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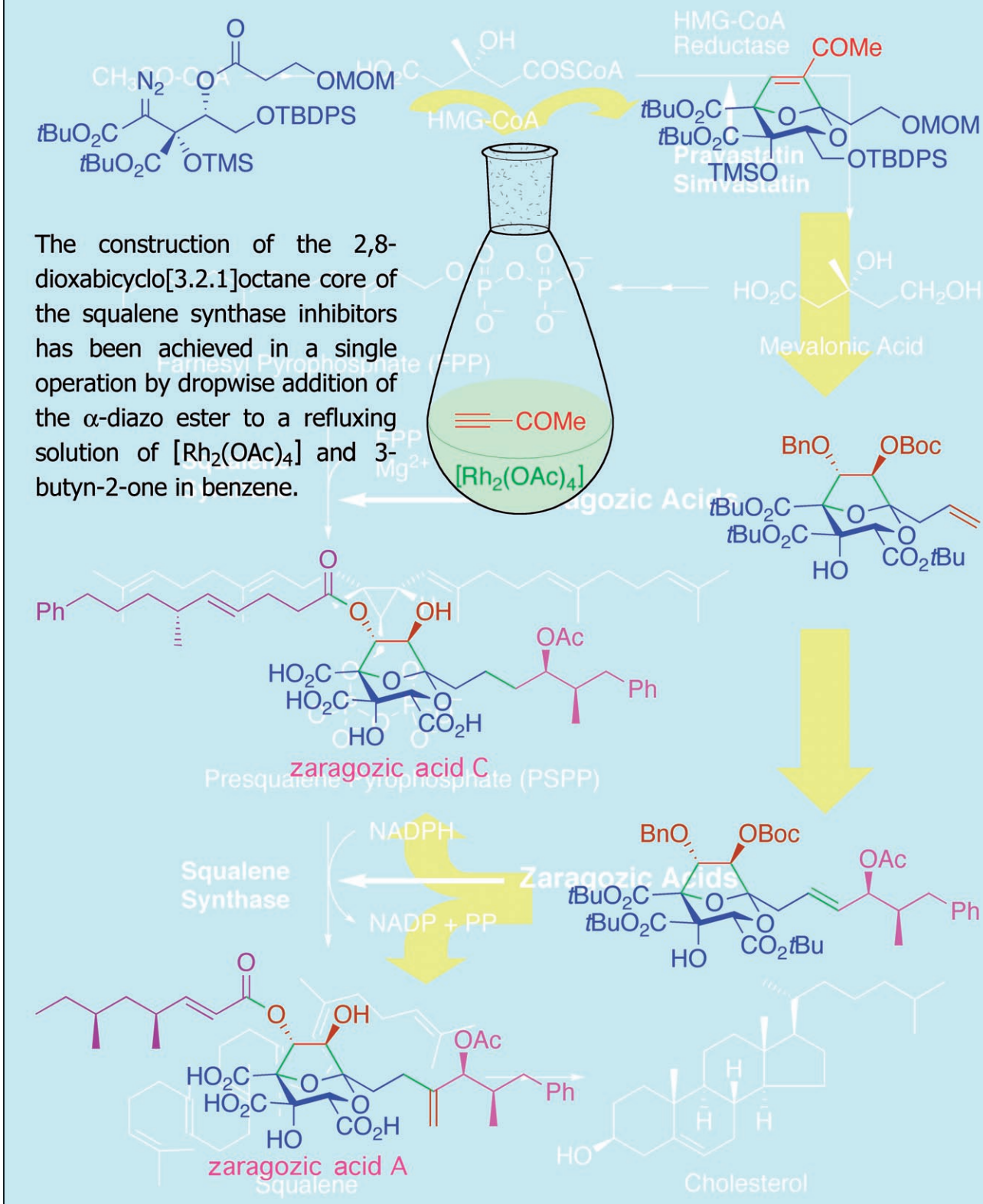
Internal Ketalization Is Not Necessary for the Total Syntheses of Zaragozic Acids A and C



The construction of the 2,8-dioxabicyclo[3.2.1]octane core of the squalene synthase inhibitors has been achieved in a single operation by dropwise addition of the α-diazo ester to a refluxing solution of $[Rh_2(OAc)_4]$ and 3-butyn-2-one in benzene.

VIP

Total Syntheses of Zaragozic Acids A and C by a Carbonyl Ylide Cycloaddition Strategy

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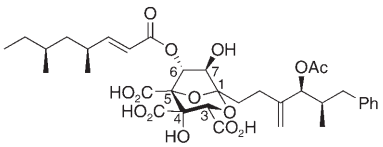
Abstract: A carbonyl ylide cycloaddition approach to the squalene synthase inhibitors zaragozic acids A and C is described. The carbonyl ylide precursor **8** was synthesized starting from di-*tert*-butyl D-tartrate (**47**) via an eleven-step sequence involving the regioselective reduction of the mono-MPM (MPM = 4-methoxybenzyl) ether **48** with $LiBH_4$ and the diastereoselective addition of sodium *tert*-butyl diazoacetate to α-keto ester **10**. The reaction of α-diazo ester **8** with 3-butyn-2-one (**40**) in the presence of a catalytic amount of $[Rh_2(OAc)_4]$ gave the desired cycloadduct **59** as a single diastereomer. The dihydroxylation of enone **59** followed by sequential transformations permitted the construction of the fully functionalized 2,8-dioxabicyclo[3.2.1]octane core **5**. Alkene **79** derived from **5** serves as a common precursor to zaragozic acids A (**1**) and C (**2**), since the elongation of the C1 alkyl side chain can be attained by olefin cross-metathesis, especially under the influence of Blechert's catalyst (**85**).

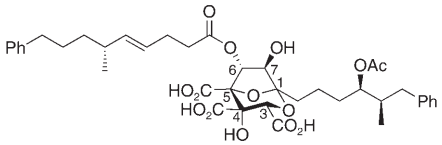
Keywords: carbonyl ylides · cycloaddition · diazo compounds · metathesis · total synthesis

Introduction

The zaragozic acids/squalestatins comprise a family of polyketide natural products that display inhibitory activity against squalene synthase[1] and farnesyl-protein transferase.[2] Since their discovery in 1992 by researchers at Merck,[2b,3] Glaxo,[4] and Tokyo Noko University/Mitsubishi Kasei Corporation,[5] zaragozic acids/squalestatins have attracted considerable attention from the synthetic community because of interest in the unique and challenging molecular architecture of these compounds coupled with their remarkable biological activity. Over 30 groups have made impressive contributions to the literature on the synthesis of these molecules.[6,7] The first total syntheses of zaragozic acid C (**2**) and zaragozic acid A (squalestatin S1, **1**) were reported from the Carreira[8] and Nicolaou[9] laboratories, respectively, in 1994. Since then, five additional total syntheses of zaragozic acids,[10–14] including our first-generation synthesis, have been reported.[15] All of these approaches utilize internal ketalization in constructing the core structure; only Heathcock adopted a stepwise approach, wherein the full C1 alkyl side chain was installed after the ketalization event.



zaragozic acid A (**1**)



zaragozic acid C (**2**)

The principal goal of our study was not simply to devise an efficient, stereocontrolled synthesis of this family of natural products, but more importantly to develop a unified strategy that would be applicable to the synthesis of core-modified analogues. The key feature of our first-generation synthesis of zaragozic acid C (**2**) is the simultaneous creation of contiguous, oxygen atom-substituted quaternary stereo-

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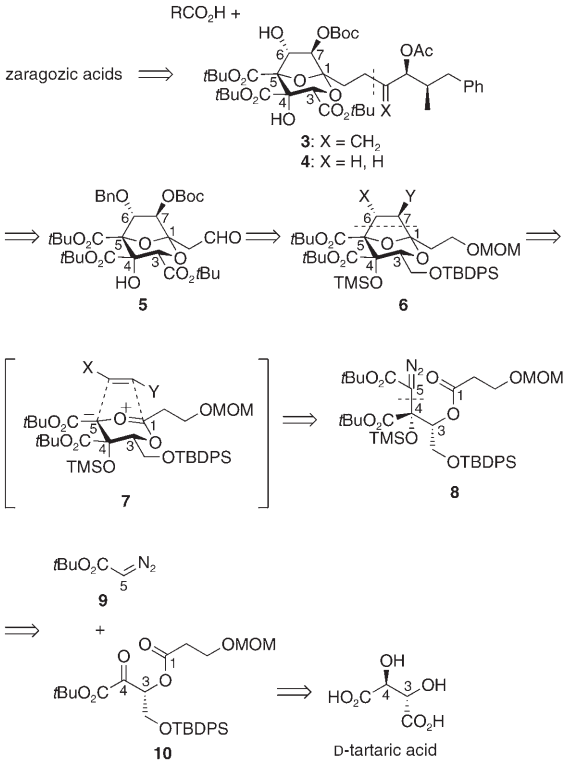
centers at C4 and C5 by a $Sn(OTf)_2$-promoted aldol coupling reaction between an α-keto ester and a silyl ketene thioacetal derived from L- and D-tartaric acids, respectively; however, the coupling incurs a stereochemical problem at C5, despite considerable effort to resolve this issue. It also became apparent that the strategy would not be amenable to analogue synthesis. As a result, we felt compelled to develop a second-generation synthesis of zaragozic acids through an entirely different route.

Metallocarbenoids, generated by the decomposition of α-diazo carbonyl compounds, form cyclic carbonyl ylides as transient species by transannular cyclization with the adjacent carbonyl groups, which undergo 1,3-dipolar cycloaddition reactions with multiple bonds to provide five-membered, oxygen-containing heterocycles.[16] The utility of this method was first demonstrated by Ibata and co-workers in 1972, wherein $Cu(acac)_2$ was used as a catalyst.[17] Since Padwa and co-workers reported that rhodium(II)-catalyzed cyclization/cycloaddition reactions proceeded under much milder conditions than was common for the classic method with $Cu(acac)_2$,[18] this process has been extensively studied and represents an attractive strategy for the synthesis of bioactive compounds.[19]

An inspection of the structure of zaragozic acids revealed the intriguing possibility of applying the tandem carbonyl ylide formation/1,3-dipolar cycloaddition sequence to construct the core structure of these molecules. In this article, we describe the details of our carbonyl ylide cycloaddition approach to the syntheses of zaragozic acids A (**1**) and C (**2**).[20,21]

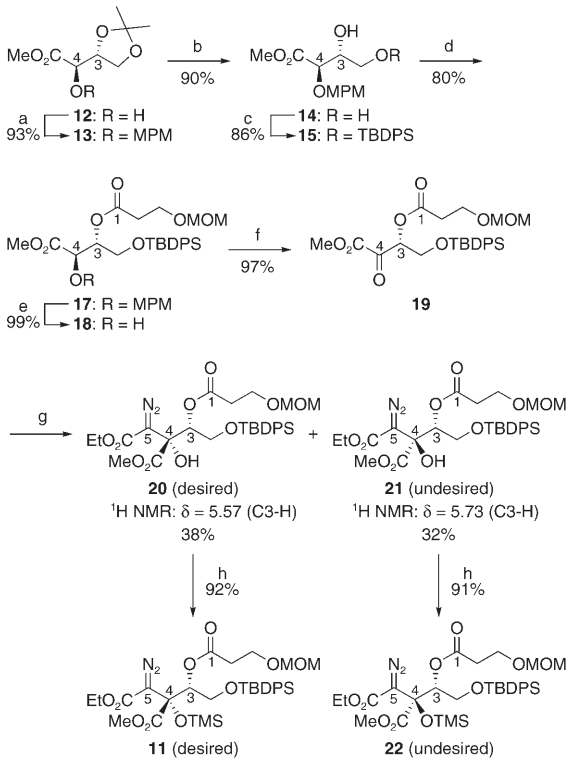
Results and Discussion

Retrosynthetic analysis: Our cycloaddition-based retrosynthetic analysis of zaragozic acids is depicted in Scheme 1. The structures of the zaragozic acids/squalestatins are characterized by 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, oxygen atom-substituted quaternary ones, and the difference between these compounds lies in the variation in the C1 alkyl and C6 acyl side chains. To enhance the convergency of the assemblage process, we planned to install the full C1 alkyl side chain late in the synthesis. The implementation of this strategy would allow the incorporation of a variety of C1 alkyl side chains into a common, fully elaborated intermediate **5**. The bicyclic compound **6** was envisioned to arise from the 1,3-dipolar cycloaddition of the cyclic carbonyl ylide **7**, generated from the α-diazo ester **8** in the presence of a rhodium(II) catalyst, with a suitable dipolarophile. A disconnection in the C4-C5 bond led to *tert*-butyl diazoacetate (**9**) and the α-keto ester **10**, which could then be traced back to D-tartaric acid. Considering our previous findings that saponification and *tert*-butyl esterification at a later stage were problematic,[12] the carboxyl groups were protected as *tert*-butyl esters throughout the synthesis.



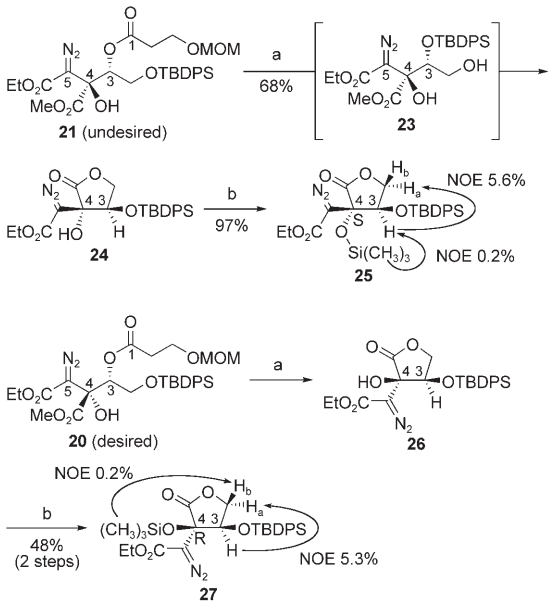
Scheme 1. Retrosynthetic analysis of zaragozic acids. Boc = *tert*-butoxycarbonyl; Bn = benzyl; MOM = methoxymethyl.

Preliminary model studies: The synthesis plan outlined in Scheme 1 necessitates the use of the α-diazo ester **8** as a carbonyl ylide precursor. Although tandem carbonyl ylide formation/1,3-dipolar cycloaddition reactions are well documented with α-diazo-β-ketoesters,[16] at the outset of our studies, α-diazo esters with an sp^3 carbon at the β-position had never been tested as substrates for these reactions.[22] In addition, it was suggested by Padwa and co-workers that alternate pathways might compete with carbonyl ylide formation in the case where the trapping carbonyl is an ester.[23] Thus, we felt it was prudent to perform exploratory experiments using a readily accessible α-diazo ester. The α-diazo ester **11** was chosen as a model substrate for the reaction. The synthesis of the α-diazo ester **11** commenced with the D-isoascorbic acid-derived alcohol **12**[24] and proceeded along the path delineated in Scheme 2. Protection of the hydroxyl group of **12** with 4-methoxybenzyl (MPM) trichloroacetimidate in the presence of Ph_3CBF_4[25] provided the MPM ether **13** in 93% yield, which, upon exposure to 10% aqueous HCl in THF, afforded the diol **14** in 90% yield. Selective silylation of the primary hydroxyl group with *tert*-butyldiphenylsilyl (TBDPS) chloride was followed by condensation with the carboxylic acid **16**[26] to give ester **17** in 69% yield over two steps. Oxidative removal of the MPM group with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[29] provided alcohol **18** in 99% yield, which underwent a Dess–Martin oxidation[30] to afford the α-keto ester **19** in 97% yield. The incorporation of the α-diazo ester functionality



Scheme 2. Synthesis of α-diazo ester **11**. a) $MPMOC(NH)CCl_3$, Ph_3CBF_4, Et_2O, 0 °C, 30 min; b) 10% aq. HCl, THF, 5 h; c) TBDPSCl, imidazole, CH_2Cl_2, 0 °C, 1 h; d) EDCI, $MOM(CH_2)_2CO_2H$ (**16**), DMAP, CH_2Cl_2, 12 h; e) DDQ, CH_2Cl_2, pH 7 phosphate buffer, 24 h; f) Dess–Martin periodinane, CH_2Cl_2, 1 h; g) LiHMDS, N_2CHCO_2Et, THF, −78 °C, 30 min; h) HMDS, imidazole, THF, 48 h. THF = tetrahydrofuran; EDCI = 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride; DMAP = 4-(dimethylamino)pyridine; HMDS = 1,1,3,3-hexamethyldisilazane.

was accomplished by employing the Wenkert protocol,[31] namely the addition of LiHMDS to a premixed solution of α-keto ester **19** and ethyl diazoacetate. The readily separable diastereomers **20** and **21** thus formed were isolated in 38 and 32% yield, respectively. The stereochemical assignments of isomers **20** and **21** were determined in two sets of experiments (Scheme 3). Treatment of isomer **21** with K_2CO_3 in MeOH effected transesterification, the migration of the TBDPS group,[32] and lactone formation to give the crystalline alcohol **24** in 68% yield, which was converted to trimethylsilyl (TMS) ether **25** in 97% yield by silylation with TMS-imidazole. Following the same reaction sequence, γ-lactone **27** was also obtained from isomer **20**, albeit in lower yield (48% in two steps without intervening purification) due to the lability of intermediate **26** to base. The ^1H NOE between $Si(CH_3)_3$ and C3-H established the (4*S*) configuration of **25**, whereas $Si(CH_3)_3$ exhibited a significant ^1H NOE interaction with H_b in lactone **27** with a 4*R* configuration. Finally, the stereochemistry of the undesired isomer **21** was unambiguously established by X-ray crystallography of the lactone **24**, as shown in Figure 1. The preparation of model compound **11** was completed in 92% yield by the silylation of **20**. The C4 isomer **22** was also prepared from **21**, in a comparative experiment.



Scheme 3. Determination of the stereochemistry at C4 of α-diazo esters **20** and **21**. a) K_2CO_3, MeOH, 0 °C, 1 h; b) TMS-imidazole, CH_2Cl_2.

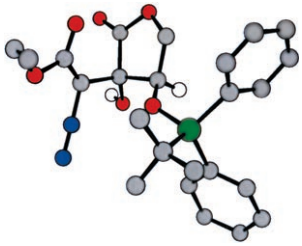
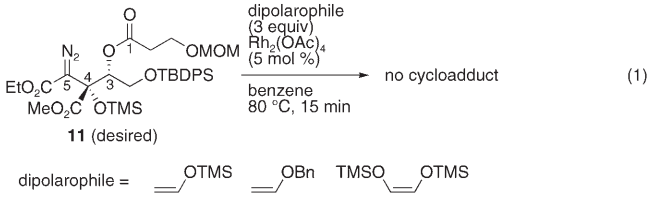


Figure 1. X-ray crystal structure of γ-lactone **24**, rendered in Chem3D. For purposes of clarity, only the protons attached to the C3 stereocenter and the oxygen atom are shown.

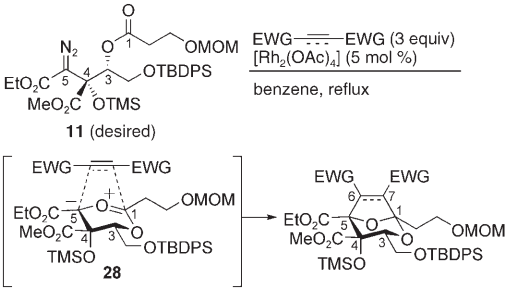
As stated earlier, the reaction of cyclic carbonyl ylides without a carbonyl group within the rings was unprecedented in the literature. Thus, several types of dipolarophile candidates were examined so as to establish the scope of the process. The reaction involved the addition of α-diazo ester **11** over a 5 min period to a refluxing solution of a dipolarophile and 5 mol% of $[Rh_2(OAc)_4]$ in benzene. When electron-rich alkenes such as trimethylsilyl vinyl ether, benzyl vinyl ether and 1,2-bis(trimethylsilyloxy)ethylene were employed as dipolarophiles, all attempts to obtain cycloadducts in even trace quantities through this reaction met with failure [Eq. (1)]. In contrast, the reaction of **11** with dimethyl acetylenedicarboxylate (**29**) proceeded with complete ste-

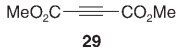
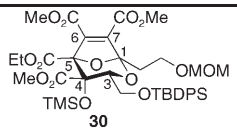
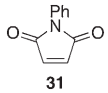
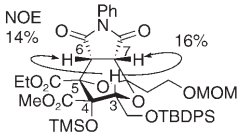
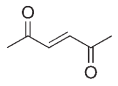
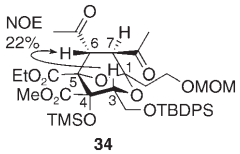
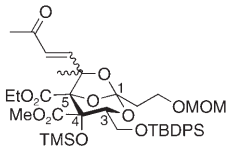


(1)

reocontrol to give cycloadduct **30** in 66% yield as a single diastereomer (Table 1, entry 1). It is noteworthy that *N*-phenylmaleimide (**31**) and (*E*)-3-hexene-2,5-dione (**33**) proved

Table 1. 1,3-Dipolar cycloaddition of carbonyl ylide **28** with symmetrical dipolarophiles.



Entry	Dipolarophile	Cycloadduct	Yield [%]
1	 **29**	 **30**	66
2[a]	 **31**	 **32**	68
3	 **33**	 **34**	47
		 **35**	31

[a] The reaction was performed using 2 equiv of **31**.

to be effective dipolarophiles for the tandem reaction, providing cycloadducts **32** and **34** as single diastereomers in 68 and 47% yield, respectively, although substantial amounts of carbonyl adduct **35** were also obtained by reaction with **33** (entries 2, 3). The stereochemical assignments for cycloadducts **32** and **34** were determined by diagnostic NOE experiments, as shown in Table 1, and the stereochemistry of **30** was assigned by analogy. These results reveal that the 1,3-dipolar cycloaddition occurred exclusively from the β-face of ylide **28** to avoid non-bonding interactions with the C4 pseudoaxial trimethylsilyloxy group. The formation of **34** is consistent with a reaction through transition state A, wherein the activating groups in **33** are nicely accommodated in a less crowded space in **28** (Figure 2). Surprisingly, under the foregoing conditions, the major product formed in the reaction of the C4 isomer **22** with **29** was cyclobutane

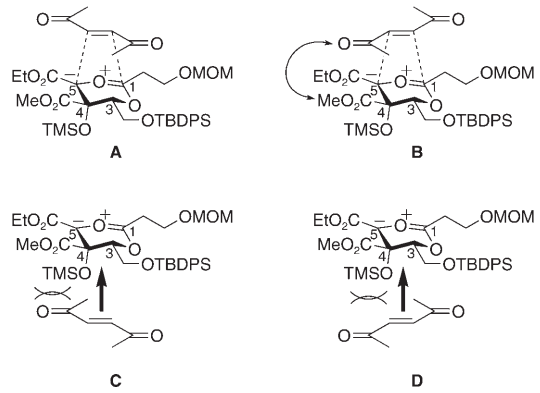
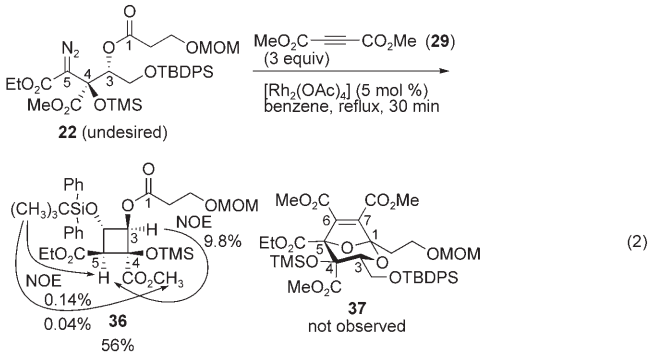


Figure 2. Stereochemical course of the 1,3-dipolar cycloaddition

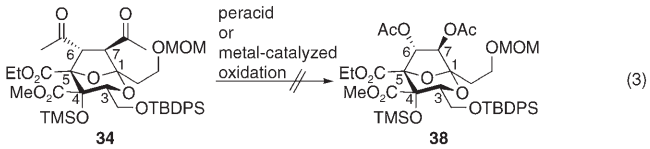
36, arising from a C-H insertion reaction, and even trace amounts of cycloadduct **37** were not detected [Eq. (2)].



(2)

These results suggest that the stereochemistry at C4 plays a pivotal role in the present system, presumably because the rhodium(II) carbenoid generated from **22** cannot adopt the required conformation for carbonyl ylide formation.

The cycloadduct **34** was anticipated to provide the suitably functionalized core compound **38** when subjected to Baeyer–Villiger conditions.[33] However, all attempts to effect the desired transformation resulted in the recovery of **34** or decomposition, principally through the loss of protecting groups [Eq. (3)]. Consequently, the judicious selection



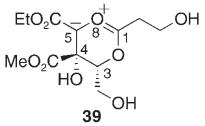
(3)

of dipolarophiles that could result in much higher yields as well as a completed synthesis became crucial to the success of our scenario.

Given the lack of information in the literature regarding the HOMO and LUMO energies for cyclic carbonyl ylides derived from α-diazo esters, calculations were performed

using the simplified dipole **39** (Table 2).[34] As anticipated, the interaction between LUMO (dipole) and HOMO (dipolarophile) is energetically favored when benzyl vinyl ether is

Table 2. HOMO and LUMO energies and coefficients for cyclic carbonyl ylide **39** and dipolarophile candidates.

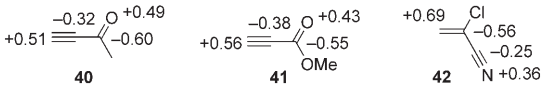


39

	Energy [eV]	Coefficient C5	O8	C1
HOMO	−8.27	+0.79	−0.14	−0.29
LUMO	−0.94	+0.23	−0.41	+0.71

Dipolarophile	Energy [eV] HOMO	LUMO	Energy separation [eV] E_I[a]	E_{II}[b]
benzyl vinyl ether	−9.36	+0.39	9.21	8.42
MeO_2C-C≡C-CO_2Me (**29**)	−11.96	−0.93	7.34	11.02
3-hexene-2,5-dione (**33**)	−10.74	−0.82	7.45	9.80
3-butyn-2-one (**40**)	−11.18	+0.05	8.32	10.24
methyl propiolate (**41**)	−11.66	+0.10	8.37	10.72
2-chloroacrylonitrile (**42**)	−10.64	−0.34	7.93	9.70

[a] E_I = [HOMO (dipole) − LUMO (dipolarophile)]. [b] E_{II} = [HOMO (dipolarophile) − LUMO (dipole)].



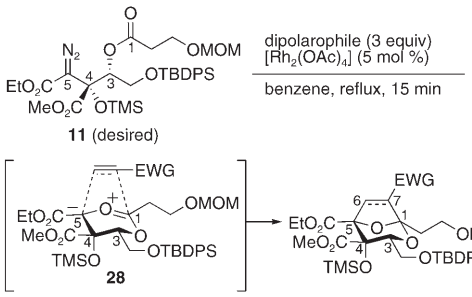
40 **41** **42**

Orbital coefficients of LUMO for **40**–**42** are indicated in the structure

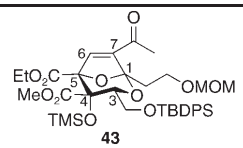
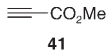
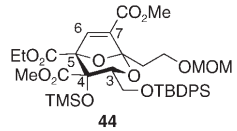
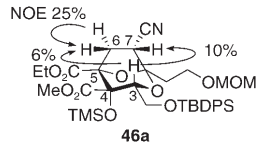
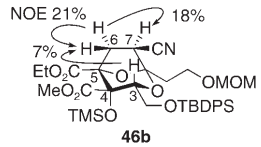
used as a dipolarophile, whereas the main interaction is the [HOMO (dipole) − LUMO (dipolarophile)] for electron-deficient alkynes and alkenes. Since carbonyl ylide **28** generated from **11** underwent 1,3-dipolar cycloaddition with electron-deficient dipolarophiles, the latter is a critical interaction that drives the present reaction. In our initial experiments, we employed symmetrical dipolarophiles with two electron-withdrawing groups, not only to enhance reactivity toward cycloaddition but also to avoid the formation of regioisomers. The calculations indicate that the energy separation between HOMO (dipole) and LUMO (dipolarophile) is extended by about 1 eV when monosubstituted, unsymmetrical alkynes **40** and **41** are employed as dipolarophiles instead of **29**. With regard to the regioselectivity of the cycloaddition, Padwa and co-workers proposed that all the results obtained could be accommodated in terms of frontier molecular orbital (FMO) theory.[18] In our system, as the atomic coefficient at C5 is larger than C1 in the HOMO for ylide **39**, the formation of C7-substituted regioisomers would be anticipated in reactions with mono- or 1,1-disubstituted, electron-deficient dipolarophiles.

Gratifyingly, monosubstituted, electron-deficient alkynes **40** and **41** could be trapped by the carbonyl ylide intermediate **28**, producing cycloadducts **43** and **44** in excellent yields with complete regio- and diastereofacial selectivity (Table 3, entries 1 and 2). *endo*/*exo* Selectivity could not be observed with acrylonitrile (**45**), affording a 3:2 mixture of C7-substituted cycloadducts **46a** and **46b** in a combined yield of 75% (entry 3). Although the LUMO energy for 2-chloroacrylonitrile (**42**) is lower than that for **40** or **41**, cycloadducts could not be obtained with **42** (entry 4), indicating that steric factors as well as energy separations should be taken into consideration for this reaction. Of the various partners tested, alkynes **40** and **41** were chosen as the dipolarophiles that would most likely lead to the completed synthesis.

Table 3. 1,3-Dipolar cycloaddition of carbonyl ylide **28** with unsymmetrical dipolarophiles.

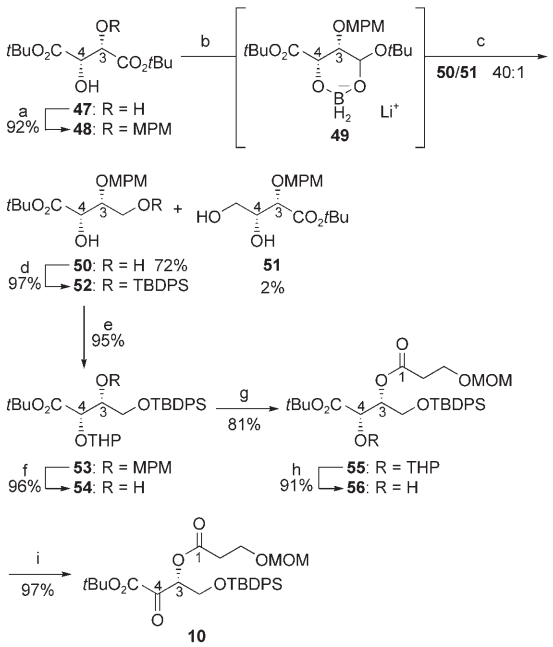


11 (desired)

Entry	Dipolarophile	Cycloadduct	Yield [%]
1	 **40**	 **43**	85
2	 **41**	 **44**	82
3	 **45**	 **46a**  **46b**	44 31
4	 **42**		[a]

[a] The cycloadduct could not be obtained.

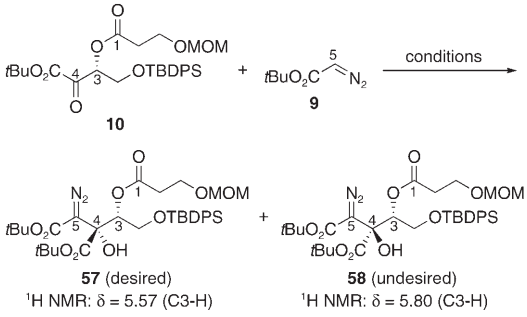
Synthesis of carbonyl ylide precursor 8: Encouraged by the results of the model studies described above, we then addressed the stereoselective synthesis of α-diazo *tert*-butyl ester **8**. The synthesis began with the mono-protection of di-*tert*-butyl D-tartrate (**47**)[35] with MPMBr via the stannylene acetal,[36] affording the MPM ether **48** in 92% yield (Scheme 4). At this point, the synthetic plan called for the selective reduction of one of the *tert*-butyl esters in **48**.[37] After considerable experimentation, $LiBH_4$ proved to be the optimal reagent for this purpose. Thus the $LiBH_4$ reduction of **48** followed by aqueous workup afforded the aldehyde, which was reduced again with $LiBH_4$ to give 1,3-diol **50** in



Scheme 4. Preparation of α-keto ester **10**. a) Bu_2SnO, toluene, reflux, 2 h, then CsF, MPMBr, DMF, 10 h; b) $LiBH_4$, THF, 4 h; c) $LiBH_4$, THF, −78 °C, 4 h; d) TBDPSCl, imidazole, CH_2Cl_2, 0 °C, 30 min; e) DHP, PPTS, CH_2Cl_2, 5 h; f) DDQ, CH_2Cl_2, pH 7 phosphate buffer, 2 h; g) EDCI, $MOMO(CH_2)_2CO_2H$ (**16**), DMAP, CH_2Cl_2, 3 h; h) TsOH, MeOH, 40 min; i) Dess–Martin periodinane, CH_2Cl_2, 2 h. DMF = *N*,*N*-dimethylformamide; DHP = 3,4-dihydro-2*H*-pyran; PPTS = pyridinium *p*-toluenesulfonate; Ts = *p*-toluenesulfonyl.

72% yield, along with 2% of the 1,2-diol **51**. This highly beneficial result can be rationalized by assuming the predominant formation of a rigid, six-membered boronate intermediate **49** that is resistant to further reduction. Selective silylation of the major isomer **50** with TBDPSCl was followed by interim protection of the remaining hydroxyl group as a tetrahydropyranyl (THP) ether and oxidative removal of the MPM ether to give **54** in 88% yield in three steps. The acylation of **54** with acid **16** followed by exposure to TsOH in MeOH provided alcohol **56** in 74% yield in two steps, which underwent a Dess–Martin oxidation to afford α-keto ester **10** in 97% yield. Our effort was then directed toward the addition of metalated *tert*-butyl diazoacetate to **10** to set up the oxygen atom-substituted quaternary center at C4, which posed a serious problem of stereocontrol. As in the case of the α-keto ester **19**, the use of LiHMDS as a base resulted in a 1:1 mixture of diastereomeric products **57** and **58**, the configurations of which at C4 were established by comparison of the ^{1}H NMR chemical shifts of C3-H to those of α-diazo esters **20** and **21** (Table 4, entry 1). Of the three alkaline metal bis(trimethylsilyl)amide surveyed, NaHMDS proved the best in terms of both yield and diastereoselectivity (entries 1–3). The reaction of α-keto ester **10** with **9** proceeded to completion within 5 min even at −93 °C (entry 4). The solvent survey revealed that unsatisfactory diastereoselectivities were obtained in donor solvents (entries 4 and 5). The use of CH_2Cl_2, which is not normally

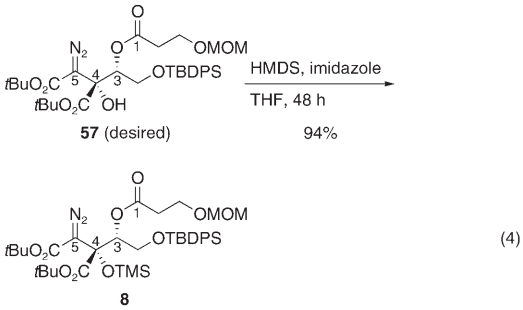
Table 4. Addition of the metalated α-diazo ester to α-keto ester **10**.



Entry	Base	Solvent	*T* [°C]	Yield [%]	**57**/**58**[a]
1	LiHMDS	THF	−78	80	1.0:1
2	NaHMDS	THF	−78	79	2.0:1
3	KHMDS	THF/PhMe 10:1	−78	26	2.1:1
4	NaHMDS	THF	−93	76	2.1:1
5	NaHMDS	Et_2O/THF 20:1	−93	64	3.2:1
6	NaHMDS	PhMe/THF 20:1	−93	62	4.3:1
7	NaHMDS	CH_2Cl_2/THF 20:1	−93	73	8.0:1

[a] The ratio was determined by 500 MHz ^{1}H NMR analysis of the crude mixture.

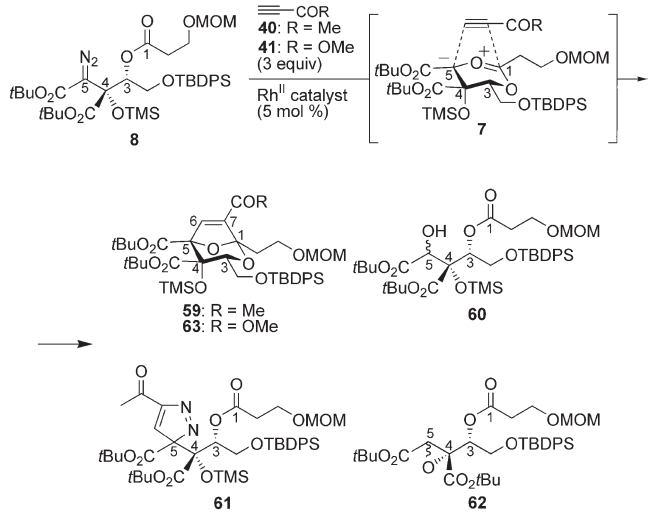
used in this type of reaction, mixed with reagent-derived THF proved to be optimal for this reaction, providing adducts in a 73% combined yield in a ratio of 8:1 favoring the anti-Felkin product **57**, although the reason for this is not clear at present (entry 7). After chromatographic separation of the diastereomers, the silylation of the desired isomer **57** produced TMS ether **8** in 94% yield [Eq. (4)], which set the stage for the tandem carbonyl ylide formation/1,3-dipolar cycloaddition sequence.



(4)

Construction of the fully functionalized 2,8-dioxabicyclo-[3.2.1]octane core: Utilizing conditions employed for compound **11**, the reaction of α-diazo ester **8** with 3-butyn-2-one (**40**) in the presence of $[Rh_2(OAc)_4]$ provided cycloadduct **59** as a single isomer in 72% yield (Table 5, entry 1). In this case, the consumption of the starting diazo compound **8** was considerably slower than that of **11**, perhaps owing to steric congestion around the reacting center. As a consequence, minor byproducts **60**–**62** were isolated in 14%, 6% and 6% yields, respectively. While the formation of alcohol **60** can be attributed to the reaction of the rhodium carbenoid inter-

Table 5. 1,3-Dipolar cycloaddition of carbonyl ylide **7** generated from α-diazo ester **8**.

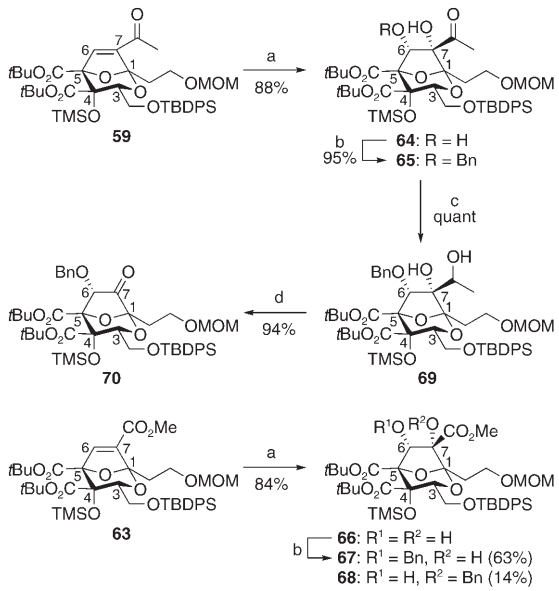


Entry	R	Rh^{II} catalyst	Solvent	T [°C]	t [min][a]	Cycloadduct		Yield [%] 60	61	62
1	Me	$[Rh_2(OAc)_4]$	benzene	80	40	**59**	72	14	6	6
2	Me	$[Rh_2(OAc)_4]$	benzene	80	140[b]	**59**	67	10	3	7
3	Me	$[Rh_2(OAc)_4]$	benzene	60	150	**59**	7	65	0	0
4	Me	$[Rh_2(OCOC_7H_{15})_4]$	benzene	80	40	**59**	71	6	0	trace
5	Me	$[Rh_2(OCOPh)_4]$	benzene	80	40	**59**	66	14	0	13
6	Me	$[Rh_2(OCOC_3F_7)_4]$	benzene	80	40	**59**	11	4	0	33
7	Me	$[Rh_2(NHAc)_4]$	benzene	80	40	**59**	72	3	0	trace
8	Me	$[Rh_2(OAc)_4]$	toluene	80	40	**59**	28	35	8	10
9	Me	$[Rh_2(OAc)_4]$	toluene	110	25	**59**	46	15	4	15
10	Me	$[Rh_2(OAc)_4]$	$(CH_2Cl)_2$	80	20	**59**	17	8	2	2
11	OMe	$[Rh_2(OAc)_4]$	benzene	80	40	**63**	78	9	–	0

[a] The reaction time includes the addition time of 15 min. [b] The reaction time includes the addition time of 120 min.

mediate with adventitious H_2O,[23] pyrazole **61** and epoxide **62** were thought to result from the direct [3+2]-cycloaddition without rhodium(II) catalysis[38] and the oxonium ylide formation-desilylation sequence, respectively, suggesting the presence of some competitive pathways during the carbonyl ylide formation process. Thus, we were poised to identify the optimal conditions for this reaction. Although it was anticipated that the decreased carbenoid concentration limited competing side reactions, the slow addition (120 min) of α-diazo ester **8** afforded no discernible benefits (entry 2). The rhodium(II)-catalyzed diazo decomposition was found to occur at 60 °C, but the major product formed at this temperature was alcohol **60**, showing that the formation of **7** and/or the 1,3-dipolar cycloaddition of **7** with **40** required a higher temperature than that for the formation of the rhodium carbenoid intermediate (entry 3). With the lone exception of $[Rh_2(OCOC_3F_7)_4]$ where **59** was produced in only 11% yield (entry 6), the chemical yield of cycloadduct **59** was nearly the same for each rhodium(II) catalyst (entries 1, 4–7). An examination of various solvents revealed that benzene was the optimal solvent for this transformation (entries 1, 8–10). Under optimal conditions, the reaction of α-diazo ester **8** with methyl propiolate (**41**) provided cycloadduct **63** in 78% yield (entry 11).

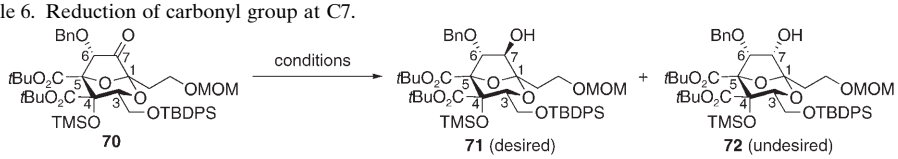
Having established a viable route to cycloadducts **59** and **63**, efforts were next focused on the installation of the C6,C7-*trans*-diol unit. The dihydroxylation of enone **59** with OsO_4 proceeded from the sterically less hindered face of the C6–C7 double bond, affording diol **64** in 88% yield, which underwent selective benzylation of the hydroxyl group at C6 to give **65** in 95% yield (Scheme 5). The stereochemistry of **65** was verified by a diagnostic ^1H NOE correlation (18%) between C3-H and C6-H. In contrast, the benzylation of diol **66**, obtained by the stereoselective dihydroxylation of enoate **63**, under the same conditions resulted in the formation of significant amounts (14%) of regioisomer **68**. With these results, the decision was made to carry the hydroxyketone **65** forward in the synthesis of natural products. The superfluous C7 acetyl group in **65** was removed in a simple two-step sequence involving reduction with diisobutylaluminum hydride (DIBALH) and oxidative cleavage of the 1,2-diol with $[Pb(OAc)_4]$.



Scheme 5. Synthesis of ketone **70**. a) OsO_4, NMO, acetone, *t*BuOH, H_2O, 3 h; b) BnBr, Ag_2O, DMF, 24 h; c) DIBALH, toluene, −78 °C, 30 min; d) $[Pb(OAc)_4]$, benzene, 30 min. NMO = 4-methylmorpholine *N*-oxide.

At this stage, we were faced with the task of reducing the C7 carbonyl group in a stereoselective manner. While the reduction of ketone **70** with $NaBH_4$ in EtOH at −45 °C gave a 2.1:1 ratio of alcohols favoring the desired isomer **71** (Table 6, entry 1), the use of K-Selectride, a bulky reducing agent, resulted in the exclusive formation of the undesired isomer **72** (entry 2). After considerable experimentation, reducing agents capable of coordination with a Lewis basic oxygen atom such as $Zn(BH_4)_2$ or DIBALH proved to be effective in preferentially providing the desired isomer **71** (entries 3–6). Finally, we found that the use of DIBALH in CH_2Cl_2 at −78 °C gave a 14.4:1 mixture of **71** and **72** (entry 5), and the diastereoselectivity was further improved to 46.4:1 in the presence of $ZnCl_2$ (entry 6). It should be noted that the selection of a benzyl protecting group for the C6 alcohol was crucial for the maximum efficiency of these transformations, particularly in terms of the essentially perfect selectivities for its installation and the C7 carbonyl reduction.

Table 6. Reduction of carbonyl group at C7.

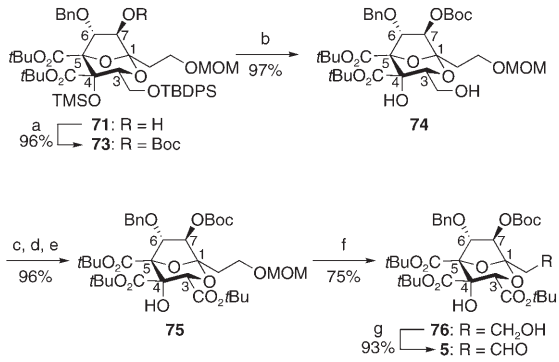


Entry	Reagent	Additive	Solvent	T [°C]	t [h]	Yield [%]	**71**:**72**[a]
1	$NaBH_4$	–	EtOH	−45	0.5	95	2.1:1
2	K-Selectride	–	THF	0	1	50	0:1
3	$Zn(BH_4)_2$	–	THF	0	6	95	2.8:1
4	DIBALH	–	toluene	−78	0.5	91	4.6:1
5	DIBALH	–	CH_2Cl_2	−78	0.5	96	14.4:1
6	DIBALH	$ZnCl_2$	CH_2Cl_2	−78	0.5	87	46.4:1

[a] The ratio was determined by HPLC (Zorbax Sil, 4.6×250 mm; eluent, 9% THF in *n*-hexane; flow rate 1.0 mL min^{-1}).

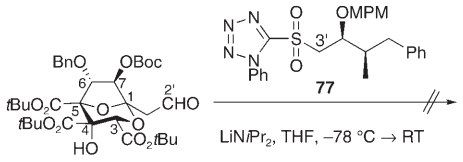
The resulting C7 alcohol was protected as the *tert*-butyl carbonate in 96% yield (Scheme 6). The remaining operations necessary for the construction of the bicyclic core of zaragozic acids involved adjustment of the oxidation state at C3. Removal of the silicon-based protecting groups with Bu_4NF afforded diol **74** in 97% yield. The diol **74** was then converted into a carboxylic acid by two successive oxidations (Dess–Martin periodinane; $NaClO_2$),[39] which was subjected to *N,N′*-diisopropyl-*O-tert*-butylisourea[40] to provide the tri-*tert*-butyl ester **75** in 96% overall yield without intervening purification. With the bicyclic core successfully functionalized, the deprotection of the C2′ alcohol was then required, preliminary to installing the full C1 side chain. We found that the use of TMSBr, generated in situ from TMSCl and Et_4NBr,[41] was effective for this purpose, affording diol **76** in 75% yield without the concomitant loss of other protecting groups. The oxidation of **76** with Dess–Martin periodinane provided aldehyde **5** in 93% yield and set the stage for the elongation of the C1 side chain.

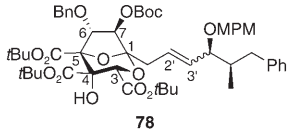
Completion of the total synthesis of zaragozic Acid C: For the full installation of the C1 alkyl side chain, two distinct olefination sequences were envisaged. One involved the Wittig reaction of aldehyde **5** with a phosphorane or, equivalently, the Julia coupling of **5** and a sulfone. The second strategy would utilize olefin cross-metathesis. We initially adapted the Kocienski–Julia olefination[42] for this task, but the attempted coupling of **5** with sulfone **77** resulted in the complete recovery of starting materials [Eq. (5)]. We then turned our attention to the use of a terminal olefin cross-metathesis.[43] The terminal olefin was uneventfully incorporated by a Wittig reaction of aldehyde **5** with methylene-triphenylphosphorane to give **79** in 93% yield [Eq. (6)]. The coupling partner, alkene **82**, was readily prepared starting from epoxide **80**, an intermediate used in our first-generation synthesis of zaragozic acid C.[44] Treatment of **80** with dimethylsulfonium methylide according to the Mioskowski–Falck protocol[45] efficiently installed the desired olefin functionality, affording allyl alcohol **81**, which was acetylated to give allyl acetate **82** in 84% overall yield [Eq. (7)].



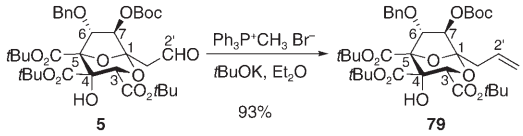
Scheme 6. Synthesis of functionalized core **5**. a) $(Boc)_2O$, Et_3N, DMAP, CH_2Cl_2, 2 h; b) Bu_4NF, THF, 0 °C, 30 min; c) Dess–Martin periodinane, CH_2Cl_2, 24 h; d) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, *t*BuOH, H_2O, 3 h; e) *i*PrN=C(O*t*Bu)NH*i*Pr, CH_2Cl_2, 48 h; f) TMSCl, Et_4NBr, CH_2Cl_2, 0 °C, 1 h, then room temperature, 20 h; g) Dess–Martin periodinane, CH_2Cl_2, 30 min.

With alkenes **79** and **82** in hand, we then proceeded to investigate the cross-metathesis reaction (Table 7). Gratifyingly, the reaction between alkenes **79** and **82** in the presence of 5 mol% of the second-generation Grubbs catalyst (**83**) in benzene at 70 °C provided the desired cross-product **87** with exclusive *E* stereochemistry in 67% yield, along with dimer **89** and alkene **91** in 8 and 4% yield, respectively (entry 1). It is apparent from this experiment that alkene **79** was the

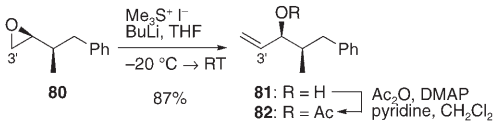




(5)

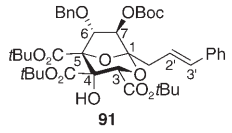


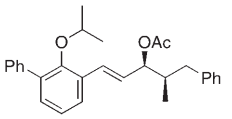
(6)



(7)

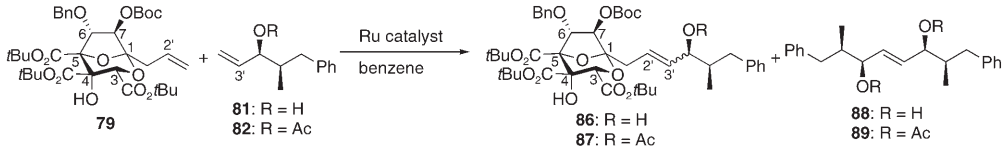
first to undergo a reaction with catalyst **83**. As might be expected from the sterically hindered nature of the olefinic functionality adjacent to the core system, the dimer **90** arising from the self-metathesis of **79** was not detected. It should be noted that the reaction of alkene **79** with dimer **89** did not occur under the same conditions, indicating that the products are the result of kinetic control. Use of 10 mol% of **83** and 2 equiv of alkene **82** did not increase the yield of the desired product **87** (entries 1 vs 2, 3). A similar result was obtained when Hoveyda's catalyst (**84**)[46] was used (entry 4). To our surprise, Blechert's catalyst (**85**)[47] exhibited a significantly different behavior in this reaction: the reaction proceeded at 60 °C, affording **87** as a 8:1 *E*/*Z* mixture of olefin isomers in 48% yield, along with dimer **89** and alkene **92** in 6 and 0.4% yield, respectively (entry 5). While no improvement was offered only with higher catalyst loadings (entry 6), increasing the amount of alkene **82** to 2 equiv coupled with the use of 20 mol% of catalyst improved the reaction efficiency, providing **87** in 90% yield (entry 7). The use of alkene **81** instead of **82** led to the exclusive formation of the self-metathesis product **88** (entry 8), suggesting that the protecting group at C4′ plays an important role in the success of this reaction.[48]

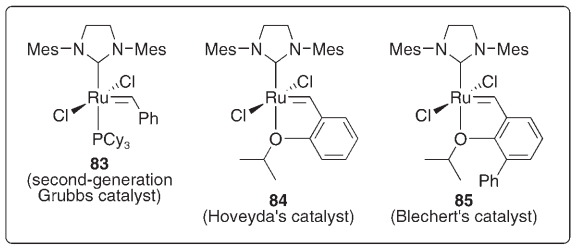


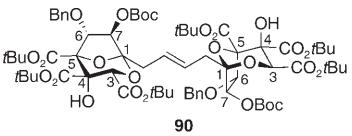


Having accomplished the elongation of the C1 alkyl side chain, the completion of the total synthesis of zaragozic acid C (**2**) required only a few finishing touches. These efforts began with the chemoselective hydrogenation of the allylic acetate in **87** (Scheme 7). A survey of a range of conditions revealed that the reaction of **87** in the presence of 5% Pd/$BaSO_4$ under a hydrogen atmosphere proceeded without the concomitant reductive cleavage of the acetoxy group to produce a partially debenzylated mixture of hydrogenation products, which upon further treatment with 20% Pd(OH)$_2$/C, furnished alcohol **4** in 98% overall yield. The route to **4** constitutes a formal synthesis of zaragozic acid C since it intersects the same intermediate employed by Carreira and Du Bois.[8b] Thus, the acylation of the hydroxyl group at C6 with (4*E*,6*R*)-6-methyl-9-phenyl-4-nonenoic acid[3e] and global deprotection

Table 7. Olefin cross-metathesis.

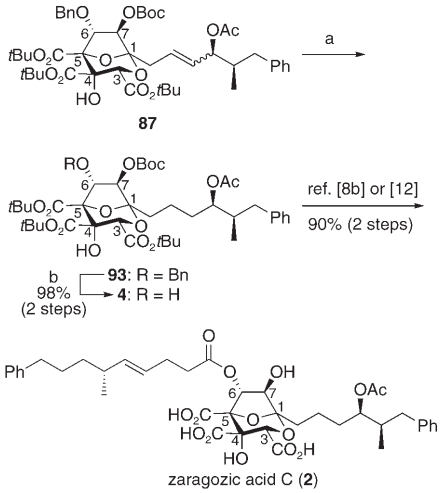






Entry	Alkene	[equiv]	Ru catalyst	[mol%]	*T* [°C]	Cross-coupling product	Yield [%]	*E*:*Z*[a]	Homodimer	Yield [%][b]
1[c]	**82**	1.2	**83**	5	70	**87**	67	*E* only	**89**	8
2[d]	**82**	1.2	**83**	10	70	**87**	60	*E* only	**89**	10
3[d]	**82**	2.0	**83**	10	70	**87**	60	*E* only	**89**	10
4	**82**	1.5	**84**	5	70	**87**	62	*E* only	**89**	4
5[e]	**82**	1.2	**85**	5	60	**87**	48	8:1	**89**	6
6[f]	**82**	1.2	**85**	20	60	**87**	46	8:1	**89**	9
7[f]	**82**	2.0	**85**	20	60	**87**	90	8:1[g]	**89**	10
8	**81**	2.0	**85**	20	80	**86**	0	–	**88**	88

[a] Determined by 500 MHz ^{1}H NMR analysis unless otherwise noted. [b] Based on alkene **81** or **82**. [c] Alkene **91** was obtained in 4% yield. [d] Alkene **91** was obtained in 8% yield. [e] Alkene **92** was obtained in 0.4% yield. [f] Alkene **92** was obtained in 1.5% yield. [g] Based on isolated yields. Mes = 2,4,6-trimethylphenyl; Cy = cyclohexyl.

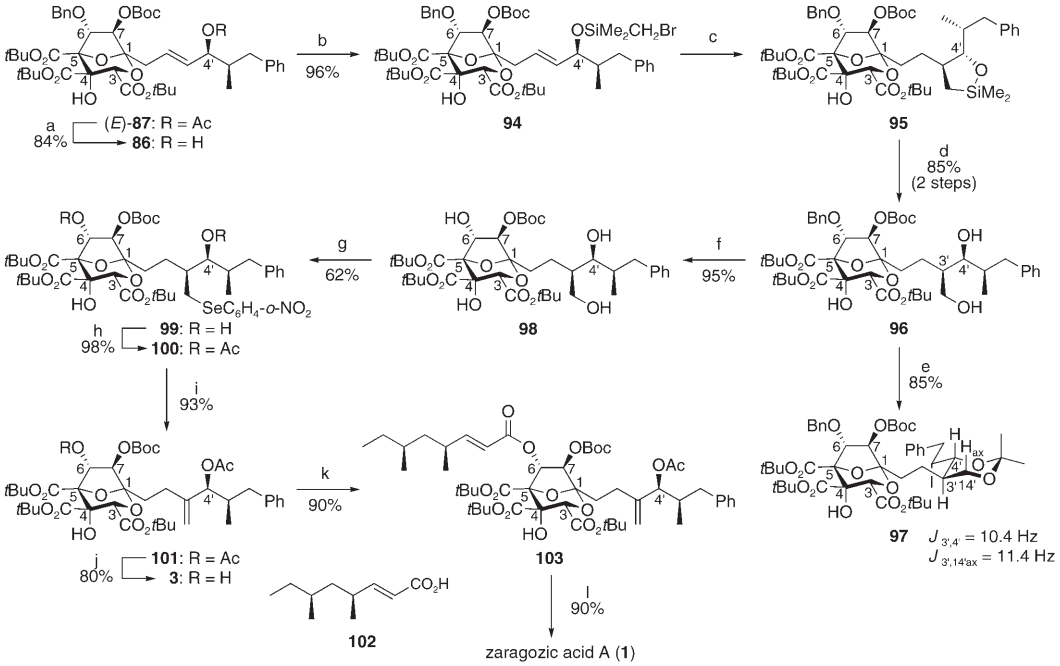


Scheme 7. Completion of the total synthesis of zaragozic acid C (**2**). a) H_2, 5% Pd/$BaSO_4$, AcOEt, 10 h; b) H_2, 20% $Pd(OH)_2$/C, AcOEt, 1 h.

with trifluoroacetic acid (TFA) completed the total synthesis of zaragozic acid C (**2**).

Total synthesis of zaragozic acid A: Since the route to zaragozic acid C (**2**) described above is, in principle, readily applicable to side chain congeners, we next addressed the synthesis of zaragozic acid A (**1**). As the only difference in carbon framework between zaragozic acids A (**1**) and C (**2**) resides at C3′, alkene **87** was anticipated to serve as a common intermediate for the synthesis of **1**. On inspection of an allylic oxygen functionality of **87**, we elected, for the manipulation at C3′, to take advantage of a radical cyclization reaction of a silyl ether that introduces a one-carbon functional chain at the α-carbon of the allylic alcohol double bond.[49]

Although, in principle, both stereoisomers (*E*)-**87** and (*Z*)-**87** could be carried forward, it was more expedient to work with a homogeneous material. Accordingly, the synthesis commenced with (*E*)-**87** (Scheme 8). While deacetylation at C4′ with 1.0 M solution of DIBALH was accompanied by some deprotection of the C7 Boc group, the use of a 0.1 M solution dramatically improved the reaction, providing diol **86** in 84% yield. As a prelude to the radical reaction, diol **86** was converted to silyl ether **94** in 96% yield by treatment with $ClSiMe_2CH_2Br$. With regard to the crucial cyclization reaction, when silyl ether **94** was subjected to Nishiyama conditions,[48a] namely the addition of a solution of Bu_3SnH and 2,2′-azobisisobutyronitrile (AIBN) to a refluxing benzene solution of **94**, the 5-*exo* product **95** was produced with complete regio- and stereoselectivity, which then underwent a Tamao oxidation[50] to give triol **96** in 85% yield in two steps. The stereochemical assignment of the newly formed stereocenter was established by ^1H NOE experiments using the acetonide **97** derived from **96**: the vicinal coupling constants ($J_{3',4'} = 10.4$ Hz and $J_{3',14'ax} = 11.4$ Hz) indicated that the 1,3-dioxane ring would adopt the chair conformation in which both C3′-H and C4′-H are axially disposed. To avoid concomitant hydrogenation of the C3′ olefin at the end of the synthesis, the benzyl protecting group in **96** should be removed at this stage. Thus benzyl



Scheme 8. Conversion of alkene (*E*)-**87** to zaragozic acid A (**1**). a) DIBALH, toluene/CH_2Cl_2 7:2, −78 °C, 1 h; b) $ClSiMe_2CH_2Br$, Et_3N, DMAP, CH_2Cl_2, 0 °C, 1 h; c) Bu_3SnH, AIBN, benzene, reflux, 4 h; d) 35% aq. H_2O_2, $NaHCO_3$, KF, THF/MeOH 1:1, 24 h; e) TsOH, $Me_2C(OMe)_2$, 1 h; f) H_2, 20% $Pd(OH)_2$/C, AcOEt, 13 h; g) 2-$NO_2C_6H_4SeCN$, Bu_3P, THF, 30 min; h) Ac_2O, DMAP, CH_2Cl_2, 0 °C, 30 min; i) 35% aq. H_2O_2, THF, 4 h; j) 0.2% K_2CO_3 in MeOH, 1 h; k) carboxylic acid **102**, DCC, DMAP, CH_2Cl_2, 5 h; l) TFA, CH_2Cl_2, 16 h. DCC = dicyclohexylcarbodiimide.

ether **96** was subjected to hydrogenolysis with 20% $Pd(OH)_2$/C to afford tetraol **98** in 95% yield. The primary alcohol in **98** was selectively transformed to the 2-nitrophenyl selenide under Grieco conditions[51] in preparation for the installation of the C3′ olefin. After acetylation of the secondary alcohols at C6 and C4′, the exposure of selenide **100** to aqueous hydrogen peroxide effected an oxidative elimination to give alkene **101** in 57% yield in three steps. Alcohol **3**, obtained by the selective transesterification of the C6 acetate with 0.2% potassium carbonate in MeOH in 80% yield, was identical in all respects (^{1}H NMR, ^{13}C NMR, IR, $[\alpha]_D$) with the intermediate reported by Tomooka and coworkers.[14] We then proceeded to complete the total synthesis by acylation of the hydroxyl group at C6 with (2*E*,4*S*,6*S*)-4,6-dimethyl-2-octenoic acid (**102**)[52] followed by global deprotection with TFA to give the fully synthetic zaragozic acid A (**1**) in 81% yield in two steps.

Conclusion

The stereocontrolled total syntheses of squalene synthase inhibitors zaragozic acids A (**1**) and C (**2**) have been achieved. The syntheses required 37 and 30 steps (longest linear sequences), respectively, and produced zaragozic acid A (**1**) in 1.5% overall yield for an average yield of 87% per step, and zaragozic acid C (**2**) in 5.7% overall yield for an average yield of 91% per step. This represents the first total syntheses of zaragozic acids that do not involve internal ketalization in constructing the 2,8-dioxabicyclo[3.2.1]octane core structure. The synthetic strategy also features the elongation of the C1 alkyl side chain through an olefin cross-metathesis as well as high convergency and flexibility. Our strategy would enable the synthesis of side chain congeners from late stage intermediates possessing a completely functionalized 2,8-dioxabicyclo[3.2.1]octane ring system.

While the carbonyl ylide cycloaddition methodology with rhodium(II) catalysts is rapidly becoming recognized as a powerful means for the construction of highly substituted oxygen-containing polycycles, a limited number of examples of the successful application of this chemistry to the complete, total synthesis of natural products, especially in optically pure form, have been reported to date.[19c,j,n,o] The present synthesis attests to the power and vitality of the tandem reaction sequence in natural product synthesis. It is also noteworthy that this is the first example of the 1,3-dipolar cycloaddition of carbonyl ylides generated from a γ-acyloxy-α-diazo ester with an sp^3 carbon at the β-position. This suggests, based on our molecular orbital calculations, that the interaction between HOMO (dipole) and LUMO (dipolarophile) is key to the success of the present reaction and the observed regioselectivity can also be explained by considering the orbital coefficients of the FMO. It is also important to note that the strategy is flexible with other types of ylides and potentially allows for the introduction of a variety of nonnatural heteroatomic substituents into the core structure. The synthesis of such analogues for biological and pharmacological investigations is currently underway, and will be reported in due course.[53]

Experimental Section

General: Melting points were determined on a Büchi 535 digital melting point apparatus and were uncorrected. Optical rotations were recorded on a JASCO P-1030 digital polarimeter. Infrared (IR) spectra were recorded on a JASCO FT/IR-5300 spectrophotometer and absorbance bands are reported in wavenumbers (cm^{-1}). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on JEOL JNM-AL400 (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. 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 compounds. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on JEOL JNM-EX270 (67.8 MHz), JEOL JNM-AL400 (100.6 MHz) or Bruker ARX500 (125.8 MHz) spectrometers with $CDCl_3$ (δ_C 77.0) as an internal standard. Electron ionization (EI) mass spectra were recorded on a JEOL JMS-FABmate spectrometer. Fast atom bombardment (FAB) mass spectra were obtained on a JEOL JMS-HX110 spectrometer in the Center for Instrumental Analysis, Hokkaido University.

Column chromatography was carried out on Kanto silica gel 60 N (40–50 μm or 63–210 μm) or Merck Kieselgel 60 (40–63 μm or 63–200 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. Dehydrated stabilizer free THF was purchased from Kanto Chemical Co., Inc. Dichloromethane was distilled from P_2O_5, and redistilled from calcium hydride prior to use. Toluene and benzene were distilled from sodium/benzophenone prior to use. Chlorotrimethylsilane (TMSCl) and 1,1,1,3,3,3-hexamethyldisilazane were distilled from calcium hydride. 4 Å molecular sieves was finely ground in mortar and heated in vacuo at 220 °C for 12 h. All reactions were conducted under an argon atmosphere unless otherwise noted.

Materials: 4-Methoxybenzyl trichloroacetimidate,[25a] Dess–Martin periodinane,[54] (*E*)-3-hexene-2,5-dione (**33**),[55] di-*tert*-butyl D-tartrate (**47**),[35] 4-methoxybenzyl bromide,[56] *tert*-butyl diazoacetate (**9**),[57] zinc borohydride $[Zn(BH_4)_2]$,[58] *N*,*N*′-diisopropyl-*O*-*tert*-butylisourea,[40] Blechert's ruthenium catalyst (**85**),[47] 2-nitrophenyl selenocyanate[59] and (2*E*,4*S*,6*S*)-4,6-dimethyl-2-octenoic acid (**102**)[52] were prepared according to literature procedures.

Methyl (2*R*,3*R*)-3,4-(dimethylmethylenedioxy)-2-(4-methoxybenzyl)oxybutanoate (13): Ph_3CBF_4 (94 mg, 0.284 mmol) was added to a stirred solution of alcohol **12**[24] (1.8 g, 9.47 mmol) and 4-methoxybenzyl trichloroacetimidate (4.0 g, 14.16 mmol) in Et_2O (80 mL) at 0 °C. After stirring for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (80 mL), and the mixture was extracted with AcOEt (40 mL). The organic extract was washed with brine (80 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (6.5 g), which was purified by column chromatography (silica gel 150 g, *n*-hexane/AcOEt 15:1) to give MPM ether **13** (2.73 g, 93%) as a colorless oil. $[\alpha]_D^{20} = +48.8$ ($c = 2.02$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 1.32 (s, 3H; acetonide CH_3), 1.40 (s, 3H; acetonide CH_3), 3.75 (s, 3H; CO_2CH_3), 3.79 (s, 3H; $C_6H_4OCH_3$), 3.93 (d, $J = 6.7$ Hz, 1H; C4-*H*), 3.95 (dd, $J = 4.9$, 8.7 Hz, 1H; OCH*H*), 4.03 (dd, $J = 6.3$, 8.7 Hz, 1H; OCH*H*), 4.31 (ddd, $J = 4.9$, 6.3, 6.7 Hz, 1H; C3-*H*), 4.42 (d, $J = 11.3$ Hz, 1H; OC*H*Ar), 4.59 (d, $J = 11.3$ Hz, 1H; OC*H*Ar), 6.87 (m, 2H; Ar*H*), 7.25 (m, 2H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 25.3$, 26.6, 52.0, 55.3, 66.4, 72.6, 75.9, 77.2, 78.8, 109.9, 113.8, 128.9, 129.8, 159.5, 171.0; IR (film): $\tilde{\nu} = 2990$, 2953, 1748, 1613, 1586, 1514, 1458, 1439, 1373, 1302,

1252, 1221 cm^{-1}; HR-MS (EI): m/z: calcd for $C_{16}H_{22}O_6$: 310.1416, found: 310.1414 [M^+].

Methyl (2*R*,3*R*)-3,4-dihydroxy-2-(4-methoxybenzyl)oxybutanoate (14): 10% Aqueous HCl (10 mL) was added to a solution of acetonide **13** (2.09 g, 6.75 mmol) in THF (20 mL) at 0°C. After stirring at room temperature for 5 h, the mixture was extracted with AcOEt (2×50 mL). The combined organic extracts were successively washed with saturated aqueous $NaHCO_3$ (30 mL) and brine (30 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (2.1 g), which was purified by column chromatography (silica gel 50 g, *n*-hexane/AcOEt 1:1) to give diol **14** (1.64 g, 90%) as a colorless oil. $[\alpha]_D^{21}=+59.6$ ($c=2.03$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=3.67$ (dd, $J=4.3$, 11.6 Hz, 1H; OCH*H*), 3.70 (dd, $J=4.6$, 11.6 Hz, 1H; OCH*H*), 3.78 (s, 3H; CO_2CH_3), 3.81 (s, 3H; $C_6H_4OCH_3$), 3.95 (ddd, $J=4.3$, 4.6, 5.6 Hz, 1H; C3-*H*), 4.08 (d, $J=5.6$ Hz, 1H; C4-*H*), 4.40 (d, $J=11.1$ Hz, 1H; OC*H*Ar), 4.67 (d, $J=11.1$ Hz, 1H; OC*H*Ar), 6.88 (m, 2H; Ar*H*), 7.26 (m, 2H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=52.1$, 55.2, 62.8, 71.9, 72.7, 78.9, 113.8, 128.8, 129.8, 130.1, 159.5, 171.6; IR (film): $\tilde{\nu}=3461$, 2953, 2839, 1732, 1613, 1588, 1514, 1441, 1397, 1248, 1105, 1033 cm^{-1}; HR-MS (EI): m/z: calcd for $C_{13}H_{18}O_6$: 270.1103, found: 270.1094 [M^+].

Methyl (2*R*,3*R*)-4-(*tert*-butyldiphenysilyl)oxy-3-hydroxy-2-(4-methoxybenzyl)oxybutanoate (15): TBDPSCl (1.63 mL, 6.27 mmol) was added to a stirred solution of diol **14** (1.54 g, 5.70 mmol) and imidazole (970 mg, 14.3 mmol) in CH_2Cl_2 (15 mL) at 0°C. After stirring for 1 h, the reaction was quenched by addition of H_2O (15 mL), and the mixture was extracted with AcOEt (30 mL). The organic extract was washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (3.6 g), which was purified by column chromatography (silica gel 40 g, *n*-hexane/AcOEt 6:1) to give TBDPS ether **15** (2.49 g, 86%) as a colorless oil. $[\alpha]_D^{27}=+12.1$ ($c=2.39$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.05$ (s, 9H; SiC(CH_3)$_3$), 2.56 (d, $J=6.9$ Hz, 1H; O*H*), 3.73 (s, 3H; CO_2CH_3), 3.78 (s, 3H; $C_6H_4OCH_3$), 3.79 (d, $J=4.4$ Hz, 2H; CH_2OTBDPS), 3.96 (ddt, $J=6.8$, 6.9, 4.4 Hz, 1H; C3-*H*), 4.09 (d, $J=6.8$ Hz, 1H; C4-*H*), 4.34 (d, $J=11.1$ Hz, 1H; OC*H*Ar), 4.57 (d, $J=11.1$ Hz, 1H; OC*H*Ar), 6.83 (m, 2H; Ar*H*), 7.18 (m, 2H; Ar*H*), 7.35–7.44 (m, 6H; Ar*H*), 7.63–7.64 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta=19.2$, 26.8, 51.9, 55.2, 63.8, 72.3, 72.4, 78.3, 113.8, 127.7, 129.0, 129.7, 129.8, 132.9, 133.0, 135.5, 159.4, 171.5; IR (film): $\tilde{\nu}=3493$, 3071, 3048, 3000, 2953, 2890, 2858, 1748, 1613, 1588, 1514, 1464, 1429, 1393, 1250, 1113, 1036 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{29}H_{36}O_6SiNa$: 531.2179, found: 531.2195 [M^++Na].

3-(Methoxymethoxy)propionic acid (16): P_2O_5 (100 g, 0.70 mol) was added in ten portions to a stirred solution of methyl 3-hydroxypropionate[27] (47.3 g, 0.45 mol) in dimethoxymethane (200 mL, 2.26 mol) and $CHCl_3$ (200 mL) at 0°C. After stirring at room temperature for 10 h, the reaction mixture was poured into an ice-cooled, two-layer mixture of Et_2O (50 mL) and saturated aqueous Na_2CO_3 (600 mL), and the mixture was extracted with AcOEt (800 mL). The organic extract was successively washed with saturated aqueous $NaHCO_3$ (300 mL) and brine (2×300 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (55.6 g), which was used without further purification.

Lithium hydroxide monohydrate (23.1 g, 0.55 mol) was added to a stirred solution of the crude methyl ester (55.6 g) in THF (300 mL)/H_2O (150 mL). After stirring for 2 h, THF was removed in vacuo, and the resultant mixture was acidified with 10% aqueous HCl (250 mL). The mixture was saturated with NaCl and extracted with AcOEt (6×400 mL). The combined organic extracts were washed with brine (2×500 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (44.1 g), which was purified by distillation to give carboxylic acid **16** (31.4 g, 52% for two steps) as a colorless oil. B.p. 138°C (13 mm Hg); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.66$ (t, $J=6.1$ Hz, 2H; C1′-H_2), 3.37 (s, 3H; OCH_3), 3.83 (t, $J=6.1$ Hz, 2H; C2′-H_2), 4.64 (s, 2H; OCH_2O); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=34.8$, 55.1, 62.8, 96.3, 177.2; IR (film): $\tilde{\nu}=3455$, 2951, 2893, 2832, 1734, 1404, 1152, 1113, 1040 cm^{-1}; HR-MS (EI): m/z: calcd for $C_5H_9O_4$: 133.0501, found: 133.0502 [M^+−H]; elemental analysis calcd (%) for $C_5H_{10}O_4$ (134.1): C 44.77, H 7.51; found: C 44.44, H 7.59.

Methyl (2*R*,3*R*)-4-(*tert*-butyldiphenylsilyl)oxy-2-(4-methoxybenzyl)oxy-3-[3-(methoxymethoxy)propionyl]oxybutanoate (17): EDCI (1.36 g, 7.11 mmol) was added to a solution of alcohol **15** (2.34 g, 4.60 mmol), carboxylic acid **16** (681 mg, 5.08 mmol) and DMAP (808 mg, 6.60 mmol) in CH_2Cl_2 (20 mL) at 0°C. After stirring at room temperature for 12 h, the reaction was quenched with 10% aqueous HCl (50 mL), and the mixture was extracted with AcOEt (50 mL). The organic extract was successively washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (3.2 g), which was purified by column chromatography (silica gel 60 g, *n*-hexane/AcOEt 7:1) to give ester **17** (2.30 g, 80%) as a colorless oil. $[\alpha]_D^{23}=+8.36$ ($c=2.25$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.02$ (s, 9H; SiC(CH_3)$_3$), 2.52 (t, $J=6.5$ Hz, 2H; C1′-H_2), 3.31 (s, 3H; OCH_3), 3.69 (s, 3H; CO_2CH_3), 3.73 (t, $J=6.5$ Hz, 2H; C2′-H_2), 3.79 (s, 3H; $C_6H_4OCH_3$), 3.84 (dd, $J=4.7$, 11.1 Hz, 1H; C*H*OTBDPS), 3.89 (dd, $J=5.4$, 11.1 Hz, 1H; C*H*OTBDPS), 4.28 (d, $J=5.6$ Hz, 1H; C4-*H*), 4.42 (d, $J=11.3$ Hz, 1H; OC*H*Ar), 4.62 (s, 2H; OCH_2O), 4.66 (d, $J=11.3$ Hz, 1H; OC*H*Ar), 5.31 (ddd, $J=4.7$, 5.4, 5.6 Hz, 1H; C3-*H*), 6.83 (m, 2H; Ar*H*), 7.24 (m, 2H; Ar*H*), 7.35–7.41 (m, 6H; Ar*H*), 7.62–7.65 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta=19.2$, 26.7, 34.9, 52.1, 52.2, 55.2, 61.5, 62.9, 72.6, 73.9, 76.0, 96.4, 113.8, 127.6, 127.7, 129.1, 129.7, 133.0, 133.2, 135.5, 135.6, 159.4, 170.3; IR (film): $\tilde{\nu}=2953$, 2888, 2859, 1750, 1613, 1588, 1514, 1464, 1429, 1391, 1362, 1302, 1250, 1175, 1105 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{34}H_{44}O_9SiNa$: 647.2652, found: 647.2672 [M^++Na].

Methyl (2*R*,3*R*)-4-(*tert*-butyldiphenylsilyl)oxy-2-hydroxy-3-[3-(methoxymethoxy)propionyl]oxybutanoate (18): DDQ (1.65 g, 7.28 mmol) was added to a stirred biphasic mixture of MPM ether **17** (1.3 g, 2.08 mmol) in CH_2Cl_2 (25 mL)/pH 7 phosphate buffer (2.5 mL). After stirring for 24 h, the reaction mixture was diluted with AcOEt (30 mL) and passed through a Celite pad. The filtrate was successively washed with saturated aqueous $NaHCO_3$ (40 mL) and brine (40 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.5 g), which was purified by column chromatography (silica gel 80 g, *n*-hexane/AcOEt 3:1) to give alcohol **18** (1.04 g, 99%) as a colorless oil. $[\alpha]_D^{20}=-29.0$ ($c=2.00$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.04$ (s, 9H; SiC(CH_3)$_3$), 2.59 (dt, $J=16.2$, 6.1 Hz, 1H; C1′-*H*), 2.60 (dt, $J=16.2$, 6.1 Hz, 1H; C1′-*H*), 3.32 (s, 3H; OCH_3), 3.35 (d, $J=6.6$ Hz, 1H; O*H*), 3.74 (s, 3H; CO_2CH_3), 3.78 (t, $J=6.1$ Hz, 2H; C2′-H_2), 3.80 (dd, $J=5.7$, 10.8 Hz, 1H; C*H*OTBDPS), 3.86 (dd, $J=6.4$, 10.8 Hz, 1H; C*H*OTBDPS), 4.49 (dd, $J=3.3$, 6.6 Hz, 1H; C4-*H*), 4.59 (s, 2H; OCH_2O), 5.33 (ddd, $J=3.3$, 5.7, 6.4 Hz, 1H; C3-*H*), 7.39–7.44 (m, 6H; Ar*H*), 7.64–7.67 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=19.1$, 26.6, 35.0, 52.6, 55.2, 61.4, 63.0, 70.2, 74.5, 96.4, 127.7, 129.8, 132.69, 132.72, 135.4, 135.5, 170.6, 172.2; IR (film): $\tilde{\nu}=3470$, 2955, 2934, 2890, 2859, 1746, 1472, 1429, 1391, 1364, 1263, 1213, 1179, 1148, 1113 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{26}H_{37}O_8Si$: 505.2258, found: 505.2263 [M^++H]; elemental analysis calcd (%) for $C_{26}H_{36}O_8Si$ (504.6): C 61.88, H 7.19; found: C 61.86, H 7.05.

Methyl (*R*)-4-(*tert*-butyldiphenylsilyl)oxy-3-[3-(methoxymethoxy)propionyl]oxy-2-oxobutanoate (19): Dess–Martin periodinane (1.43 g, 3.36 mmol) was added to a stirred solution of alcohol **18** (1.55 g, 3.07 mmol) in CH_2Cl_2 (20 mL). After stirring for 1 h, the reaction mixture was poured into an ice-cooled mixture of saturated aqueous $NaHCO_3$ (15 mL) and 10% aqueous $Na_2S_2O_3{\cdot}H_2O$ (10 mL), and the whole was extracted with AcOEt (20 mL). The organic extract was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.9 g), which was purified by column chromatography (silica gel 30 g, *n*-hexane/AcOEt 3:1) to give α-keto ester **19** (1.49 g, 97%) as a colorless oil. $[\alpha]_D^{20}=-14.6$ ($c=2.05$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.00$ (s, 9H; SiC(CH_3)$_3$), 2.69 (dt, $J=9.0$, 6.4 Hz, 1H; C1′-*H*), 2.70 (dt, $J=9.0$, 6.4 Hz, 1H; C1′-*H*), 3.34 (s, 3H; OCH_3), 3.79 (dt, $J=11.1$, 6.4 Hz, 1H; C2′-*H*), 3.81 (dt, $J=11.1$, 6.4 Hz, 1H; C2′-*H*), 3.87 (s, 3H; CO_2CH_3), 3.99 (dd, $J=3.8$, 11.3 Hz, 1H; C*H*OTBDPS), 4.32 (dd, $J=4.7$, 11.3 Hz, 1H; C*H*OTBDPS), 4.62 (s, 2H; OCH_2O), 5.83 (dd, $J=3.8$, 4.7 Hz, 1H; C3-*H*), 7.36–7.46 (m, 6H; Ar*H*), 7.62–7.65 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=19.1$, 26.5, 26.6, 34.6, 53.0, 55.2, 62.9, 63.1, 77.2, 96.5, 96.6, 127.7, 127.8, 128.0, 129.9, 130.2, 132.3, 132.5, 135.4, 135.6, 160.0, 170.5, 187.6; IR (film): $\tilde{\nu}=3455$, 2934, 2890, 1738, 1472, 1429, 1391, 1364, 1256, 1177, 1113, 1038, 704 cm^{-1};

HR-MS (FAB): m/z: calcd for $C_{26}H_{35}O_5Si$: 503.2101, found: 503.2129 [M^++H].

4-Ethyl 1-methyl [2*R*,2(1*R*)]-2-[2-(*tert*-butyldiphenylsilyl)oxy-1-[3-(methoxymethoxy)propionyl]oxyethyl]-3-diazo-2-hydroxybutanedioate (20) and 4-ethyl 1-methyl [2*S*,2(1*R*)]-2-[2-(*tert*-butyldiphenylsilyl)oxy-1-[3-(methoxymethoxy)propionyl]oxyethyl]-3-diazo-2-hydroxybutanedioate (21): A 0.35 M solution of lithium bis(trimethylsilyl)amide in THF (6.26 mL, 2.19 mmol) was added to a stirred mixture of α-keto ester **19** (1.0 g, 1.99 mmol) and ethyl diazoacetate (272 mg, 2.39 mmol) in THF (20 mL) at −78 °C. After stirring for 30 min, the solution was poured into saturated aqueous NH_4Cl (20 mL), and the mixture was extracted with AcOEt (30 mL). The organic extract was washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.3 g), which was purified by flash column chromatography (silica gel 20 g, *n*-hexane/Et_2O 2:1) to give α-diazo esters **20** (467 mg, 38 %) and **21** (394 mg, 32 %) as yellow oils.

Data for [2*R*,2(1*R*)]-isomer **20**: $[\alpha]_D^{27}=+17.5$ ($c=1.45$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.03$ (s, 9H; SiC(CH_3)$_3$), 1.24 (t, $J=7.3$ Hz, 3H; $CO_2CH_2CH_3$), 2.61 (dt, $J=12.6$, 6.2 Hz, 1H; C1′-*H*), 2.63 (dt, $J=12.6$, 6.2 Hz, 1H; C1′-*H*), 3.33 (s, 3H; OCH_3), 3.70 (s, 3H; CO_2CH_3), 3.78 (m, 2H; C2′-H_2), 3.90 (dd, $J=4.2$, 11.2 Hz, 1H; C*H*OTBDPS), 3.99 (dd, $J=6.0$, 11.2 Hz, 1H; C*H*OTBDPS), 4.19 (q, $J=7.3$ Hz, 2H; $CO_2CH_2CH_3$), 4.58 (s, 2H; OCH_2O), 5.18 (s, 1H; O*H*), 5.57 (dd, $J=4.2$, 6.0 Hz, 1H; C3-*H*), 7.38–7.45 (m, 6H; Ar*H*), 7.63–7.65 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=14.3$, 19.1, 26.6, 35.0, 53.5, 55.2, 61.3, 62.5, 62.8, 74.0, 74.6, 96.5, 127.8, 129.9, 132.5, 135.5, 165.8, 170.2, 171.0; IR (film): $\tilde{\nu}=3463$, 2934, 2890, 2859, 2105, 1750, 1699, 1589, 1470, 1429, 1308, 1111, 706 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{30}H_{41}O_{10}Si$: 589.2469, found: 589.2458 [M^+-N_2+H].

Data for [2*S*,2(1*R*)]-isomer **21**: $[\alpha]_D^{25}=-21.9$ ($c=1.11$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.02$ (s, 9H; SiC(CH_3)$_3$), 1.23 (t, $J=7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.58 (dt, $J=10.7$, 6.4 Hz, 1H; C1′-*H*), 2.59 (dt, $J=10.7$, 6.4 Hz, 1H; C1′-*H*), 3.32 (s, 3H; OCH_3), 3.75 (m, 2H; C2′-H_2), 3.76 (s, 3H; CO_2CH_3), 3.90 (dd, $J=6.1$, 11.3 Hz, 1H; C*H*OTBDPS), 3.98 (dd, $J=4.2$, 11.3 Hz, 1H; C*H*OTBDPS), 4.17 (dq, $J=10.6$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.20 (dq, $J=10.6$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.59 (s, 2H; OCH_2O), 4.85 (s, 1H; O*H*), 5.73 (dd, $J=4.2$, 6.1 Hz, 1H; C3-*H*), 7.37–7.45 (m, 6H; Ar*H*), 7.63–7.66 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=14.2$, 19.0, 26.6, 34.9, 53.4, 55.2, 61.2, 62.3, 62.8, 73.3, 73.9, 96.4, 127.8, 129.8, 132.4, 132.6, 135.45, 135.54, 165.1, 169.8, 171.1; IR (film): $\tilde{\nu}=3466$, 2934, 2890, 2859, 2106, 1752, 1699, 1472, 1429, 1393, 1370, 1307, 1113, 756 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{30}H_{41}O_{10}Si$: 589.2469, found: 589.2463 [M^+-N_2+H].

4-Ethyl 1-methyl [2*R*,2(1*R*)]-2-[2-(*tert*-butyldiphenylsilyl)oxy-1-[3-(methoxymethoxy)propionyl]oxyethyl]-3-diazo-2-(trimethylsilyl)oxybutanedioate (11): HMDS (0.18 mL, 0.818 mmol) was added to a stirred solution of α-diazo ester **20** (119 mg, 0.193 mmol) and imidazole (28 mg, 0.408 mmol) in THF (2 mL). After stirring for 48 h, the volatile elements were removed in vacuo. Purification of the residue (150 mg) by column chromatography (silica gel 10 g, *n*-hexane/AcOEt 10:1) afforded TMS ether **11** (122 mg, 92 %) as a yellow oil. $[\alpha]_D^{25}=-17.1$ ($c=1.04$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.08$ (s, 9H; Si(CH_3)$_3$), 1.01 (s, 9H; SiC(CH_3)$_3$), 1.23 (t, $J=7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.60 (dt, $J=16.0$, 6.5 Hz, 1H; C1′-*H*), 2.64 (dt, $J=16.0$, 6.5 Hz, 1H; C1′-*H*), 3.34 (s, 3H; OCH_3), 3.62 (s, 3H; CO_2CH_3), 3.76–3.81 (m, 2H; C2′-H_2), 3.80 (dd, $J=7.6$, 11.1 Hz, 1H; C*H*OTBDPS), 3.85 (dd, $J=3.7$, 11.1 Hz, 1H; C*H*OTBDPS), 4.16 (dq, $J=10.3$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.17 (dq, $J=10.3$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.59 (s, 2H; OCH_2O), 5.70 (dd, $J=3.7$, 7.6 Hz, 1H; C3-*H*), 7.38–7.42 (m, 6H; Ar*H*), 7.63–7.67 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=1.0$, 14.4, 19.1, 26.6, 35.0, 52.8, 55.2, 61.0, 62.5, 62.8, 76.7, 77.2, 96.4, 127.7, 129.6, 129.7, 133.0, 133.2, 135.5, 135.6, 164.3, 169.2, 170.1; IR (film): $\tilde{\nu}=2955$, 2892, 2859, 2103, 1755, 1703, 1466, 1429, 1391, 1370, 1304, 1254, 1113, 1036, 847 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{33}H_{49}O_{10}Si_2$: 661.2864, found: 661.2885 [M^+-N_2+H].

4-Ethyl 1-methyl [2*S*,2(1*R*)]-2-[2-(*tert*-butyldiphenylsilyl)oxy-1-[3-(methoxymethoxy)propionyl]oxyethyl]-3-diazo-2-(trimethylsilyl)oxybutanedioate (22): HMDS (0.19 mL, 0.876 mmol) was added to a stirred solution of α-diazo ester **21** (127 mg, 0.206 mmol) and imidazole (30 mg, 0.438 mmol) in THF (2 mL). After stirring for 48 h, the volatile elements were removed in vacuo. Purification of the residue (162 mg) by column chromatography (silica gel 10 g, *n*-hexane/AcOEt 10:1) afforded TMS ether **22** (129 mg, 91 %) as a yellow oil. $[\alpha]_D^{29}=+32.8$ ($c=1.03$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.10$ (s, 9H; Si(CH_3)$_3$), 1.00 (s, 9H; SiC(CH_3)$_3$), 1.19 (t, $J=7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.58 (t, $J=6.5$ Hz, 2H; C1′-H_2), 3.32 (s, 3H; OCH_3), 3.67 (dd, $J=7.7$, 11.0 Hz, 1H; C*H*OTBDPS), 3.68 (s, 3H; CO_2CH_3), 3.73 (dt, $J=9.9$, 6.5 Hz, 1H; C2′-*H*), 3.81 (dt, $J=9.9$, 6.5 Hz, 1H; C2′-*H*), 3.96 (dd, $J=4.0$, 11.0 Hz, 1H; C*H*OTBDPS), 4.12 (dq, $J=11.3$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.13 (dq, $J=11.3$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.58 (s, 2H; OCH_2O), 5.90 (dd, $J=4.0$, 7.7 Hz, 1H; C3-*H*), 7.36–7.41 (m, 6H; Ar*H*), 7.63–7.67 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta=1.2$, 14.2, 19.1, 26.6, 35.0, 52.6, 55.2, 60.9, 62.3, 62.9, 75.2, 75.6, 96.4, 127.6, 127.7, 129.6, 129.7, 133.1, 133.2, 135.5, 135.6, 135.7, 164.2, 169.59, 169.63; IR (film): $\tilde{\nu}=2955$, 2890, 2859, 2105, 1755, 1699, 1472, 1429, 1391, 1370, 1306, 1254, 1171, 1150 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{33}H_{49}O_{10}Si_2$: 661.2864, found: 661.2844 [M^+-N_2+H].

(2*S*,3*R*)-3-(*tert*-Butyldiphenylsilyl)oxy-2-[diazo(ethoxycarbonyl)methyl]-2-hydroxy-4-butanolide (24): K_2CO_3 (91 mg, 0.66 mmol) was added to a stirred solution of alcohol **21** (101 mg, 0.164 mmol) in MeOH (1.5 mL) at 0 °C. After stirring for 1 h, the mixture was poured into an ice-cooled, two-layer mixture of Et_2O (5 mL) and H_2O (5 mL), and the whole was extracted with AcOEt (10 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (105 mg), which was purified by column chromatography (silica gel 10 g, *n*-hexane/AcOEt 20:1) to give lactone **24** (52.5 mg, 68 %) as a yellow solid. M.p. 107–108 °C (yellow prisms from *n*-hexane/*n*-Bu_2O 10:1); $[\alpha]_D^{22}=-55.7$ ($c=1.03$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.06$ (s, 9H; SiC(CH_3)$_3$), 1.31 (t, $J=7.2$ Hz, 3H; $CO_2CH_2CH_3$), 3.90 (dd, $J=4.0$, 9.4 Hz, 1H; one of lactone CH_2), 4.03 (dd, $J=4.7$, 9.4 Hz, 1H; one of lactone CH_2), 4.25 (dq, $J=10.7$, 7.2 Hz, 1H; CO_2CHHCH_3), 4.29 (dq, $J=10.7$, 7.2 Hz, 1H; CO_2CHHCH_3), 4.50 (dd, $J=4.0$, 4.7 Hz, 1H; C3-*H*), 7.41–7.48 (m, 6H; Ar*H*), 7.61–7.63 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=14.4$, 19.1, 26.6, 61.5, 71.9, 76.0, 76.1, 76.3, 76.8, 77.2, 127.9, 128.0, 128.1, 130.38, 130.42, 131.6, 132.7, 135.5, 135.6, 166.6, 172.6; IR ($CHCl_3$): $\tilde{\nu}=3021$, 2114, 1790, 1686, 1472, 1427, 1395, 1373, 1327, 1181, 1152 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{24}H_{29}N_2O_6Si$: 469.1795, found: 469.1778 [M^++H].

(2*S*,3*R*)-3-(*tert*-Butyldiphenylsilyl)oxy-2-[diazo(ethoxycarbonyl)methyl]-2-(trimethylsilyl)oxy-4-butanolide (25): TMS-imidazole (0.1 mL, 0.672 mmol) was added to a stirred solution of alcohol **24** (52.5 mg, 0.112 mmol) in CH_2Cl_2 (1 mL). After stirring for 12 h, the mixture was evaporated in vacuo. Purification of the residue by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 20:1) afforded TMS ether **25** (58.7 mg, 97 %) as a yellow oil. $[\alpha]_D^{22}=-9.62$ ($c=2.94$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.17$ (s, 9H; Si(CH_3)$_3$), 1.04 (s, 9H; SiC(CH_3)$_3$), 1.27 (t, $J=7.0$ Hz, 3H; $CO_2CH_2CH_3$), 3.87 (dd, $J=4.5$, 9.2 Hz, 1H; H_b of lactone CH_2), 3.92 (dd, $J=4.9$, 9.2 Hz, 1H; H_a of lactone CH_2), 4.19 (dq, $J=10.5$, 7.0 Hz, 1H; CO_2CHHCH_3), 4.20 (dq, $J=10.5$, 7.0 Hz, 1H; CO_2CHHCH_3), 4.55 (dd, $J=4.5$, 4.9 Hz, 1H; C3-*H*), 7.39–7.48 (m, 6H; Ar*H*), 7.62–7.66 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=0.8$, 14.4, 19.1, 26.6, 61.1, 71.1, 77.3, 127.9, 128.0, 130.2, 130.3, 131.8, 133.0, 135.5, 135.7, 164.9, 172.3; IR (film): $\tilde{\nu}=2961$, 2934, 2899, 2108, 1786, 1701, 1472, 1429, 1392, 1372, 1318, 1256, 1219, 1188, 1115 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{27}H_{37}N_2O_6Si_2$: 541.2190, found: 541.2195 [M^++H].

(2*R*,3*R*)-3-(*tert*-Butyldiphenylsilyl)oxy-2-[diazo(ethoxycarbonyl)methyl]-2-(trimethylsilyl)oxy-4-butanolide (27): K_2CO_3 (51 mg, 0.37 mmol) was added to a stirred solution of alcohol **20** (52 mg, 0.084 mmol) in MeOH (1 mL) at 0 °C. After stirring for 1 h, the mixture was poured into an ice-cooled, two-layer mixture of Et_2O (5 mL) and H_2O (5 mL), and the whole was extracted with AcOEt (10 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude lactone **26** (23.3 mg), which was used without further purification.

TMS-imidazole (0.02 mL, 0.149 mmol) was added to a stirred solution of the crude lactone **26** (23.3 mg) in CH_2Cl_2 (0.5 mL). After stirring for

20 h, the mixture was evaporated in vacuo. Purification of the residue by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 20:1) afforded TMS ether **27** (21.8 mg, 48% for two steps) as a yellow oil. $[\alpha]_D^{19} = +17.0$ ($c = 1.08$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.26$ (s, 9H; Si(CH_3)$_3$), 1.08 (s, 9H; SiC(CH_3)$_3$), 1.46 (t, $J = 7.3$ Hz, 3H; $CO_2CH_2CH_3$), 3.96 (dq, $J = 10.7$, 7.3 Hz, 1H; CO_2CHHCH_3), 3.98 (dq, $J = 10.7$, 7.3 Hz, 1H; CO_2CHHCH_3), 4.04 (dd, $J = 6.0$, 8.9 Hz, 1H; H_b of lactone CH_2), 4.20 (dd, $J = 5.7$, 8.9 Hz, 1H; H_a of lactone CH_2), 4.59 (dd, $J = 5.7$, 6.0 Hz, 1H; C3-*H*), 7.38–7.45 (m, 6H; Ar*H*), 7.62–7.66 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 0.8$, 14.1, 19.3, 26.8, 61.0, 70.9, 72.7, 73.9, 77.2, 127.7, 127.9, 130.0, 130.2, 132.5, 133.0, 135.6, 135.7, 163.9, 172.1; IR ($CHCl_3$): $\tilde{\nu} = 3023$, 2108, 1794, 1688, 1474, 1427, 1321, 1256, 1221, 1175, 1119 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{27}H_{36}N_2O_6Si_2Na$: 563.2010, found: 563.1992 [M^++Na].

Typical procedure for tandem carbonyl ylide formation/1,3-dipolar cycloaddition reaction of α-diazo ester 11: **5-ethyl 4,6,7-trimethyl (1*S*,3*R*,4*S*,5*R*)-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]oct-6-ene-4,5,6,7-tetracarboxylate (30)**: A solution of α-diazo ester **11** (15.4 mg, 0.022 mmol) in benzene (0.6 mL) was added dropwise over 5 min to a refluxing solution of dimethyl acetylenedicarboxylate (**29**, 9.4 mg, 0.066 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (0.5 mg, 5 mol%) in benzene (0.8 mL), and the mixture was stirred for 25 min. After cooling, the volatile elements were removed in vacuo, and the greenish residue (19 mg) was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 10:1) to give cycloadduct **30** (11.9 mg, 66%) as a colorless oil. $[\alpha]_D^{23} = -42.9$ ($c = 0.60$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = -0.04$ (s, 9H; Si(CH_3)$_3$), 1.04 (s, 9H; SiC(CH_3)$_3$), 1.29 (t, $J = 7.0$ Hz, 3H; $CO_2CH_2CH_3$), 2.19 (dt, $J = 15.0$, 4.9 Hz, 1H; C1′-*H*), 2.41 (ddd, $J = 6.2$, 9.2, 15.0 Hz, 1H; C1′-*H*), 3.28 (s, 3H; OCH_3), 3.56 (s, 3H; CO_2CH_3), 3.63 (ddd, $J = 4.9$, 6.2, 14.4 Hz, 1H; C2′-*H*), 3.66 (dd, $J = 5.9$, 10.9 Hz, 1H; C*H*OTBDPS), 3.70 (dd, $J = 5.9$, 10.9 Hz, 1H; C*H*OTBDPS), 3.76 (ddd, $J = 4.9$, 9.2, 14.4 Hz, 1H; C2′-*H*), 3.82 (s, 6H; $2 \times CO_2CH_3$), 4.22 (dq, $J = 10.7$, 7.0 Hz, 1H; CO_2CHHCH_3), 4.27 (dq, $J = 10.7$, 7.0 Hz, 1H; CO_2CHHCH_3), 4.41 (t, $J = 5.9$ Hz, 1H; C3-*H*), 4.49 (d, $J = 6.6$ Hz, 1H; one of OCH_2O), 4.52 (d, $J = 6.6$ Hz, 1H; one of OCH_2O), 7.36–7.41 (m, 6H; Ar*H*), 7.62–7.66 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 2.2$, 13.8, 19.3, 26.8, 33.8, 52.1, 52.3, 55.2, 62.0, 62.2, 63.1, 78.1, 78.7, 90.0, 96.4, 109.2, 127.6, 127.7, 129.6, 133.2, 133.6, 135.6, 135.8, 138.3, 141.1, 161.4, 162.8, 165.3, 170.5; IR (film): $\tilde{\nu} = 2953$, 2890, 2859, 2774, 1732, 1651, 1589, 1435, 1372, 1252, 1200, 1113, 1036, 951 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{39}H_{54}O_{14}Si_2Na$: 825.2950, found: 825.2941 [M^++Na].

1-Ethyl 10-methyl (1*R*,2*R*,6*S*,7*S*,9*R*,10*S*)-9-[(*tert*-butyldiphenylsilyl)oxymethyl]-7-[2-(methoxymethoxy)ethyl]-3,5-dioxo-4-phenyl-10-(trimethylsilyl)oxy-4-aza-8,11-dioxatricyclo[5.3.1.0^{2,6}]undecane-1,10-dicarboxylate (32): The tandem carbonyl ylide formation/1,3-dipolar cycloaddition reaction was performed according to the typical procedure (1.8 mL benzene, reflux, 30 min) employing α-diazo ester **11** (45 mg, 0.065 mmol), *N*-phenylmaleimide (**31**, 34 mg, 0.196 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (1.4 mg, 5 mol%). The crude product (82 mg) was purified by flash column chromatography (silica gel 10 g, *n*-hexane/AcOEt 6:1) to give cycloadduct **32** (37.0 mg, 68%) as a colorless oil. $[\alpha]_D^{22} = -37.9$ ($c = 1.85$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = -0.05$ (s, 9H; Si(CH_3)$_3$), 1.06 (s, 9H; SiC(CH_3)$_3$), 1.24 (t, $J = 7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.23 (ddd, $J = 5.2$, 10.2, 15.3 Hz, 1H; C1′-*H*), 2.39 (ddd, $J = 5.5$, 10.4, 15.3 Hz, 1H; C1′-*H*), 3.32 (s, 3H; OCH_3), 3.47 (d, $J = 7.1$ Hz, 1H; C7-*H*), 3.62 (d, $J = 5.4$ Hz, 2H; CH_2OTBDPS), 3.73 (s, 3H; CO_2CH_3), 3.77 (ddd, $J = 5.2$, 10.4, 15.4 Hz, 1H; C2′-*H*), 3.90 (ddd, $J = 5.5$, 10.2, 15.4 Hz, 1H; C2′-*H*), 4.16 (t, $J = 5.4$ Hz, 1H; C3-*H*), 4.18 (dq, $J = 10.7$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.23 (dq, $J = 10.7$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.59 (s, 2H; OCH_2O), 4.75 (d, $J = 7.1$ Hz, 1H; C6-*H*), 7.20 (m, 2H; Ar*H*), 7.37–7.46 (m, 9H; Ar*H*), 7.64–7.65 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 2.1$, 13.7, 19.2, 26.8, 35.1, 49.4, 51.8, 52.7, 55.2, 62.3, 63.0, 63.2, 76.2, 89.2, 96.6, 106.4, 126.4, 127.7, 127.8, 129.0, 129.2, 129.9, 131.4, 133.0, 133.1, 135.58, 135.64, 165.8, 170.7, 172.6, 173.1; IR (film): $\tilde{\nu} = 2955$, 2893, 2859, 1759, 1721, 1597, 1501, 1472, 1429, 1389, 1310, 1252, 1202, 1111, 1026, 912 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{43}H_{55}NO_{12}Si_2Na$: 856.3161, found: 856.3164 [M^++Na].

5-Ethyl 4-methyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*S*)-6,7-diacetyl-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (34): The tandem carbonyl ylide formation/1,3-dipolar cycloaddition reaction was performed according to the typical procedure (23 mL benzene, reflux, 1 h) employing α-diazo ester **11** (820 mg, 1.19 mmol), (*E*)-3-hexene-2,5-dione (**33**, 400 mg, 3.57 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (30 mg, 5 mol%). Purification by flash column chromatography (silica gel 80 g, *n*-hexane/AcOEt 4:1) afforded cycloadduct **34** (430 mg, 47%), along with cycloadduct **35** (284 mg, 31%, dr 4:1), as colorless oils. $[\alpha]_D^{25} = -20.1$ ($c = 0.39$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.02$ (s, 9H; Si(CH_3)$_3$), 1.02 (s, 9H; SiC(CH_3)$_3$), 1.22 (t, $J = 7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.20 (s, 3H; $COCH_3$), 2.31 (s, 3H; $COCH_3$), 2.40 (t, $J = 6.4$ Hz, 2H; C1′-H_2), 3.35 (s, 3H; OCH_3), 3.46 (d, $J = 5.7$ Hz, 2H; CH_2OTBDPS), 3.59 (d, $J = 6.1$ Hz, 1H; C7-*H*), 3.73 (s, 3H; CO_2CH_3), 3.76 (dt, $J = 10.1$, 6.4 Hz, 1H; C2′-*H*), 3.89 (dt, $J = 10.1$, 6.4 Hz, 1H; C2′-*H*), 4.12 (dq, $J = 9.4$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.14 (dq, $J = 9.4$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.25 (t, $J = 5.7$ Hz, 1H; C3-*H*), 4.60 (d, $J = 6.5$ Hz, 1H; one of OCH_2O), 4.63 (d, $J = 6.5$ Hz, 1H; one of OCH_2O), 5.19 (d, $J = 6.1$ Hz, 1H; C6-*H*), 7.37–7.46 (m, 6H; Ar*H*), 7.60–7.63 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 2.1$, 13.6, 19.0, 26.6, 29.4, 30.6, 36.5, 52.4, 55.2, 61.6, 63.1, 63.2, 63.6, 75.7, 77.9, 88.6, 96.7, 105.2, 127.6, 129.6, 132.88, 132.93, 135.4, 167.2, 170.3, 202.3, 206.3; IR (film): $\tilde{\nu} = 2955$, 2893, 2859, 1753, 1726, 1589, 1472, 1429, 1391, 1360, 1250, 1198, 1111, 1034, 937 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{39}H_{56}O_{12}Si_2$: 772.3310, found: 772.3278 [M^+].

Data for **35**: $[\alpha]_D^{22} = -52.1$ ($c = 1.07$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.03$ (s, 9H; Si(CH_3)$_3$), 1.02 (s, 9H; SiC(CH_3)$_3$), 1.24 (s, 3H; C6-CH_3), 1.31 (t, $J = 7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.30 (t, $J = 7.8$ Hz, 2H; C1′-H_2), 2.33 (s, 3H; $COCH_3$), 3.35 (s, 3H; OCH_3), 3.52 (dd, $J = 5.9$, 10.8 Hz, 1H; C*H*OTBDPS), 3.54 (dd, $J = 5.9$, 10.8 Hz, 1H; C*H*OTBDPS), 3.60 (s, 3H; CO_2CH_3), 3.72 (dt, $J = 9.6$, 7.8 Hz, 1H; C2′-*H*), 3.77 (dt, $J = 9.6$, 7.8 Hz, 1H; C2′-*H*), 4.22 (dq, $J = 10.3$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.26 (dq, $J = 10.3$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.53 (t, $J = 5.9$ Hz, 1H; C3-*H*), 4.62 (s, 2H; OCH_2O), 6.48 (d, $J = 15.6$ Hz, 1H; =*CH*COCH$_3$), 6.95 (d, $J = 15.6$ Hz, 1H; =*CH*), 7.34–7.45 (m, 6H; Ar*H*), 7.57–7.65 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 2.1$, 13.8, 19.1, 25.8, 26.7, 28.5, 35.8, 52.6, 55.1, 62.0, 62.7, 74.4, 77.7, 84.3, 89.4, 96.5, 118.1, 126.2, 127.5, 129.6, 133.0, 133.2, 135.2, 135.4, 143.9, 165.4, 169.2, 197.9; IR (film): $\tilde{\nu} = 2955$, 2893, 2859, 1753, 1726, 1589, 1472, 1429, 1391, 1360, 1250, 1198, 1111, 1034, 937 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{39}H_{57}O_{12}Si_2$: 773.3388, found: 773.3389 [M^++H].

2-Ethyl 1-methyl (1*S*,2*S*,3*S*,4*R*)-3-(*tert*-butyldiphenylsilyl)oxy-4-[3-(methoxymethoxy)propionyl]oxy-1-(trimethylsilyl)oxycyclobutane-1,2-dicarboxylate (36): A solution of α-diazo ester **22** (16.8 mg, 0.024 mmol) in benzene (0.5 mL) was added dropwise over 15 min to a refluxing solution of dimethyl acetylenedicarboxylate (**29**, 10 mg, 0.072 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (0.5 mg, 5 mol%) in benzene (0.5 mL), and the mixture was stirred for 15 min. After cooling, the volatile elements were removed in vacuo, and the greenish residue (18 mg) was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 10:1) to give cyclobutane **36** (8.8 mg, 56%) as a colorless oil. $[\alpha]_D^{23} = +43.9$ ($c = 0.98$ in $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6): $\delta = 0.30$ (s, 9H; Si(CH_3)$_3$), 0.94 (t, $J = 7.1$ Hz, 3H; $CO_2CH_2CH_3$), 1.21 (s, 9H; SiC(CH_3)$_3$), 2.33 (ddd, $J = 6.3$, 10.0, 16.6 Hz, 1H; C1′-*H*), 2.36 (ddd, $J = 6.3$, 10.0, 16.6 Hz, 1H; C1′-*H*), 3.18 (s, 3H; OCH_3), 3.38 (s, 3H; CO_2CH_3), 3.63 (ddd, $J = 6.3$, 10.0, 12.8 Hz, 1H; C2′-*H*), 3.66 (ddd, $J = 6.3$, 10.0, 12.8 Hz, 1H; C2′-*H*), 3.74 (d, $J = 8.4$ Hz, 1H; C5-*H*), 3.86 (dq, $J = 10.7$, 7.1 Hz, 1H; CO_2CHHCH_3), 3.99 (dq, $J = 10.7$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.45 (s, 2H; OCH_2O), 5.33 (dd, $J = 7.0$, 8.4 Hz, 1H; C*H*OTBDPS), 5.55 (d, $J = 7.0$ Hz, 1H; C3-*H*), 7.24–7.28 (m, 6H; Ar*H*), 7.85–7.90 (m, 4H; Ar*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 1.8$, 14.1, 19.2, 26.8, 34.4, 52.8, 53.1, 55.2, 60.8, 62.5, 70.2, 75.2, 76.8, 96.4, 127.46, 127.48, 129.7, 133.0, 133.2, 135.6, 167.2, 170.1, 170.7; IR (film): $\tilde{\nu} = 2957$, 2893, 2861, 1746, 1589, 1471, 1429, 1391, 1370, 1341, 1296, 1250, 1227, 1152, 1111, 1071, 1036 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{33}H_{49}O_{10}Si_2$: 661.2864, found: 661.2859 [M^++H]; elemental analysis calcd (%) for $C_{33}H_{48}O_{10}Si_2$ (660.9): C 59.97, H 7.32; found: C 59.94, H 7.28.

5-Ethyl 4-methyl (1*S*,3*R*,4*S*,5*R*)-7-acetyl-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]oct-6-ene-4,5-dicarboxylate (43): The tandem carbonyl ylide formation/1,3-dipolar cycloaddition reaction was performed according to the typical procedure (2 mL benzene, reflux, 15 min) employing α-diazo ester **11** (20 mg, 0.029 mmol), 3-butyn-2-one (**40**, 5.9 mg, 0.087 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (0.6 mg, 5 mol%). Purification by column chromatography (silica gel 3 g, *n*-hexane/AcOEt 3:1) afforded cycloadduct **43** (17.9 mg, 85%) as a colorless oil. $[\alpha]_D^{23} = -20.2$ ($c = 0.62$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.09$ (s, 9H; $Si(CH_3)_3$), 1.02 (s, 9H; $SiC(CH_3)_3$), 1.29 (t, $J = 7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.27 (dt, $J = 15.0$, 4.9 Hz, 1H; C1′-*H*), 2.33 (s, 3H; $COCH_3$), 2.52 (ddd, $J = 6.7$, 8.9, 15.0 Hz, 1H; C1′-*H*), 3.27 (s, 3H; OCH_3), 3.61 (dd, $J = 5.3$, 10.8 Hz, 1H; C*H*OTBDPS), 3.61–3.69 (m, 2H; C2′-H_2), 3.65 (s, 3H; CO_2CH_3), 3.69 (dd, $J = 6.3$, 10.8 Hz, 1H; C*H*OTBDPS), 4.21 (dd, $J = 5.3$, 6.3 Hz, 1H; C3-*H*), 4.22 (q, $J = 7.1$ Hz, 2H; $CO_2CH_2CH_3$), 4.48 (d, $J = 6.4$ Hz, 1H; one of CH_2O), 4.50 (d, $J = 6.4$ Hz, 1H; one of CH_2O), 7.13 (s, 1H; C6-*H*), 7.34–7.41 (m, 6H; Ar*H*), 7.59–7.61 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 2.4$, 14.0, 19.2, 26.9, 27.9, 29.7, 33.4, 52.5, 55.1, 62.1, 62.4, 62.9, 79.5, 90.0, 96.2, 108.8, 127.6, 129.7, 133.2, 133.3, 135.6, 135.7, 141.6, 141.8, 166.3, 170.8, 194.1; IR (film): $\tilde{\nu} = 2955$, 2890, 2859, 1759, 1736, 1688, 1250, 1211, 1113, 1026 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{37}H_{53}O_{11}Si_2$: 729.3126, found: 729.3153 [M^++H].

5-Ethyl 4,7-dimethyl (1*S*,3*R*,4*S*,5*R*)-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo-[3.2.1]oct-6-ene-4,5,7-tricarboxylate (44): The tandem carbonyl ylide formation/1,3-dipolar cycloaddition reaction was performed according to the typical procedure (1.4 mL benzene, reflux, 15 min) employing α-diazo ester **11** (20 mg, 0.029 mmol), methyl propiolate (**41**, 7.3 mg, 0.087 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (0.6 mg, 5 mol%). Purification by column chromatography (silica gel 4 g, *n*-hexane/AcOEt 6:1) afforded cycloadduct **44** (17.7 mg, 82%) as a colorless oil. $[\alpha]_D^{24} = -23.0$ ($c = 0.69$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.08$ (s, 9H; $Si(CH_3)_3$), 1.03 (s, 9H; $SiC(CH_3)_3$), 1.27 (t, $J = 7.2$ Hz, 3H; $CO_2CH_2CH_3$), 2.29 (dt, $J = 14.5$, 5.0 Hz, 1H; C1′-*H*), 2.53 (ddd, $J = 6.9$, 8.7, 14.5 Hz, 1H; C1′-*H*), 3.28 (s, 3H; OCH_3), 3.62 (dd, $J = 5.6$, 10.7 Hz, 1H; C*H*OTBDPS), 3.64–3.74 (m, 2H; C2′-H_2), 3.65 (s, 3H; CO_2CH_3), 3.70 (dd, $J = 5.6$, 10.7 Hz, 1H; C*H*OTBDPS), 3.81 (s, 3H; CO_2CH_3), 4.20 (q, $J = 7.2$ Hz, 2H; $CO_2CH_2CH_3$), 4.31 (t, $J = 5.6$ Hz, 1H; C3-*H*), 4.49 (d, $J = 6.6$ Hz, 1H; one of CH_2O), 4.52 (d, $J = 6.6$ Hz, 1H; one of CH_2O), 7.29 (s, 1H; C6-*H*), 7.35–7.41 (m, 6H; Ar*H*), 7.60–7.62 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 2.4$, 14.0, 19.2, 26.8, 33.6, 51.9, 52.5, 55.1, 62.1, 62.4, 63.0, 77.2, 79.5, 90.0, 96.3, 108.4, 127.6, 127.8, 129.7, 133.2, 133.4, 134.8, 135.7, 143.4, 162.8, 166.1, 170.7; IR (film): $\tilde{\nu} = 2953$, 2890, 2859, 2774, 1732, 1651, 1589, 1435, 1372, 1252, 1200, 1113, 1036, 951 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{37}H_{53}O_{12}Si_2$: 745.3076, found: 745.3062 [M^++H].

5-Ethyl 4-methyl (1*S*,3*R*,4*S*,5*R*)-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-7-cyano-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (46): The tandem carbonyl ylide formation/1,3-dipolar cycloaddition reaction was performed according to the typical procedure (3 mL benzene, reflux, 15 min) employing α-diazo ester **11** (100 mg, 0.145 mmol), acrylonitrile (**45**, 23.1 mg, 0.435 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (3.2 mg, 5 mol%). Purification by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 6:1) afforded cycloadducts **46a** (45.9 mg, 44%) and **46b** (31.6 mg, 31%) as colorless oils.

Data for (1*S*,3*R*,4*S*,5*R*,7*R*)-isomer **46a**: $[\alpha]_D^{23} = -10.7$ ($c = 0.59$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.03$ (s, 9H; $Si(CH_3)_3$), 1.03 (s, 9H; $SiC(CH_3)_3$), 1.28 (t, $J = 7.2$ Hz, 3H; $CO_2CH_2CH_3$), 2.23 (dd, $J = 5.5$, 13.6 Hz, 1H; C6-*H*), 2.32–2.47 (m, 2H; C1′-H_2), 3.19 (dd, $J = 5.5$, 8.6 Hz, 1H; C7-*H*), 3.30 (s, 3H; OCH_3), 3.55–3.78 (m, 5H; C6-*H*, C2′-H_2, CH_2OTBDPS), 3.67 (s, 3H; CO_2CH_3), 4.08 (t, $J = 5.9$ Hz, 1H; C3-*H*), 4.15–4.24 (m, 2H; $CO_2CH_2CH_3$), 4.57 (d, $J = 6.3$ Hz, 1H; one of CH_2O), 4.60 (d, $J = 6.3$ Hz, 1H; one of CH_2O), 7.37–7.47 (m, 6H; Ar*H*), 7.61–7.64 (m, 4H; Ar*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 2.3$, 14.1, 19.3, 26.9, 35.4, 36.6, 37.0, 52.6, 55.2, 62.1, 62.2, 63.2, 75.7, 76.9, 86.9, 96.3, 105.9, 119.4, 127.5, 127.6, 129.7, 132.8, 135.39, 135.44, 167.5, 170.3; IR ($CHCl_3$): $\tilde{\nu} = 3021$, 2957, 2934, 2892, 2861, 2249, 1759, 1732, 1464, 1429, 1393, 1373, 1316, 1285, 1113, 1038 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{36}H_{51}NO_{10}Si_2Na$: 736.2949, found: 736.2889 [M^++Na].

Data for (1*S*,3*R*,4*S*,5*R*,7*S*)-isomer **46b**: $[\alpha]_D^{22} = +3.45$ ($c = 0.54$ in EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.05$ (s, 9H; $Si(CH_3)_3$), 1.06 (s, 9H; $SiC(CH_3)_3$), 1.26 (t, $J = 7.1$ Hz, 3H; $CO_2CH_2CH_3$), 2.11–2.27 (m, 2H; C1′-H_2), 2.42 (dd, $J = 11.7$, 14.8 Hz, 1H; C6-*H*), 3.34 (s, 3H; OCH_3), 3.38 (dd, $J = 5.1$, 11.7 Hz, 1H; C7-*H*), 3.51 (dd, $J = 5.1$, 14.8 Hz, 1H; C6-*H*), 3.60 (dd, $J = 5.7$, 10.5 Hz, 1H; C*H*OTBDPS), 3.63 (dd, $J = 5.7$, 10.5 Hz, 1H; C*H*OTBDPS), 3.67 (dt, $J = 10.9$, 5.0 Hz, 1H; C2′-*H*), 3.69 (s, 3H; CO_2CH_3), 3.77 (dt, $J = 10.9$, 5.0 Hz, 1H; C2′-*H*), 4.17 (dq, $J = 14.2$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.19 (dq, $J = 14.2$, 7.1 Hz, 1H; CO_2CHHCH_3), 4.60 (d, $J = 6.5$ Hz, 1H; one of OCH_2O), 4.61 (d, $J = 6.5$ Hz, 1H; one of OCH_2O), 4.75 (t, $J = 5.7$ Hz, 1H; C3-*H*), 7.36–7.43 (m, 6H; Ar*H*), 7.65–7.67 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 2.4$, 14.1, 19.3, 26.9, 34.9, 35.1, 36.8, 52.7, 55.5, 62.0, 62.4, 63.0, 75.9, 76.7, 87.1, 96.7, 105.1, 117.5, 127.55, 127.59, 129.5, 129.6, 132.8, 133.1, 135.4, 167.6, 170.2; IR (film): $\tilde{\nu} = 3073$, 3050, 2955, 2892, 2859, 2249, 1755, 1464, 1429, 1393, 1319, 1113, 1030 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{36}H_{51}NO_{10}Si_2Na$: 736.2949, found: 736.2999 [M^++Na].

Di-*tert*-butyl (2*S*,3*S*)-2-hydroxy-3-(4-methoxybenzyl)oxybutanedioate (48): In a flask equipped with a Dean–Stark apparatus whose sidearm was filled with 4 Å molecular sieves, Bu_2SnO (29.0 g, 0.117 mol) was added to a solution of di-*tert*-butyl D-tartrate (**47**, 30.0 g, 0.114 mol) in toluene (300 mL), and the mixture was refluxed for 2 h. After cooling, the solvent was evaporated in vacuo, and cesium fluoride (35.0 g, 0.228 mol) was added to the resulting white solid. The mixture was suspended in DMF (120 mL), and 4-methoxybenzyl bromide (21 mL, 0.148 mol) was added. After stirring for 10 h, Et_2O (200 mL) and water (100 mL) were added at 0 °C, and the mixture was extracted with Et_2O (2×150 mL). The combined organic extracts were stirred vigorously with saturated aqueous $NaHCO_3$ (200 mL) for 2 h, during which time a white precipitate formed. The mixture was filtered through a Celite pad, and the layers were separated. The organic layer was washed with brine (200 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (55.7 g), which was purified by column chromatography (silica gel 200 g, *n*-hexane/AcOEt 20:1) to give MPM ether **48** (40.1 g, 92%) as a colorless oil. $[\alpha]_D^{24} = -49.7$ ($c = 2.17$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.44$ (s, 9H; $CO_2C(CH_3)_3$), 1.52 (s, 9H; $CO_2C(CH_3)_3$), 3.04 (d, $J = 8.8$ Hz, 1H; O*H*), 3.80 (s, 3H; $C_6H_4OCH_3$), 4.19 (d, $J = 2.3$ Hz, 1H; C3-*H*), 4.39 (d, $J = 10.9$ Hz, 1H; OC*H*Ar), 4.44 (dd, $J = 2.3$, 8.8 Hz, 1H; C4-*H*), 4.74 (d, $J = 10.9$ Hz, 1H; OC*H*Ar), 6.85 (m, 2H; Ar*H*), 7.24 (m, 2H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 27.9$, 28.1, 55.2, 72.6, 78.6, 82.2, 82.8, 113.7, 129.1, 129.8, 159.4, 168.5, 170.3; IR (film): $\tilde{\nu} = 3499$, 2978, 2936, 2839, 1746, 1613, 1588, 1514, 1460, 1395, 1370, 1155, 1098, 1034 cm^{-1}; HR-MS (EI): *m*/*z*: calcd for $C_{20}H_{30}O_7$: 382.1992, found: 382.1971 [M^+].

***tert*-Butyl (2*S*,3*R*)-2,4-dihydroxy-3-(4-methoxybenzyl)oxybutanoate (50)**: A solution of ester **48** (38.0 g, 99.4 mmol) in THF (180 mL) was added to a 1.69 M solution of $LiBH_4$ in THF (100 mL, 169 mmol) at 0 °C. After stirring at room temperature for 4 h, the mixture was poured into 1 N aqueous HCl (300 mL) at 0 °C, and the whole was extracted with AcOEt (2× 300 mL). The combined organic extracts were successively washed with saturated aqueous $NaHCO_3$ (300 mL) and brine (300 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude aldehyde (29.1 g), which was used without further purification.

A solution of the crude aldehyde (29.1 g) in THF (180 mL) was added to a 1.69 M solution of $LiBH_4$ in THF (100 mL, 169 mmol) at −78 °C. After stirring for 4 h, the mixture was poured into 1 N aqueous HCl (300 mL) at 0 °C, and the whole was extracted with AcOEt (2×300 mL). The combined organic extracts were successively washed with saturated aqueous $NaHCO_3$ (300 mL) and brine (300 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (29.0 g), which was purified by column chromatography (silica gel 300 g, *n*-hexane/AcOEt 2:1) to give 1,3-diol **50** (24.5 g, 72%) as a white solid, along with 1,2-diol **51** (620 mg, 2%) as a white solid.

Data for **50**: M.p. 59.7–63.6 °C (colorless needles from *n*-hexane/AcOEt 10:1); $[\alpha]_D^{27} = +10.6$ ($c = 2.05$ in benzene); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.49$ (s, 9H; $CO_2C(CH_3)_3$), 2.46 (brs, 1H; CH_2OH), 3.20 (d, $J =$

7.5 Hz, 1H; C4-O*H*), 3.76–3.87 (m, 3H; C3-*H*, CH_2OH), 3.79 (s, 3H; $C_6H_4OCH_3$), 4.22 (dd, J=1.9, 7.5 Hz, 1H; C4-*H*), 4.53 (d, J=11.1 Hz, 1H; OC*H*Ar), 4.56 (d, J=11.1 Hz, 1H; OC*H*Ar), 6.86 (m, 2H; Ar*H*), 7.25 (m, 2H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=28.0, 55.2, 61.7, 71.9, 72.3, 78.9, 82.8, 113.8, 129.4, 129.9, 159.3, 171.9; IR (Nujol): $\tilde{\nu}$= 3457, 2978, 2936, 1732, 1613, 1514, 1462, 1370, 1173, 1130, 1084 cm^{-1}; HR-MS (EI): m/z: calcd for $C_{16}H_{24}O_6$: 312.1573, found: 312.1589 [M^+]; elemental analysis calcd (%) for $C_{16}H_{24}O_6$ (312.4): C 61.52, H 7.74; found: C 61.42, H 7.80.

Data for **51**: m.p. 79.5–80.5 °C (colorless needles from *n*-hexane/AcOEt 10:1); $[\alpha]_D^{21}=-83.7$ (c=1.11 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.51 (s, 9H; $CO_2C(CH_3)_3$), 2.33 (br s, 1H; O*H*), 2.84 (br s, 1H; O*H*), 3.64 (m, 1H; one of CH_2OH), 3.67 (dt, J=4.2, 11.3 Hz, 1H; C4-*H*), 3.80 (s, 3H; $C_6H_4OCH_3$), 3.90 (d, J=4.2 Hz, 1H; C3-*H*), 3.92 (m, 1H; one of CH_2OH), 4.38 (d, J=11.1 Hz, 1H; OC*H*Ar), 4.73 (d, J=11.1 Hz, 1H; OC*H*Ar), 6.88 (m, 2H; Ar*H*), 7.27 (m, 2H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=28.1, 55.2, 63.6, 72.2, 72.4, 78.6, 82.3, 113.9, 129.0, 129.1, 130.0, 159.6, 169.7; IR (Nujol): $\tilde{\nu}$=3443, 2924, 2855, 1744, 1611, 1517, 1464, 1372, 1285, 1221, 1182, 1159, 1140, 1084, 1069, 1049, 1022, 997 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{16}H_{25}O_6$: 313.1651, found: 313.1642 [M^+ +H]; elemental analysis calcd (%) for $C_{16}H_{24}O_6$ (312.4): C 61.52, H 7.74; found: C 61.41, H 7.69.

***tert*-Butyl (2*S*,3*R*)-4-(*tert*-butyldiphenylsilyl)oxy-2-hydroxy-3-(4-methoxybenzyl)oxybutanoate (52)**: TBDPSCl (1.2 mL, 4.62 mmol) was added to a stirred solution of diol **50** (1.31 g, 4.20 mmol) and imidazole (715 mg, 10.5 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After stirring for 30 min, the reaction was quenched with H_2O (20 mL), and the mixture was extracted with AcOEt (30 mL). The organic extract was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (2.75 g), which was purified by column chromatography (silica gel 30 g, *n*-hexane/AcOEt 10:1) to give TBDPS ether **52** (2.24 g, 97%) as a colorless oil. $[\alpha]_D^{22}=-11.1$ (c=2.11 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.06 (s, 9H; $SiC(CH_3)_3$), 1.49 (s, 9H; $CO_2C(CH_3)_3$), 2.90 (d, J=8.1 Hz, 1H; O*H*), 3.76 (dd, J=3.8, 9.0 Hz, 1H; C*H*OTBDPS), 3.77 (s, 3H; $C_6H_4OCH_3$), 3.84 (dd, J=5.8, 9.0 Hz, 1H; C*H*OTBDPS), 3.85 (ddd, J=3.8, 5.8, 7.3 Hz, 1H; C3-*H*), 4.31 (dd, J=7.3, 8.1 Hz, 1H; C4-*H*), 4.35 (d, J=11.1 Hz, 1H; OC*H*Ar), 4.44 (d, J= 11.1 Hz, 1H; OC*H*Ar), 6.79 (m, 2H; Ar*H*), 7.10 (m, 2H; Ar*H*), 7.35–7.45 (m, 6H; Ar*H*), 7.65–7.68 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=19.1, 26.8, 28.1, 55.2, 62.4, 70.7, 72.9, 79.9, 82.3, 113.7, 127.7, 129.3, 129.7, 130.1, 133.2, 133.4, 135.6, 159.2, 172.5; IR (film): $\tilde{\nu}$=3511, 1736, 1514, 1300, 1250, 1173, 1113 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{32}H_{43}O_6Si$: 551.2830, found: 551.2814 [M^++H].

***tert*-Butyl (2*S*,3*R*)-4-(*tert*-butyldiphenylsilyl)oxy-3-(4-methoxybenzyl)oxy-2-(tetrahydropyran-2-yl)oxybutanoate (53)**: PPTS (196 mg, 0.78 mmol) was added to a stirred solution of alcohol **52** (4.27 g, 7.76 mmol) and DHP (1.4 mL, 15.5 mmol) in CH_2Cl_2 (50 mL). After stirring for 5 h, the reaction was quenched with Et_3N (5 mL), and the volatile elements were removed in vacuo. Purification of the residue (6.2 g) by column chromatography (silica gel 80 g, *n*-hexane/AcOEt 15:1) afforded THP ether **53** (4.67 g, 95%) as a colorless oil. $[\alpha]_D^{24}=-17.1$ (c=2.51 in EtOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.04 (s, 4.5H; $SiC(CH_3)_3$), 1.05 (s, 4.5H; $SiC(CH_3)_3$), 1.41 (s, 4.5H; $CO_2C(CH_3)_3$), 1.42 (s, 4.5H; $CO_2C(CH_3)_3$), 1.51–1.60 (m, 3H; three of THP ether CH_2), 1.64–1.92 (m, 3H; three of THP ether CH_2), 3.38–3.48 (m, 1H; one of THP ether OCH_2), 3.65 (dd, J=6.1, 10.6 Hz, 0.5H; C*H*OTBDPS), 3.72–3.75 (m, 1H; C3-*H*, C*H*OTBDPS), 3.75 (s, 1.5H; $C_6H_4OCH_3$), 3.77 (s, 1.5H; $C_6H_4OCH_3$), 3.86 (dt, J=11.2, 5.4 Hz, 0.5H; one of THP ether OCH_2), 3.91 (dd, J= 6.7, 10.0 Hz, 0.5H; C*H*OTBDPS), 3.95 (m, 0.5H; C3-*H*), 3.97 (dd, J=6.7, 10.6 Hz, 0.5H; C*H*OTBDPS), 4.01 (dt, J=10.9, 3.0 Hz, 0.5H; one of THP ether OCH_2), 4.24 (d, J=5.0 Hz, 0.5H; C4-*H*), 4.47 (d, J=11.3 Hz, 0.5H; OC*H*Ar), 4.49 (d, J=11.3 Hz, 0.5H; OC*H*Ar), 4.50 (d, J=5.7 Hz, 0.5H; C4-*H*), 4.51 (d, J=11.3 Hz, 0.5H; OC*H*Ar), 4.56 (d, J=11.3 Hz, 0.5H; OC*H*Ar), 4.77 (t, J=3.0 Hz, 0.5H; THP ether OC*H*O), 4.80 (t, J= 2.7 Hz, 0.5H; THP ether OC*H*O), 6.76–6.79 (m, 2H; Ar*H*), 7.13–7.18 (m, 2H; Ar*H*), 7.35–7.42 (m, 6H; Ar*H*), 7.63–7.67 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=18.5, 18.8, 19.10, 19.14, 25.3, 25.4, 26.8, 27.9, 28.1, 30.0, 30.1, 55.2, 61.6, 61.9, 62.4, 62.7, 73.0, 73.2, 73.4, 77.2, 77.9, 80.1, 80.3, 81.1, 81.5, 96.4, 100.3, 113.5, 113.6, 127.6, 129.5, 129.55, 129.63, 130.5, 130.6, 133.2, 133.3, 133.5, 135.56, 135.63, 159.0, 170.3, 170.4; IR (film): $\tilde{\nu}$=2936, 1740, 1612, 1514, 1248, 1113, 1080, 1035 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{37}H_{50}O_7SiNa$: 657.3224, found: 657.3205 [M^+ +Na].

***tert*-Butyl (2*S*,3*R*)-4-(*tert*-butyldiphenylsilyl)oxy-3-hydroxy-2-(tetrahydropyran-2-yl)oxybutanoate (54)**: DDQ (878 mg, 3.87 mmol) was added to a stirred biphasic mixture of MPM ether **53** (1.17 g, 1.84 mmol) in CH_2Cl_2 (20 mL)/pH 7 phosphate buffer (1 mL). After stirring for 2 h, the reaction mixture was diluted with AcOEt (30 mL) and passed through a Celite pad. The filtrate was successively washed with saturated aqueous $NaHCO_3$ (40 mL) and brine (40 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.65 g), which was purified by column chromatography (silica gel 50 g, *n*-hexane/AcOEt 20:1) to give alcohol **54** (914 mg, 96%) as a colorless oil. $[\alpha]_D^{24}=-20.8$ (c=2.01 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.067 (s, 4.5H; $SiC(CH_3)_3$), 1.073 (s, 4.5H; $SiC(CH_3)_3$), 1.45 (s, 4.5H; $CO_2C(CH_3)_3$), 1.47 (s, 4.5H; $CO_2C(CH_3)_3$), 1.50–1.60 (m, 3H; three of THP ether CH_2), 1.64–1.87 (m, 3H; three of THP ether CH_2), 2.41 (d, J= 6.7 Hz, 0.5H; O*H*), 2.51 (d, J=6.7 Hz, 0.5H; O*H*), 3.44–3.47 (m, 1H; one of THP ether OCH_2), 3.66 (dd, J=6.9, 10.1 Hz, 0.5H; C*H*OTBDPS), 3.70 (dd, J=5.9, 9.9 Hz, 0.5H; C*H*OTBDPS), 3.75 (dd, J=6.4, 10.1 Hz, 0.5H; C*H*OTBDPS), 3.76 (m, 1H; C3-*H*), 3.79 (dd, J=6.9, 9.9 Hz, 0.5H; C*H*OTBDPS), 4.00 (m, 0.5H; one of THP ether OCH_2), 4.08 (ddd, J= 2.5, 7.1, 9.1 Hz, 0.5H; one of THP ether OCH_2), 4.23 (d, J=3.8 Hz, 0.5H; C4-*H*), 4.47 (d, J=2.7 Hz, 0.5H; C4-*H*), 4.74 (t, J=3.1 Hz, 0.5H; THP ether OC*H*O), 4.83 (t, J=2.5 Hz, 0.5H; THP ether OC*H*O), 7.36–7.43 (m, 6H; Ar*H*), 7.65–7.69 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=18.6, 18.8, 19.2, 25.2, 25.3, 26.8, 27.9, 28.1, 30.0, 30.1, 61.8, 62.1, 63.5, 64.3, 72.7, 72.8, 73.0, 77.1, 77.2, 81.5, 81.9, 96.5, 100.2, 127.6, 127.7, 129.7, 129.8, 133.06, 133.10, 133.2, 133.4, 135.5, 135.6, 170.2, 170.4; IR (film): $\tilde{\nu}$=3482, 3071, 1741, 1514, 1472, 1370, 1244, 1113 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{29}H_{43}O_6Si$: 515.2829, found: 515.2802 [M^+ +H]; elemental analysis calcd (%) for $C_{29}H_{42}O_6Si$ (514.7): C 67.54, H 8.40; found: C 67.74, H 8.26.

***tert*-Butyl (2*S*,3*R*)-4-(*tert*-butyldiphenylsilyl)oxy-3-[3-(methoxymethoxy)-propionyl]oxy-2-(tetrahydropyran-2-yl)oxybutanoate (55)**: EDCI (2.46 g, 12.8 mmol) was added to a solution of alcohol **54** (3.44 g, 6.69 mmol), 3-(methoxymethoxy)propionic acid (**16**, 1.08 g, 8.03 mmol) and DMAP (1.17 g, 12.05 mmol) in CH_2Cl_2 (60 mL) at 0 °C. After stirring at room temperature for 3 h, the reaction was quenched with 10% aqueous HCl (70 mL), and the mixture was extracted with AcOEt (100 mL). The organic extract was successively washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (4.6 g), which was purified by column chromatography (silica gel 60 g, *n*-hexane/AcOEt 10:1) to give **55** (3.42 g, 81%) as a colorless oil. $[\alpha]_D^{21}=-13.4$ (c=2.81 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H; $SiC(CH_3)_3$), 1.42 (s, 9H; $CO_2C(CH_3)_3$), 1.51 (m, 2H; two of THP ether OCH_2), 1.62 (m, 2H; two of THP ether OCH_2), 1.72 (m, 2H; two of THP ether OCH_2), 2.55–2.59 (m, 2H; C1′-H_2), 3.30 (s, 3H; OCH_3), 3.40–3.45 (m, 1H; one of THP ether OCH_2), 3.75 (dt, J=7.8, 5.0 Hz, 1H; one of THP ether OCH_2), 3.75–3.78 (m, 2.5H; C2′-H_2, C*H*OTBDPS), 3.82 (dd, J=5.8, 10.4 Hz, 0.5H; C*H*OTBDPS), 3.90 (dd, J=6.0, 10.7 Hz, 0.5H; C*H*OTBDPS), 3.98 (m, 0.5H; C2′-*H*), 4.31 (d, J=4.4 Hz, 0.5H; C4-*H*), 4.53 (d, J=3.2 Hz, 0.5H; C4-*H*), 4.55 (s, 1H; one of OCH_2O), 4.56 (s, 1H; one of OCH_2O), 4.72 (t, J=3.2 Hz, 0.5H; THP ether OC*H*O), 4.78 (t, J=2.5 Hz, 0.5H; THP ether OC*H*O), 5.34 (dt, J=4.4, 6.0 Hz, 0.5H; C3-*H*), 5.50 (ddd, J= 3.2, 5.8, 6.4 Hz, 0.5H; C3-*H*), 7.26–7.41 (m, 6H; Ar*H*), 7.66–7.69 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=18.6, 18.8, 19.1, 25.2, 25.3, 26.7, 27.8, 27.9, 30.0, 30.1, 34.8, 55.1, 61.2, 61.8, 62.1, 62.9, 71.8, 73.7, 73.8, 75.9, 77.2, 81.5, 82.0, 96.4, 100.4, 127.6, 127.66, 127.69, 129.66, 129.74, 132.96, 133.01, 133.1, 133.2, 135.5, 168.8, 169.0, 170.3, 170.4; IR (film): $\tilde{\nu}$=2935, 1748, 1471, 1429, 1392, 1370, 1282, 1256, 1113 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{34}H_{51}O_9Si$: 631.3302, found: 631.3307 [M^++H]; elemental analysis calcd (%) for $C_{34}H_{50}O_9Si$ (630.8): C 64.73, H 7.99; found: C 64.80, H 7.94.

***tert*-Butyl (2*S*,3*R*)-4-(*tert*-butyldiphenylsilyl)oxy-2-hydroxy-3-[3-(methoxymethoxy)propionyl]oxybutanoate (56)**: *p*-Toluenesulfonic acid monohydrate (94 mg, 0.49 mmol) was added to a stirred solution of THP ether **55** (6.20 g, 9.84 mmol) in MeOH (80 mL). After stirring for 40 min, H_2O (100 mL) was added, and the mixture was extracted with AcOEt (2× 300 mL). The combined organic extracts were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (5.50 g), which was purified by column chromatography (silica gel 100 g, *n*-hexane/AcOEt 6:1) to give alcohol **56** (4.88 g, 91%) as a colorless oil. $[\alpha]_D^{23}=-2.61$ ($c=2.22$ in benzene); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.05$ (s, 9H; SiC(CH_3)$_3$), 1.47 (s, 9H; $CO_2C(CH_3)_3$), 2.53 (t, $J=6.3$ Hz, 2H; C1′-H_2), 2.97 (d, $J=7.1$ Hz, 1H; O*H*), 3.29 (s, 3H; OCH_3), 3.73 (t, $J=6.3$ Hz, 2H; C2′-H_2), 3.79 (dd, $J=6.5$, 10.1 Hz, 1H; C*H*OTBDPS), 3.85 (dd, $J=7.4$, 10.1 Hz, 1H; C*H*OTBDPS), 4.38 (dd, $J=1.8$, 7.1 Hz, 1H; C4-*H*), 4.55 (s, 2H; OCH_2O), 5.39 (ddd, $J=1.8$, 6.5, 7.4 Hz, 1H; C3-*H*), 7.32–7.45 (m, 6H; Ar*H*), 7.65–7.70 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=19.1$, 26.7, 27.8, 34.8, 55.1, 61.5, 62.8, 69.5, 73.7, 83.1, 96.4, 127.7, 129.7, 133.0, 133.1, 135.5, 135.6, 170.0, 171.5; IR (film): $\tilde{\nu}=3499$, 3073, 2934, 2888, 2859, 1742, 1285, 1256, 1179, 1113, 1044 cm^{-1}; HR-MS (EI): *m*/*z*: calcd for $C_{25}H_{33}O_8Si$: 489.1945, found: 489.1952 [$M^+-C_4H_9$]; elemental analysis calcd (%) for $C_{29}H_{42}O_8Si$ (546.7): C 63.71, H 7.74; found: C 63.88, H 7.71.

***tert*-Butyl (*R*)-4-(*tert*-butyldiphenylsilyl)oxy-3-[3-(methoxymethoxy)propionyl]oxy-2-oxobutanoate (10)**: Dess–Martin periodinane (8.30 g, 19.5 mmol) was added to a stirred solution of alcohol **56** (8.90 g, 16.2 mmol) in CH_2Cl_2 (160 mL). After stirring for 2 h, the reaction mixture was poured into an ice-cooled saturated aqueous $NaHCO_3$ (100 mL) containing $Na_2S_2O_3\cdot H_2O$ (10 g), and the layers were separated. The organic layer was washed with brine (100 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (9.6 g), which was purified by column chromatography (silica gel 150 g, *n*-hexane/AcOEt 6:1) to give α-keto ester **10** (8.60 g, 97%) as a colorless oil. $[\alpha]_D^{23}=-6.57$ ($c=2.15$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=$ 1.01 (s, 9H; SiC(CH_3)$_3$), 1.54 (s, 9H; $CO_2C(CH_3)_3$), 2.68 (dt, $J=15.4$, 6.2 Hz, 1H; C1′-*H*), 2.72 (dt, $J=15.4$, 6.2 Hz, 1H; C1′-*H*), 3.34 (s, 3H; OCH_3), 3.80 (dt, $J=9.5$, 6.2 Hz, 1H; C2′-*H*), 3.85 (dt, $J=9.5$, 6.2 Hz, 1H; C2′-*H*), 3.98 (dd, $J=2.7$, 11.4 Hz, 1H; C*H*OTBDPS), 4.36 (dd, $J=4.5$, 11.4 Hz, 1H; C*H*OTBDPS), 4.62 (s, 2H; OCH_2O), 5.81 (dd, $J=2.7$, 4.5 Hz, 1H; C3-*H*), 7.37–7.45 (m, 6H; Ar*H*), 7.61–7.67 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=19.1$, 26.5, 27.7, 34.6, 55.1, 62.8, 63.1, 77.1, 84.5, 96.4, 127.6, 127.7, 129.8, 132.3, 132.7, 135.4, 135.5, 159.0, 170.4, 188.1; IR (film): $\tilde{\nu}=3482$, 3073, 3052, 2934, 2888, 1748, 1725, 1308, 1256, 1150, 1113, 1036 cm^{-1}; HR-MS (EI): *m*/*z*: calcd for $C_{25}H_{31}O_8Si$: 487.1788, found: 487.1759 [$M^+-C_4H_9$].

Di-*tert*-butyl [2*R*,2(1*R*)]-2-[2-(*tert*-butyldiphenylsilyl)oxy-1-[3-(methoxymethoxy)propionyl]oxyethyl]-3-diazo-2-hydroxybutanedioate (57): A 1.0 M solution of sodium bis(trimethylsilyl)amide in THF (0.6 mL, 0.604 mmol) was added to a stirred solution of α-keto ester **10** (300 mg, 0.549 mmol) and *tert*-butyl diazoacetate (**9**, 94 mg, 0.659 mmol) in CH_2Cl_2 (12 mL) at −93 °C. After stirring for 5 min, the reaction mixture was poured into saturated aqueous NH_4Cl (10 mL), and the mixture was extracted with AcOEt (20 mL). The organic extract was washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (402 mg), which was purified by flash column chromatography (silica gel 20 g, toluene/AcOEt 20:1) to give α-diazo ester **57** (245 mg, 65%) as a yellow oil, along with isomer **58** (30.5 mg, 8%) as a yellow oil.

Data for **57**: $[\alpha]_D^{27}=+33.7$ ($c=2.14$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.01$ (s, 9H; SiC(CH_3)$_3$), 1.35 (s, 9H; $CO_2C(CH_3)_3$), 1.44 (s, 9H; $CO_2C(CH_3)_3$), 2.65 (dt, $J=12.9$, 6.4 Hz, 1H; C1′-*H*), 2.69 (dt, $J=$ 12.9, 6.4 Hz, 1H; C1′-*H*), 3.34 (s, 3H; OCH_3), 3.80 (dt, $J=10.4$, 6.4 Hz, 1H; C2′-*H*), 3.82 (dd, $J=2.8$, 11.3 Hz, 1H; C*H*OTBDPS), 3.83 (dt, $J=$ 10.4, 6.4 Hz, 1H; C2′-*H*), 3.99 (dd, $J=7.7$, 11.3 Hz, 1H; C*H*OTBDPS), 4.61 (s, 2H; OCH_2O), 5.57 (dd, $J=2.8$, 7.7 Hz, 1H; C3-*H*), 7.36–7.44 (m, 6H; Ar*H*), 7.63–7.66 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=$ 19.0, 26.6, 27.5, 28.2, 35.0, 55.2, 62.7, 62.8, 74.3, 75.1, 82.5, 84.0, 96.5, 127.7, 129.8, 132.7, 135.5, 165.2, 169.3, 170.2; IR (film): $\tilde{\nu}=3461$, 3073, 3052, 2978, 2934, 2890, 2861, 2099, 1746, 1699, 1321, 1254, 1150, 1115, 1047 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{35}H_{50}N_2O_{10}SiNa$: 709.3132, found: 709.3149 [M^++Na].

Data for [2*S*,2(1*R*)]-isomer **58**: $[\alpha]_D^{27}=-30.2$ ($c=2.62$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.01$ (s, 9H; SiC(CH_3)$_3$), 1.43 (s, 9H; $CO_2C(CH_3)_3$), 1.44 (s, 9H; $CO_2C(CH_3)_3$), 2.36 (s, 1H; O*H*), 2.61 (t, $J=6.6$ Hz, 2H; C1′-H_2), 3.31 (s, 3H; OCH_3), 3.74 (dt, $J=11.9$, 6.6 Hz, 1H; C2′-*H*), 3.76 (dt, $J=11.9$, 6.6 Hz, 1H; C2′-*H*), 3.86 (dd, $J=7.5$, 11.1 Hz, 1H; C*H*OTBDPS), 3.95 (dd, $J=4.0$, 11.1 Hz, 1H; C*H*OTBDPS), 4.56 (s, 2H; OCH_2O), 5.80 (dd, $J=4.0$, 7.5 Hz, 1H; C3-*H*), 7.36–7.42 (m, 6H; Ar*H*), 7.63–7.67 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=19.1$, 26.6, 27.6, 28.2, 34.8, 55.2, 62.4, 62.7, 73.5, 73.7, 82.5, 83.9, 96.4, 127.7, 128.0, 129.8, 132.7, 132.8, 135.5, 135.6, 164.5, 169.6, 169.7; IR (film): $\tilde{\nu}=3461$, 3073, 3052, 2934, 2890, 2859, 2101, 1748, 1699, 1318, 1256, 1148, 1113, 1046 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{35}H_{50}N_2O_{10}SiNa$: 709.3132, found: 709.3124 [M^++Na].

Di-*tert*-butyl [2*R*,2(1*R*)]-2-[2-(*tert*-butyldiphenylsilyl)oxy-1-[3-(methoxymethoxy)propionyl]oxyethyl]-3-diazo-2-(trimethylsilyl)oxybutanedioate (8): HMDS (3.4 mL, 16.0 mmol) was added to a stirred solution of α-diazo ester **57** (3.66 g, 5.33 mmol) and imidazole (545 mg, 8.00 mmol) in THF (40 mL). After stirring for 48 h, the volatile elements were removed in vacuo. Purification of the residue (4.3 g) by column chromatography (silica gel 40 g, *n*-hexane/AcOEt 10:1) afforded TMS ether **8** (3.78 g, 94%) as a yellow oil. $[\alpha]_D^{26}=+9.53$ ($c=2.04$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.10$ (s, 9H; Si(CH_3)$_3$), 1.00 (s, 9H; SiC(CH_3)$_3$), 1.30 (s, 9H; $CO_2C(CH_3)_3$), 1.47 (s, 9H; $CO_2C(CH_3)_3$), 2.61 (dt, $J=13.9$, 6.8 Hz, 1H; C1′-*H*), 2.65 (dt, $J=13.9$, 6.8 Hz, 1H; C1′-*H*), 3.35 (s, 3H; OCH_3), 3.79 (dt, $J=10.0$, 6.8 Hz, 1H; C2′-*H*), 3.81–3.84 (m, 2H; CH_2OTBDPS), 3.82 (dt, $J=10.0$, 6.8 Hz, 1H; C2′-*H*), 4.60 (s, 2H; OCH_2O), 5.79 (dd, $J=3.8$, 7.3 Hz, 1H; C3-*H*), 7.35–7.41 (m, 6H; Ar*H*), 7.62–7.66 (m, 4H; Ar*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=1.4$, 19.1, 26.7, 27.6, 28.3, 35.1, 55.2, 62.80, 62.84, 77.2, 77.8, 82.1, 83.1, 96.4, 127.57, 127.64, 129.5, 129.6, 133.0, 133.1, 135.4, 135.5, 163.5, 167.0, 169.8; IR (film): $\tilde{\nu}=2934$, 2890, 2859, 2097, 1755, 1701, 1370, 1318, 1252, 1148, 1115, 1040 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{38}H_{58}N_2O_{10}Si_2Na$: 781.3528, found: 781.3518 [M^++Na].

Typical procedure for tandem carbonyl ylide formation/1,3-dipolar cycloaddition reaction of α-diazo *tert*-butyl ester 8: **di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*)-7-acetyl-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]oct-6-ene-4,5-dicarboxylate (59)**: A solution of α-diazo ester **8** (1.55 g, 2.04 mmol) in benzene (12 mL) was added dropwise over 15 min to a refluxing solution of 3-butyn-2-one (**40**, 0.48 mL, 6.13 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (42 mg, 5 mol%) in benzene (8 mL), and the mixture was stirred for 25 min. After cooling, the volatile elements were removed in vacuo, and the greenish residue (1.70 g) was purified by column chromatography (silica gel 40 g, *n*-hexane/AcOEt 10:1) to give cycloadduct **59** (1.18 g, 72%) as a colorless oil, along with alcohol **60** (214 mg, 14%, dr 10:1), pyrazole **61** (101 mg, 6%, dr 9:1) and epoxide **62** (81 mg, 6%, dr 4.2:1) as colorless oils. $[\alpha]_D^{20}=-20.8$ ($c=1.92$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=-0.05$ (s, 9H; Si(CH_3)$_3$), 1.02 (s, 9H; SiC(CH_3)$_3$), 1.44 (s, 9H; $CO_2C(CH_3)_3$), 1.46 (s, 9H; $CO_2C(CH_3)_3$), 2.34 (dt, $J=14.9$, 4.5 Hz, 1H; C1′-*H*), 2.37 (s, 3H; $COCH_3$), 2.64 (ddd, $J=6.9$, 8.9, 14.9 Hz, 1H; C1′-*H*), 3.30 (s, 3H; OCH_3), 3.50 (dd, $J=1.9$, 11.5 Hz, 1H; C*H*OTBDPS), 3.64–3.74 (m, 3H; C2′-H_2, C*H*OTBDPS), 4.21 (dd, $J=1.9$, 8.0 Hz, 1H; C3-*H*), 4.51 (d, $J=6.4$ Hz, 1H; one of OCH_2O), 4.54 (d, $J=6.4$ Hz, 1H; one of OCH_2O), 7.15 (s, 1H; C6-*H*), 7.34–7.40 (m, 6H; Ar*H*), 7.60–7.70 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=$ 2.5, 19.2, 26.7, 27.7, 27.9, 28.1, 28.2, 33.8, 55.1, 62.7, 64.3, 78.7, 79.7, 82.9, 83.3, 89.7, 96.3, 108.7, 127.5, 127.6, 129.5, 133.2, 133.9, 135.5, 135.8, 141.5, 142.8, 165.3, 169.1, 194.1; IR (film): $\tilde{\nu}=2934$, 2890, 2861, 1742, 1688, 1248, 1155, 1113, 1047, 1020 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{42}H_{62}O_{11}Si_2Na$: 821.3728, found: 821.3732 [M^++Na]; elemental analysis calcd (%) for $C_{42}H_{62}O_{11}Si_2$ (799.1): C 63.13, H 7.82; found: C 62.84, H 7.79.

Data for **60**: $[\alpha]_D^{22}=+4.28$ ($c=1.21$ in benzene); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.09$ (s, 9H; Si(CH_3)$_3$), 1.01 (s, 9H; SiC(CH_3)$_3$), 1.38 (s, 9H; $CO_2C(CH_3)_3$), 1.44 (s, 9H; $CO_2C(CH_3)_3$), 2.66 (dt, $J=10.0$, 6.8 Hz, 1H;

C1′-*H*), 2.67 (dt, *J* = 10.0, 6.8 Hz, 1H; C1′-*H*), 3.06 (d, *J* = 8.8 Hz, 1H; O*H*), 3.34 (s, 3H; OCH_3), 3.81 (dt, *J* = 9.9, 6.8 Hz, 1H; C2′-*H*), 3.86 (dt, *J* = 9.9, 6.8 Hz, 1H; C2′-*H*), 3.92 (dd, *J* = 2.3, 10.8 Hz, 0.1H; C*H*OTBDPS), 3.93 (dd, *J* = 2.6, 10.8 Hz, 0.9H; C*H*OTBDPS), 3.99 (dd, *J* = 5.3, 10.8 Hz, 0.1H; C*H*OTBDPS), 4.00 (dd, *J* = 9.1, 10.8 Hz, 0.9H; C*H*OTBDPS), 4.26 (d, *J* = 8.8 Hz, 1H; C5-*H*), 4.58 (s, 1.8H; OCH_2O), 4.60 (s, 0.2H; OCH_2O), 5.63 (dd, *J* = 2.3, 5.3 Hz, 0.1H; C3-*H*), 5.63 (dd, *J* = 2.6, 9.1 Hz, 0.9H; C3-*H*), 7.35–7.41 (m, 6H; Ar*H*), 7.64–7.68 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 2.4, 19.3, 26.7, 28.0, 28.1, 34.8, 35.4, 37.0, 55.4, 62.7, 64.5, 77.3, 77.6, 83.3, 83.5, 87.2, 96.9, 105.2, 117.7, 127.6, 127.7, 129.6, 133.2, 133.7, 135.6, 135.8, 166.7, 168.7; IR (film): $\tilde{\nu}$ = 3493, 2934, 2893, 2859, 1734, 1698, 1460, 1427, 1393, 1370, 1354, 1254, 1177, 1113, 1040, 947 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{38}H_{60}O_{11}Si_2Na$: 771.3572, found: 771.3572 [M^++Na].

Data for **61**: $[\alpha]_D^{22}$ = +20.5 (*c* = 1.21 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.08 (s, 0.9H; Si(CH_3)$_3$), 0.01 (s, 8.1H; Si(CH_3)$_3$), 1.01 (s, 8.1H; SiC(CH_3)$_3$), 1.04 (s, 0.9H; SiC(CH_3)$_3$), 1.31 (s, 8.1H; CO_2C(CH_3)$_3$), 1.32 (s, 0.9H; CO_2C(CH_3)$_3$), 1.50 (s, 0.9H; CO_2C(CH_3)$_3$), 1.52 (s, 8.1H; CO_2C(CH_3)$_3$), 2.49 (s, 3H; COCH_3), 2.56 (dt, *J* = 9.7, 6.8 Hz, 1H; C1′-*H*), 2.57 (dt, *J* = 9.7, 6.8 Hz, 1H; C1′-*H*), 3.29 (s, 0.3H; OCH_3), 3.32 (s, 2.7H; OCH_3), 3.76 (dt, *J* = 8.8, 6.8 Hz, 0.9H; C2′-*H*), 3.77 (m, 0.2H; C2′-H_2), 3.78 (dt, *J* = 8.8, 6.8 Hz, 0.9H; C2′-*H*), 3.84 (dd, *J* = 9.0, 11.1 Hz, 0.9H; C*H*OTBDPS), 3.89 (dd, *J* = 8.9, 11.2 Hz, 0.1H; C*H*OTBDPS), 4.06 (dd, *J* = 1.8, 11.1 Hz, 0.9H; C*H*OTBDPS), 4.18 (dd, *J* = 2.4, 11.2 Hz, 0.1H; C*H*OTBDPS), 4.49 (s, 0.2H; OCH_2O), 4.56 (s, 1.8H; OCH_2O), 6.40 (dd, *J* = 1.8, 9.0 Hz, 0.9H; C3-*H*), 6.56 (dd, *J* = 2.4, 8.9 Hz, 0.1H; C3-*H*), 7.24 (s, 0.9H; =C*H*), 7.26 (s, 0.1H; =C*H*), 7.34–7.40 (m, 6H; Ar*H*), 7.62–7.65 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 1.3, 19.1, 26.4, 26.6, 27.6, 28.1, 35.0, 35.2, 55.1, 62.8, 63.2, 76.0, 82.5, 82.7, 83.2, 83.7, 91.7, 96.4, 112.7, 127.6, 127.7, 129.59, 129.64, 133.2, 133.3, 135.56, 135.62, 136.6, 148.4, 157.6, 165.1, 169.6, 193.6; IR (film): $\tilde{\nu}$ = 2934, 2893, 2859, 1734, 1698, 1460, 1427, 1393, 1370, 1354, 1254, 1177, 1113, 1040, 947 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{42}H_{62}N_2O_{11}Si_2Na$: 849.3790, found: 849.3767 [M^++Na].

Data for **62**: $[\alpha]_D^{22}$ = +15.8 (*c* = 0.53 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 7.2H; SiC(CH_3)$_3$), 1.04 (s, 1.8H; SiC(CH_3)$_3$), 1.45 (s, 14.4H; 2 × CO_2C(CH_3)$_3$), 1.46 (s, 3.6H; 2 × CO_2C(CH_3)$_3$), 2.65 (m, 0.4H; C1′-H_2), 2.66 (dt, *J* = 9.6, 6.6 Hz, 0.8H; C1′-*H*), 2.68 (dt, *J* = 9.6, 6.6 Hz, 0.8H; C1′-*H*), 3.33 (s, 0.6H; OCH_3), 3.34 (s, 2.4H; OCH_3), 3.81 (m, 1.6H; C2′-H_2), 3.82 (m, 0.4H; C2′-H_2), 3.97 (dd, *J* = 7.4, 11.2 Hz, 0.2H; C*H*OTBDPS), 3.98 (dd, *J* = 3.1, 11.4 Hz, 0.8H; C*H*OTBDPS), 4.06 (dd, *J* = 5.4, 11.4 Hz, 0.8H; C*H*OTBDPS), 4.14 (dd, *J* = 4.2, 11.2 Hz, 0.2H; C*H*OTBDPS), 4.59 (s, 0.4H; OCH_2O), 4.60 (s, 1.6H; OCH_2O), 4.62 (s, 0.8H; C5-*H*), 4.63 (s, 0.2H; C5-*H*), 5.58 (dd, *J* = 3.1, 5.4 Hz, 0.8H; C3-*H*), 5.83 (dd, *J* = 4.2, 7.4 Hz, 0.2H; C3-*H*), 7.26–7.43 (m, 6H; Ar*H*), 7.61–7.65 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 19.2, 19.3, 26.6, 26.65, 26.68, 27.8, 27.9, 28.0, 28.1, 29.7, 34.8, 34.9, 44.4, 55.3, 62.6, 63.0, 63.1, 63.3, 63.6, 63.8, 65.0, 72.8, 78.5, 81.5, 81.6, 83.2, 83.3, 83.4, 96.4, 104.0, 127.67, 127.68, 127.76, 127.79, 129.67, 129.72, 129.85, 129.89, 132.7, 132.8, 133.1, 133.3, 135.55, 135.59, 135.63, 163.2, 163.4, 164.1, 166.2, 169.9, 170.4, 170.5, 172.4, 196.6; IR (film): $\tilde{\nu}$ = 2934, 2888, 2859, 1730, 1657, 1474, 1429, 1393, 1370, 1308, 1256, 1150, 1113, 1042, 999, 920 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{35}H_{50}O_{10}SiNa$: 681.3071, found: 681.3071 [M^++Na].

4,5-Di-*tert*-butyl 7-methyl (1*S*,3*R*,4*S*,5*R*)-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]oct-6-ene-4,5,7-tricarboxylate (63): A solution of α-diazo ester **8** (50 mg, 0.066 mmol) in benzene (0.6 mL) was added dropwise over 15 min to a refluxing solution of methyl propiolate (**41**, 17 mg, 0.198 mmol) and bis(methanol) adduct of $[Rh_2(OAc)_4]$ (1.5 mg, 5 mol%) in benzene (0.8 mL), and the mixture was stirred for 25 min. After cooling, the volatile elements were removed in vacuo, and the greenish residue was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 10:1) to give cycloadduct **63** (42 mg, 78%) as a colorless oil, along with alcohol **60** (4.4 mg, 9%) as a colorless oil. $[\alpha]_D^{24}$ = −28.3 (*c* = 2.20 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.05 (s, 9H; Si(CH_3)$_3$), 1.02 (s, 9H; SiC(CH_3)$_3$), 1.44 (s, 9H; CO_2C(CH_3)$_3$), 1.45 (s, 9H; CO_2C-(CH_3)$_3$), 2.35 (dt, *J* = 14.3, 5.0 Hz, 1H; C1′-*H*), 2.64 (ddd, *J* = 7.1, 8.6, 14.3 Hz, 1H; C1′-*H*), 3.31 (s, 3H; OCH_3), 3.33 (dd, *J* = 8.1, 11.5 Hz, 1H; C*H*OTBDPS), 3.52 (dd, *J* = 1.7, 11.5 Hz, 1H; C*H*OTBDPS), 3.67–3.80 (m, 2H; C2′-H_2), 3.82 (s, 3H; CO_2CH_3), 4.28 (dd, *J* = 1.7, 8.1 Hz, 1H; C3-*H*), 4.54 (d, *J* = 6.5 Hz, 1H; one of OCH_2O), 4.55 (d, *J* = 6.5 Hz, 1H; one of OCH_2O), 7.32 (s, 1H; C6-*H*), 7.34–7.39 (m, 6H; Ar*H*), 7.61–7.71 (m, 4H; Ar*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 2.6, 19.4, 26.7, 27.8, 27.9, 28.0, 28.1, 33.8, 51.8, 55.2, 62.8, 64.3, 78.7, 79.6, 82.9, 83.3, 89.8, 96.4, 108.4, 127.4, 127.5, 127.7, 129.4, 133.2, 134.0, 134.3, 135.4, 135.5, 135.6, 135.8, 144.4, 162.9, 165.1, 168.9; IR (film): $\tilde{\nu}$ = 2934, 2890, 2859, 1732, 1631, 1589, 1429, 1392, 1370, 1252, 1150 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{42}H_{62}O_{12}Si_2Na$: 837.3678, found: 837.3660 [M^++Na].

Di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*R*)-7-acetyl-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-6,7-dihydroxy-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)-oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (64): A 4% solution of OsO_4 in *tert*-butyl alcohol (0.6 mL, 0.074 mmol) was added to a stirred solution of enone **59** (510 mg, 0.639 mmol) and NMO (50% in H_2O, 0.4 mL, 1.20 mmol) in acetone (4.4 mL)/H_2O (0.6 mL) at 0 °C. After stirring at room temperature for 3 h, the reaction was quenched by addition of 10% aqueous $Na_2S_2O_3$ (5 mL), and the mixture was extracted with AcOEt (15 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (600 mg), which was purified by column chromatography (silica gel 20 g, *n*-hexane/AcOEt 4:1) to give diol **64** (467 mg, 88%) as a colorless amorphous. $[\alpha]_D^{21}$ = +9.49 (*c* = 2.11 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.10 (s, 9H; Si(CH_3)$_3$), 1.02 (s, 9H; SiC(CH_3)$_3$), 1.46 (s, 9H; CO_2C(CH_3)$_3$), 1.50 (s, 9H; CO_2C(CH_3)$_3$), 2.24 (ddd, *J* = 6.0, 7.5, 13.9 Hz, 1H; C1′-*H*), 2.45 (s, 3H; COCH_3), 2.54 (dt, *J* = 13.9, 7.5 Hz, 1H; C1′-*H*), 3.19 (d, *J* = 7.5 Hz, 1H; C6-O*H*), 3.38 (s, 3H; OCH_3), 3.39 (dd, *J* = 1.1, 11.2 Hz, 1H; C*H*OTBDPS), 3.54 (dd, *J* = 7.9, 11.2 Hz, 1H; C*H*OTBDPS), 3.82 (ddd, *J* = 6.0, 7.5, 13.9 Hz, 1H; C2′-*H*), 3.87 (dt, *J* = 13.9, 7.5 Hz, 1H; C2′-*H*), 4.43 (dd, *J* = 1.1, 7.9 Hz, 1H; C3-*H*), 4.63 (d, *J* = 6.4 Hz, 1H; one of OCH_2O), 4.67 (d, *J* = 6.4 Hz, 1H; one of OCH_2O), 4.91 (br s, 1H; C7-O*H*), 5.74 (d, *J* = 7.5 Hz, 1H; C6-*H*), 7.35–7.40 (m, 6H; Ar*H*), 7.59–7.66 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 2.4, 19.2, 25.9, 26.6, 28.0, 28.3, 33.4, 55.3, 63.3, 64.9, 73.6, 77.5, 77.7, 83.4, 83.5, 86.8, 90.9, 96.6, 106.9, 127.6, 127.7, 129.6, 133.1, 133.4, 135.4, 135.6, 165.5, 169.0, 204.1; IR (Nujol): $\tilde{\nu}$ = 3347, 2728, 2361, 1742, 1462, 1377, 1306, 1250, 1206, 1155, 1038 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{42}H_{64}O_{13}Si_2Na$: 855.3783, found: 855.3777 [M^++Na].

Di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*R*)-7-acetyl-6-benzyloxy-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-7-hydroxy-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (65): Benzyl bromide (1.0 mL, 7.98 mmol) was added to a stirred solution of diol **64** (1.11 g, 1.33 mmol) and Ag_2O (618 mg, 2.67 mmol) in DMF (13 mL). After stirring for 24 h in the dark, the reaction was quenched by addition of H_2O (30 mL), and the resulting mixture was stirred for another 24 h. The whole mixture was extracted with AcOEt (3 × 40 mL), and 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 (3.5 g), which was purified by column chromatography (silica gel 40 g, *n*-hexane/AcOEt 15:1) to give benzyl ether **65** (1.17 g, 95%) as a colorless oil. $[\alpha]_D$ = +16.4 (*c* = 2.04 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.11 (s, 9H; Si(CH_3)$_3$), 1.02 (s, 9H; SiC(CH_3)$_3$), 1.35 (s, 9H; CO_2C(CH_3)$_3$), 1.55 (s, 9H; CO_2C(CH_3)$_3$), 2.20 (ddd, *J* = 5.6, 10.5, 13.7 Hz, 1H; C1′-*H*), 2.36 (s, 3H; COCH_3), 2.63 (ddd, *J* = 6.2, 10.2, 13.7 Hz, 1H; C1′-*H*), 3.34 (dd, *J* = 1.7, 11.1 Hz, 1H; C*H*OTBDPS), 3.37 (s, 3H; OCH_3), 3.49 (dd, *J* = 7.5, 11.1 Hz, 1H; C*H*OTBDPS), 3.84 (m, 2H; C2′-H_2), 3.95 (s, 1H; O*H*), 4.38 (dd, *J* = 1.7, 7.5 Hz, 1H; C3-*H*), 4.46 (d, *J* = 10.9 Hz, 1H; OC*H*Ph), 4.63 (d, *J* = 10.9 Hz, 1H; OC*H*Ph), 4.64 (d, *J* = 6.4 Hz, 1H; one of OCH_2O), 4.67 (d, *J* = 6.4 Hz, 1H; one of OCH_2O), 5.80 (s, 1H; C6-*H*), 7.24–7.42 (m, 9H; Ar*H*), 7.59–7.66 (m, 6H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 3.0, 19.3, 25.9, 26.7, 27.5, 28.1, 28.3, 33.1, 55.2, 63.8, 65.0, 75.4, 77.3, 77.9, 81.8, 82.9, 83.4, 86.8, 89.8, 96.8, 107.1, 127.6, 127.7, 128.0, 128.41, 128.44, 128.5, 128.6, 129.7, 133.2, 133.6, 135.5, 135.6, 136.2, 165.2, 168.9, 204.4; IR (film): $\tilde{\nu}$ = 3447, 2934, 2890, 2859, 1744, 1728, 1250, 1202, 1152, 1113, 1071, 1042 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{49}H_{70}O_{13}Si_2Na$: 945.4253, found: 945.4285 [M^++Na]; elemental analysis calcd (%) for $C_{49}H_{70}O_{13}Si_2$ (923.2): C 63.75, H 7.64; found: C 63.62, H 7.74.

4,5-Di-*tert*-butyl 7-methyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*S*)-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-6,7-dihydroxy-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5,7-tricarboxylate (66): A 4% solution of OsO_4 in *tert*-butyl alcohol (0.02 mL, 2.5 μmol) was added to a stirred solution of enoate **63** (42 mg, 0.052 mmol) and NMO (50% in H_2O, 0.03 mL, 0.092 mmol) in acetone (1 mL)/H_2O (0.1 mL) at 0 °C. After stirring at room temperature for 3 h, the reaction was quenched by addition of 10% aqueous $Na_2S_2O_3$ (5 mL), and the mixture was extracted with AcOEt (15 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (51 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 4:1) to give diol **66** (37.1 mg, 84%) as a colorless amorphous. $[\alpha]_D^{21}=+7.57$ ($c=1.16$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=-0.11$ (s, 9H; Si(CH_3)$_3$), 1.03 (s, 9H; SiC(CH_3)$_3$), 1.46 (s, 9H; $CO_2C(CH_3)_3$), 1.52 (s, 9H; $CO_2C(CH_3)_3$), 2.25 (dt, $J=14.7$, 6.2 Hz, 1H; C1′-*H*), 2.53 (dt, $J=14.7$, 7.3 Hz, 1H; C1′-*H*), 3.34 (d, $J=7.7$ Hz, 1H; C6-O*H*), 3.37 (s, 3H; OCH_3), 3.44 (dd, $J=1.2$, 11.4 Hz, 1H; C*H*OTBDPS), 3.53 (dd, $J=7.7$, 11.4 Hz, 1H; C*H*OTBDPS), 3.77 (ddd, $J=6.2$, 7.3, 10.2 Hz, 1H; C2′-*H*), 3.82 (s, 3H; CO_2CH_3), 3.84 (ddd, $J=6.2$, 7.3, 10.2 Hz, 1H; C2′-*H*), 4.63 (d, $J=6.6$ Hz, 1H; one of OCH_2O), 4.67 (d, $J=6.6$ Hz, 1H; one of OCH_2O), 4.68 (dd, $J=1.2$, 7.7 Hz, 1H; C3-*H*), 5.07 (s, 1H; C7-O*H*), 5.80 (d, $J=7.7$ Hz, 1H; C6-*H*), 7.35–7.39 (m, 6H; Ar*H*), 7.61–7.67 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=2.4$, 19.3, 26.7, 28.0, 28.3, 33.3, 53.2, 55.5, 62.9, 65.4, 75.0, 77.2, 77.7, 77.9, 82.6, 83.2, 91.3, 96.6, 107.3, 127.6, 127.7, 129.7, 133.2, 133.5, 135.4, 135.6, 165.2, 169.1, 170.7; IR (film): $\tilde{\nu}=3389$, 3052, 2978, 2934, 2860, 1740, 1474, 1458, 1429, 1393, 1370, 1325, 1248, 1154, 1073, 1038, 999 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{42}H_{64}O_{14}Si_2Na$: 871.3732, found: 871.3739 [M^++Na].

4,5-Di-*tert*-butyl 7-methyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*S*)-6-benzyloxy-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-7-hydroxy-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5,7-tricarboxylate (67): Benzyl bromide (18 mg, 0.108 mmol) was added to a stirred solution of diol **66** (23 mg, 0.027 mmol) and Ag_2O (13 mg, 0.054 mmol) in DMF (0.5 mL). After stirring for 24 h in the dark, the reaction was quenched by addition of H_2O (5 mL), and the resulting mixture was stirred for 4 h. The whole mixture was extracted with AcOEt (15 mL), and the organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (46 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 10:1 → 4:1) to give benzyl ether **67** (15.9 mg, 63%) as a colorless oil, along with isomer **68** (3.2 mg, 14%) as a colorless oil.

Data for **67**: $[\alpha]_D^{21}=+16.9$ ($c=0.63$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=-0.13$ (s, 9H; SiC(CH_3)$_3$), 1.03 (s, 9H; Si(CH_3)$_3$), 1.34 (s, 9H; $CO_2C(CH_3)_3$), 1.55 (s, 9H; $CO_2C(CH_3)_3$), 2.42 (dt, $J=14.1$, 7.9 Hz, 1H; C1′-*H*), 2.51 (dt, $J=14.1$, 7.9 Hz, 1H; C1′-*H*), 3.36 (s, 3H; OCH_3), 3.37 (dd, $J=1.0$, 11.2 Hz, 1H; C*H*OTBDPS), 3.49 (dd, $J=7.7$, 11.2 Hz, 1H; C*H*OTBDPS), 3.78 (s, 3H; CO_2CH_3), 3.83 (t, $J=7.9$ Hz, 2H; C2′-H_2), 4.08 (s, 1H; C7-O*H*), 4.49 (dd, $J=1.0$, 7.7 Hz, 1H; C3-*H*), 4.60 (d, $J=10.9$ Hz, 1H; OC*H*Ph), 4.63 (d, $J=6.5$ Hz, 1H; one of OCH_2O), 4.66 (d, $J=6.5$ Hz, 1H; one of OCH_2O), 4.69 (d, $J=10.9$ Hz, 1H; OC*H*Ph), 5.88 (s, 1H; C6-*H*), 7.31–7.40 (m, 11H; Ar*H*), 7.60–7.66 (m, 4H; Ar*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=2.6$, 19.4, 26.7, 28.2, 28.3, 32.3, 52.9, 55.2, 63.7, 65.2, 75.6, 77.6, 77.8, 83.1, 83.4, 90.0, 96.6, 107.6, 127.5, 127.6, 128.4, 128.5, 129.6, 133.0, 133.5, 135.3, 135.6, 136.0, 168.9, 170.1; IR (film): $\tilde{\nu}=3455$, 2978, 2934, 2860, 1740, 1589, 1474, 1456, 1429, 1393, 1370, 1323, 1248, 1209, 1152, 1074, 1037, 999 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{49}H_{71}O_{14}Si_2$: 939.4382, found: 939.4409 [M^++H].

Data for **68**: $[\alpha]_D^{21}=+3.88$ ($c=0.22$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=-0.14$ (s, 9H; Si(CH_3)$_3$), 1.04 (s, 9H; SiC(CH_3)$_3$), 1.41 (s, 9H; $CO_2C(CH_3)_3$), 1.56 (s, 9H; $CO_2C(CH_3)_3$), 2.54 (t, $J=6.9$ Hz, 2H; C1′-H_2), 2.55 (d, $J=12.4$ Hz, 1H; C6-O*H*), 3.36 (s, 3H; OCH_3), 3.37 (dd, $J=1.0$, 11.4 Hz, 1H; C*H*OTBDPS), 3.48 (dd, $J=7.6$, 11.4 Hz, 1H; C*H*OTBDPS), 3.76 (s, 3H; CO_2CH_3), 3.84 (dt, $J=9.6$, 6.9 Hz, 1H; C2′-*H*), 3.85 (dt, $J=9.6$, 6.9 Hz, 1H; C2′-*H*), 4.37 (dd, $J=1.0$, 7.6 Hz, 1H; C3-*H*), 4.57 (d, $J=10.8$ Hz, 1H; OC*H*Ph), 4.62 (d, $J=10.8$ Hz, 1H; OC*H*Ph), 4.63 (d, $J=6.4$ Hz, 1H; one of OCH_2O), 4.66 (d, $J=6.4$ Hz, 1H; one of OCH_2O), 5.91 (d, $J=12.4$ Hz, 1H; C6-*H*), 7.35–7.41 (m, 11H; Ar*H*), 7.61–7.68 (m, 4H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta=2.4$, 19.3, 26.3, 26.7, 28.1, 28.3, 29.7, 32.8, 52.7, 55.2, 63.9, 65.3, 70.7, 75.3, 83.4, 83.5, 90.5, 92.0, 96.8, 107.6, 127.3, 127.6, 127.7, 128.0, 128.5, 129.65, 129.69, 133.1, 133.5, 135.4, 135.6, 137.0, 165.1, 168.3, 168.9; IR (film): $\tilde{\nu}=3544$, 2932, 1740, 1589, 1456, 1393, 1370, 1113, 920, 887 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{49}H_{71}O_{14}Si_2$: 939.4382, found: 939.4390 [M^++H].

Di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*S*)-6-benzyloxy-3-[(*tert*-butyldiphenylsilyl)-oxymethyl]-7-hydroxy-7-(1-hydroxyethyl)-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (69): DIBALH in toluene (1.0 M, 2.64 mL, 2.64 mmol) was added to a stirred solution of ketone **65** (973 mg, 1.06 mmol) in toluene (13 mL) at −78 °C. After stirring for 30 min, the reaction was quenched by addition of MeOH (2 mL) followed by 15% aqueous potassium sodium tartrate (10 mL). After stirring at room temperature for 10 h, the mixture was extracted with AcOEt (30 mL). The organic extract was washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.5 g), which was purified by column chromatography (silica gel 30 g, *n*-hexane/AcOEt 7:1) to give diol **69** (972 mg, quant.) as a colorless oil. $[\alpha]_D^{20}=+6.89$ ($c=2.61$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=-0.09$ (s, 9H; Si(CH_3)$_3$), 1.05 (s, 9H; SiC(CH_3)$_3$), 1.32 (s, 9H; $CO_2C(CH_3)_3$), 1.33 (d, $J=6.4$ Hz, 3H; CH(OH)CH_3), 1.53 (s, 9H; $CO_2C(CH_3)_3$), 2.38 (d, $J=7.2$ Hz, 1H; CHO*H*), 2.43 (dt, $J=14.7$, 7.6 Hz, 1H; C1′-*H*), 2.47 (dt, $J=14.7$, 7.6 Hz, 1H; C1′-*H*), 3.36 (s, 3H; OCH_3), 3.42 (dd, $J=0.5$, 11.1 Hz, 1H; C*H*OTBDPS), 3.59 (dd, $J=7.7$, 11.1 Hz, 1H; C*H*OTBDPS), 3.81 (s, 1H; C7-O*H*), 3.84 (t, $J=7.6$ Hz, 2H; C2′-H_2), 4.14 (dq, $J=7.2$, 6.4 Hz, 1H; C*H*(OH)CH$_3$), 4.25 (dd, $J=0.5$, 7.7 Hz, 1H; C3-*H*), 4.60 (d, $J=10.5$ Hz, 1H; OC*H*Ph), 4.62 (d, $J=6.4$ Hz, 1H; one of OCH_2O), 4.65 (d, $J=6.4$ Hz, 1H; one of OCH_2O), 4.77 (d, $J=10.5$ Hz, 1H; OC*H*Ph), 5.05 (s, 1H; C6-*H*), 7.29–7.41 (m, 11H; Ar*H*), 7.63–7.71 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=2.5$, 19.2, 19.4, 26.7, 28.1, 28.2, 33.3, 55.1, 64.0, 65.2, 68.2, 75.6, 77.2, 77.9, 82.4, 82.7, 83.3, 90.2, 96.5, 108.3, 127.7, 128.1, 128.2, 128.4, 129.6, 129.7, 132.9, 133.6, 135.4, 135.7, 136.6, 166.1, 169.8; IR ($CHCl_3$): $\tilde{\nu}=3490$, 3073, 3017, 2982, 2957, 1746, 1725, 1589, 1427, 1393, 1370, 1325, 1252, 1144, 1111, 1069, 997 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{49}H_{72}O_{13}Si_2Na$: 947.4409, found: 947.4460 [M^++Na].

Di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*,6*S*)-6-benzyloxy-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-7-oxo-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (70): [Pb(OAc)$_4$] (529 mg, 1.19 mmol) was added to a stirred solution of diol **69** (920 mg, 0.995 mmol) in benzene (15 mL). After stirring for 30 min, the reaction was quenched by addition of ethylene glycol (1 mL) and 10% aqueous $Na_2S_2O_3$ (10 mL), and the mixture was extracted with AcOEt (15 mL). 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 (1.20 g), which was purified by column chromatography (silica gel 30 g, *n*-hexane/AcOEt 15:1) to give ketone **70** (822 mg, 94%) as a colorless oil. $[\alpha]_D^{22}=-69.4$ ($c=2.45$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=-0.09$ (s, 9H; Si(CH_3)$_3$), 1.01 (s, 9H; SiC(CH_3)$_3$), 1.28 (s, 9H; $CO_2C(CH_3)_3$), 1.42 (s, 9H; $CO_2C(CH_3)_3$), 2.19 (ddd, $J=4.9$, 7.8, 14.4 Hz, 1H; C1′-*H*), 2.29 (dt, $J=14.4$, 7.8 Hz, 1H; C1′-*H*), 3.33 (s, 3H; OCH_3), 3.37 (dd, $J=0.9$, 11.6 Hz, 1H; C*H*OTBDPS), 3.57 (dd, $J=7.6$, 11.6 Hz, 1H; C*H*OTBDPS), 3.75 (dt, $J=13.8$, 7.8 Hz, 1H; C2′-*H*), 3.76 (ddd, $J=4.9$, 7.8, 13.8 Hz, 1H; C2′-*H*), 4.09 (dd, $J=0.9$, 7.6 Hz, 1H; C3-*H*), 4.51 (br s, 1H; C6-*H*), 4.56 (d, $J=6.5$ Hz, 1H; one of OCH_2O), 4.61 (d, $J=6.5$ Hz, 1H; one of OCH_2O), 4.73 (d, $J=12.3$ Hz, 1H; OC*H*Ph), 4.84 (d, $J=12.3$ Hz, 1H; OC*H*Ph), 7.34–7.41 (m, 11H; Ar*H*), 7.57–7.64 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta=2.5$, 19.2, 26.7, 27.7, 28.2, 32.0, 55.1, 62.2, 64.9, 72.0, 74.5, 77.2, 78.0, 79.4, 83.4, 83.5, 88.4, 96.7, 100.5, 127.6, 127.7, 128.1, 128.4, 128.6, 129.6, 132.8, 133.4, 135.4, 135.7, 136.5, 168.0, 208.5; IR (film): $\tilde{\nu}=3071$, 2934, 2890, 2861, 1771, 1746, 1730, 1250, 1211, 1154, 1113 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{47}H_{66}O_{12}Si_2Na$: 901.3991, found: 901.3975 [M^++Na].

Typical procedure for the reduction of ketone 70: **di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*R*)-6-benzyloxy-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-7-hydroxy-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (71)**: DIBALH in CH_2Cl_2 (1.0 M,

0.17 mL, 0.17 mmol) was added to a stirred solution of ketone **70** (50 mg, 0.057 mmol) and $ZnCl_2$ (23 mg, 0.171 mmol) in CH_2Cl_2 (0.5 mL) at −78 °C. After stirring for 30 min, the reaction was quenched by addition of MeOH (0.5 mL) followed by 15% aqueous potassium sodium tartrate (5 mL). After stirring at room temperature for 2 h, the mixture was extracted with AcOEt (15 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (81 mg), from which a diastereomeric mixture of alcohol (43.7 mg, 87%) was obtained as a colorless oil after column chromatography (silica gel 5 g, *n*-hexane/AcOEt 10:1). The diastereomeric ratio (**71**/**72** 46.4:1) was determined by HPLC analysis [column, Zorbax Sil, 4.6×250 mm; eluent, *n*-hexane/THF 10:1; flow rate, 1.0 mL min^{-1}; detection, 254 nm; t_R (7*R* isomer **71**) = 22.2 min, t_R (7*S* isomer **72**) = 19.3 min]. The diastereomers were separated by flash column chromatography (silica gel 10 g, toluene/AcOEt 40:1) to afford alcohol **71** (42.7 mg, 85%) as a colorless oil, along with undesired isomer **72** (1.0 mg, 2%) as a colorless oil. $[\alpha]_D^{23} = -9.07$ ($c = 2.15$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = -0.06$ (s, 9H; $Si(CH_3)_3$), 1.03 (s, 9H; $SiC(CH_3)_3$), 1.34 (s, 9H; $CO_2C(CH_3)_3$), 1.38 (s, 9H; $CO_2C(CH_3)_3$), 2.14 (ddd, $J = 3.9$, 11.6, 14.5 Hz, 1H; C1′-*H*), 2.24 (dt, $J = 14.5$, 3.9 Hz, 1H; C1′-*H*), 3.31 (s, 3H; OCH_3), 3.45 (dd, $J = 0.6$, 11.3 Hz, 1H; C*H*OTBDPS), 3.70 (dd, $J = 8.1$, 11.3 Hz, 1H; C*H*OTBDPS), 3.72 (dt, $J = 10.0$, 3.9 Hz, 1H; C2′-*H*), 3.95–3.99 (m, 2H; C3-*H*, C2′-*H*), 4.21 (br s, 1H; C7-O*H*), 4.59 (d, $J = 12.3$ Hz, 1H; OC*H*Ph), 4.61 (d, $J = 6.4$ Hz, 1H; one of OCH_2O), 4.63 (d, $J = 6.4$ Hz, 1H; one of OCH_2O), 4.66 (m, 1H; C7-*H*), 4.77 (d, $J = 12.3$ Hz, 1H; OC*H*Ph), 4.96 (br s, 1H; C6-*H*), 7.35–7.39 (m, 11H; Ar*H*), 7.63–7.69 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta =$ 2.6, 19.2, 21.3, 26.6, 27.7, 28.1, 36.8, 55.5, 63.2, 64.7, 71.1, 77.3, 78.6, 82.4, 82.55, 82.59, 84.9, 90.2, 96.3, 104.1, 125.2, 127.4, 127.5, 127.6, 127.7, 127.8, 128.1, 128.9, 129.47, 129.52, 133.2, 133.4, 135.4, 135.5, 137.7, 165.4, 168.8; IR (film): $\tilde{\nu} = 3470$, 2976, 2934, 2859, 1740, 1474, 1456, 1429, 1393, 1370, 1329, 1250, 1152, 1011, 925 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{47}H_{68}O_{12}Si_2Na$: 903.4147, found: 903.4152 [M^++Na]; elemental analysis calcd (%) for $C_{47}H_{68}O_{12}Si_2$ (881.2): C 64.06, H 7.78; found: C 63.91, H 7.75.

Data for **72**: $[\alpha]_D^{21} = -9.50$ ($c = 2.21$ in benzene); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = -0.06$ (s, 9H; $Si(CH_3)_3$), 1.03 (s, 9H; $SiC(CH_3)_3$), 1.38 (s, 9H; $CO_2C(CH_3)_3$), 1.45 (s, 9H; $CO_2C(CH_3)_3$), 2.26 (dt, $J = 12.9$, 5.6 Hz, 1H; C1′-*H*), 2.32 (dt, $J = 12.9$, 6.9 Hz, 1H; C1′-*H*), 3.35 (s, 3H; OCH_3), 3.36 (d, $J = 5.3$ Hz, 1H; C7-O*H*), 3.41 (dd, $J = 0.8$, 11.2 Hz, 1H; C*H*OTBDPS), 3.60 (dd, $J = 7.8$, 11.2 Hz, 1H; C*H*OTBDPS), 3.79 (dt, $J = 9.4$, 5.6 Hz, 1H; C2′-*H*), 3.84 (dt, $J = 9.4$, 6.9 Hz, 1H; C2′-*H*), 4.01 (dd, $J = 0.8$, 7.8 Hz, 1H; C3-*H*), 4.23 (dd, $J = 5.3$, 6.0 Hz, 1H; C7-*H*), 4.62 (d, $J = 6.7$ Hz, 1H; one of OCH_2O), 4.63 (d, $J = 11.4$ Hz, 1H; OC*H*Ph), 4.64 (d, $J = 6.7$ Hz, 1H; one of OCH_2O), 4.67 (d, $J = 11.4$ Hz, 1H; OC*H*Ph), 5.17 (d, $J = 6.0$ Hz, 1H; C6-*H*), 7.33–7.40 (m, 11H; Ar*H*), 7.62–7.68 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 2.6$, 19.2, 26.7, 27.9, 28.0, 28.2, 33.3, 55.1, 63.4, 64.7, 73.7, 75.2, 77.2, 77.8, 79.7, 82.7, 82.8, 91.3, 96.5, 108.0, 127.6, 127.7, 127.9, 128.1, 128.3, 128.4, 129.6, 133.0, 133.5, 135.4, 135.6, 136.7, 165.6, 169.4; IR (film): $\tilde{\nu} = 3486$, 2932, 2859, 1744, 1726, 1146, 1111, 1063 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{47}H_{68}O_{12}Si_2Na$: 903.4147, found: 903.4136 [M^++Na]; elemental analysis calcd (%) for $C_{47}H_{68}O_{12}Si_2$ (881.2): C 64.06, H 7.78; found: C 63.84, H 7.85.

Di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*R*)-6-benzyloxy-7-(*tert*-butoxycarbonyl)oxy-3-[(*tert*-butyldiphenylsilyl)oxymethyl]-1-[2-(methoxymethoxy)ethyl]-4-(trimethylsilyl)oxy-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (73): $(Boc)_2O$ (1.14 mL, 4.96 mmol) was added to a stirred solution of alcohol **71** (627 mg, 0.708 mmol), Et_3N (0.38 mL, 2.83 mmol) and DMAP (130 mg, 1.06 mmol) in CH_2Cl_2 (12 mL) at 0 °C. After stirring at room temperature for 2 h, the reaction was quenched with 10% aqueous K_2HPO_4 (10 mL), and the mixture was extracted with AcOEt (10 mL). 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 (710 mg), which was purified by column chromatography (silica gel 15 g, *n*-hexane/AcOEt 15:1) to give carbonate **73** (663 mg, 96%) as a colorless oil. $[\alpha]_D^{24} = +3.51$ ($c = 2.30$ in benzene); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = -0.09$ (s, 9H; $Si(CH_3)_3$), 1.03 (s, 9H; $SiC(CH_3)_3$), 1.36 (s, 9H; $CO_2C(CH_3)_3$), 1.38 (s, 9H; $CO_2C(CH_3)_3$), 1.47 (s, 9H; $OCO_2C(CH_3)_3$), 2.22 (dt, $J = 14.0$, 6.2 Hz, 1H; C1′-*H*), 2.27 (dt, $J = 14.0$, 6.2 Hz, 1H; C1′-*H*), 3.35 (s, 3H; OCH_3), 3.42 (dd, $J = 0.9$, 11.3 Hz, 1H; C*H*OTBDPS), 3.60 (dd, $J = 7.8$, 11.3 Hz, 1H; C*H*OTBDPS), 3.73 (dt, $J = 9.4$, 6.2 Hz, 1H; C2′-*H*), 3.84 (dt, $J = 9.4$, 6.2 Hz, 1H; C2′-*H*), 4.42 (dd, $J = 0.9$, 7.8 Hz, 1H; C3-*H*), 4.59 (d, $J = 11.8$ Hz, 1H; OC*H*Ph), 4.61 (d, $J = 6.4$ Hz, 1H; one of OCH_2O), 4.63 (d, $J = 6.4$ Hz, 1H; one of OCH_2O), 4.74 (d, $J = 11.8$ Hz, 1H; OC*H*Ph), 4.95 (br s, 1H; C7-*H*), 5.21 (d, $J = 1.6$ Hz, 1H; C6-*H*), 7.29–7.39 (m, 11H; Ar*H*), 7.63–7.72 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 2.5$, 19.2, 26.6, 27.6, 27.7, 28.1, 36.4, 55.0, 62.8, 64.5, 65.7, 71.9, 77.8, 78.0, 82.2, 82.5, 82.7, 83.1, 90.5, 96.4, 103.4, 127.4, 127.5, 128.05, 128.14, 129.4, 133.0, 133.8, 135.4, 135.7, 137.4, 152.7, 159.7, 168.9; IR (film): $\tilde{\nu} = 2934$, 1748, 1688, 1589, 1456, 1429, 1393, 1370, 922, 841, 791, 741 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{52}H_{76}O_{14}Si_2Na$: 1003.4671, found: 1003.4680 [M^++Na].

Di-*tert*-butyl (1*S*,3*R*,4*S*,5*R*,6*R*,7*R*)-6-benzyloxy-7-(*tert*-butoxycarbonyl)-oxy-4-hydroxy-3-(hydroxymethyl)-1-[2-(methoxymethoxy)ethyl]-2,8-dioxabicyclo[3.2.1]octane-4,5-dicarboxylate (74): Bu_4NF in THF (1.0 M, 1.25 mL, 1.25 mmol) was added to a stirred solution of bis-silyl ether **73** (601 mg, 0.612 mmol) in THF (9 mL) at 0 °C. After stirring for 30 min, the reaction was quenched with H_2O (10 mL), and the mixture was extracted with AcOEt (20 mL). 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 (520 mg), which was purified by column chromatography (silica gel 10 g, *n*-hexane/AcOEt 1:1) to give diol **74** (402 mg, 97%) as a colorless oil. $[\alpha]_D^{24} = -18.9$ ($c = 2.01$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.42$ (s, 9H; $CO_2C(CH_3)_3$), 1.46 (s, 9H; $CO_2C(CH_3)_3$), 1.52 (s, 9H; $OCO_2C(CH_3)_3$), 1.91 (dd, $J = 4.3$, 8.2 Hz, 1H; CH_2OH), 2.21 (dt, $J = 14.1$, 6.7 Hz, 1H; C1′-*H*), 2.29 (dt, $J = 14.1$, 6.7 Hz, 1H; C1′-*H*), 3.33 (s, 3H; OCH_3), 3.63 (ddd, $J = 5.2$, 8.2, 11.6 Hz, 1H; C*H*OH), 3.70 (ddd, $J = 0.8$, 4.3, 11.6 Hz, 1H; C*H*OH), 3.71 (dt, $J = 10.1$, 6.7 Hz, 1H; C2′-*H*), 3.83 (dt, $J = 10.1$, 6.7 Hz, 1H; C2′-*H*), 3.88 (s, 1H; C4-O*H*), 4.33 (dd, $J = 0.8$, 5.2 Hz, 1H; C3-*H*), 4.59 (d, $J = 6.3$ Hz, 1H; one of OCH_2O), 4.61 (d, $J = 6.3$ Hz, 1H; one of OCH_2O), 4.63 (d, $J = 11.9$ Hz, 1H; OC*H*Ph), 4.77 (d, $J = 11.9$ Hz, 1H; OC*H*Ph), 4.80 (br s, 1H; C7-*H*), 5.29 (br s, 1H; C6-*H*), 7.27–7.34 (m, 5H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 27.5$, 27.7, 35.8, 54.9, 61.0, 62.1, 71.8, 74.2, 74.7, 82.66, 82.71, 83.1, 84.5, 90.7, 96.1, 103.2, 127.6, 128.0, 137.1, 152.3, 164.8, 169.5; IR (film): $\tilde{\nu} = 3461$, 2978, 2934, 1732, 1456, 1395, 1370, 1333, 1278, 1161, 1117 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{33}H_{50}O_{14}Na$: 693.3098, found: 693.3080 [M^++Na].

Tri-*tert*-butyl (1*S*,3*S*,4*S*,5*R*,6*R*,7*R*)-6-benzyloxy-7-(*tert*-butoxycarbonyl)-oxy-4-hydroxy-1-[2-(methoxymethoxy)ethyl]-2,8-dioxabicyclo[3.2.1]-octane-3,4,5-tricarboxylate (75): Dess–Martin periodinane (335 mg, 0.791 mmol) was added to a stirred solution of diol **74** (265 mg, 0.395 mmol) in CH_2Cl_2 (5 mL). After stirring for 24 h, the mixture was diluted with AcOEt (10 mL) and poured into an ice-cooled saturated aqueous $NaHCO_3$ (5 mL) containing $Na_2S_2O_3 \cdot H_2O$ (200 mg). 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 furnished the crude product (380 mg), which was used without further purification.

$NaClO_2$ (175 mg, 1.19 mmol) was added to a stirred mixture of the crude aldehyde (380 mg) and NaH_2PO_4 (94.0 mg, 1.19 mmol) in *tert*-butyl alcohol (5 mL)/H_2O (1 mL)/2-methyl-2-butene (20 mL, 2.49 mmol) at 0 °C. After stirring at room temperature for 3 h, the reaction mixture was acidified with 10% aqueous $NaHSO_4$ (10 mL) and 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 (290 mg), which was used without further purification.

N,*N*′-Diisopropyl-*O*-*tert*-butylisourea (0.32 mL, 1.58 mmol) was added to a stirred solution of the crude carboxylic acid (290 mg) in CH_2Cl_2 (5 mL). After stirring for 48 h, the solvent was removed in vacuo. Purification by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 4:1) afforded triester **75** (279 mg, 96% for three steps) as a colorless oil. $[\alpha]_D^{22} = -10.4$ ($c = 1.58$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.43$ (s, 9H; $CO_2C(CH_3)_3$), 1.448 (s, 9H; $CO_2C(CH_3)_3$), 1.452 (s, 9H; $CO_2C(CH_3)_3$), 1.52 (s, 9H; $OCO_2C(CH_3)_3$), 2.28 (dt, $J = 14.2$, 6.7 Hz, 1H; C1′-*H*), 2.36 (dt, $J = 14.2$, 6.7 Hz, 1H; C1′-*H*), 3.33 (s, 3H; OCH_3), 3.79 (dt, $J = 10.1$, 6.7 Hz, 1H; C2′-*H*), 3.89 (dt, $J = 10.1$, 6.7 Hz, 1H; C2′-*H*), 4.02 (s, 1H; C4-O*H*), 4.59 (d, $J = 6.4$ Hz, 1H; one of OCH_2O), 4.61 (d, $J = 6.4$ Hz, 1H; one of

OCH_2O), 4.64 (d, J=11.9 Hz, 1H; OCHPh), 4.77 (s, 1H; C3-H), 4.78 (d, J=11.9 Hz, 1H; OCHPh), 4.82 (brs, 1H; C7-H), 5.30 (d, J=0.9 Hz, 1H; C6-H), 7.28–7.34 (m, 5H; ArH); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=27.7, 27.9, 28.0, 36.1, 55.1, 62.5, 71.7, 73.9, 75.5, 82.6, 83.0, 83.2, 83.4, 84.9, 91.3, 96.4, 103.2, 127.8, 128.28, 128.34, 137.2, 152.4, 164.7, 165.7, 168.8; IR (film): $\tilde{\nu}$=3453, 2980, 2934, 1744, 1456, 1395, 1370, 1333, 1277, 1256, 1155, 1116 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{37}H_{56}O_{15}Na$: 763.3517, found: 763.3530 [M^++Na].

Tri-*tert*-butyl (1*S*,3*S*,4*S*,5*R*,6*R*,7*R*)-6-benzyloxy-7-(*tert*-butoxycarbonyl)-oxy-4-hydroxy-1-(2-hydroxyethyl)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (76): TMSCl (60 μL, 0.456 mmol) was added to a stirred solution of MOM ether **75** (56 mg, 0.076 mmol) and Et_4NBr (96 mg, 0.456 mmol) in CH_2Cl_2 (2 mL) at 0 °C. The reaction mixture was stirred for 1 h and then allowed to warm to room temperature. After stirring for 20 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL), and the mixture was extracted with AcOEt (15 mL). 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 (70 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 3:1) to give diol **76** (40 mg, 75%) as a colorless oil. $[\alpha]_D^{24}=-9.35$ (c=1.25 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.45 (s, 9H; $CO_2C(CH_3)_3$), 1.46 (s, 18H; 2×$CO_2C(CH_3)_3$), 1.53 (s, 9H; $OCO_2C(CH_3)_3$), 2.10 (ddd, J=1.4, 5.3, 14.8 Hz, 1H; C1′-H), 2.32 (ddd, J=2.8, 9.6, 14.8 Hz, 1H; C1′-H), 3.76 (m, 1H; C2′-H), 4.06 (brs, 1H; C4-OH), 4.18 (m, 1H; C2′-H), 4.59 (d, J=12.0 Hz, 1H; OCHPh), 4.74 (d, J=12.0 Hz, 1H; OCHPh), 4.80 (s, 1H; C3-H), 4.81 (brs, 1H; C7-H), 5.12 (d, J=1.4 Hz, 1H; C6-H), 7.28–7.32 (m, 5H; ArH); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=27.7, 27.9, 28.0, 38.0, 58.4, 71.8, 73.6, 75.7, 77.2, 82.3, 83.1, 83.5, 83.8, 83.9, 85.4, 91.1, 105.0, 128.0, 128.3, 128.4, 136.9, 152.4, 164.4, 165.8, 168.7; IR (film): $\tilde{\nu}$=3545, 3455, 2982, 2936, 1732, 1456, 1395, 1370, 1275, 1115, 984, 918 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{35}H_{53}O_{14}$: 697.3435, found: 697.3412 [M^++H].

Tri-*tert*-butyl (1*S*,3*S*,4*S*,5*R*,6*R*,7*R*)-6-benzyloxy-7-(*tert*-butoxycarbonyl)-oxy-1-(formylmethyl)-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (5): Dess–Martin periodinane (37 mg, 0.086 mmol) was added to a stirred solution of diol **76** (40 mg, 0.057 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After stirring at room temperature for 30 min, the reaction mixture was diluted with AcOEt (15 mL) and poured into an ice-cooled saturated aqueous $NaHCO_3$ (10 mL) containing $Na_2S_2O_3{\cdot}H_2O$ (1.0 g). The layers were separated, and the organic layer was washed with brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (39 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 10:1) to give aldehyde **5** (37 mg, 93%) as a colorless oil. $[\alpha]_D^{23}=-4.06$ (c=1.65 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.45 (s, 18H; 2×$CO_2C(CH_3)_3$), 1.47 (s, 9H; $CO_2C(CH_3)_3$), 1.52 (s, 9H; $OCO_2C(CH_3)_3$), 2.98 (d, J=2.3 Hz, 2H; C1′-H_2), 4.11 (s, 1H; C4-OH), 4.60 (d, J=12.0 Hz, 1H; OCHPh), 4.75 (d, J=12.0 Hz, 1H; OCHPh), 4.83 (s, 1H; C3-H), 4.86 (brs, 1H; C7-H), 5.14 (d, J=1.1 Hz, 1H; C6-H), 7.29–7.32 (m, 5H; ArH), 9.94 (t, J=2.3 Hz, 1H; CHO); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=27.7, 27.9, 27.98, 28.03, 48.9, 72.1, 73.8, 75.6, 77.2, 82.1, 83.0, 83.5, 83.7, 83.9, 85.5, 91.4, 102.2, 128.0, 128.3, 128.4, 136.9, 152.2, 164.3, 165.4, 168.6, 198.7; IR (film): $\tilde{\nu}$=3449, 2982, 2936, 1732, 1476, 1458, 1395, 1372, 1258, 1155 cm^{-1}; elemental analysis calcd (%) for $C_{35}H_{50}O_{14}$ (694.8): C 60.51, H 7.25; found: C 60.29, H 7.37.

Tri-*tert*-butyl (1*S*,3*S*,4*S*,5*R*,6*R*,7*R*)-1-allyl-6-benzyloxy-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (79): *t*BuOK (258 mg, 2.30 mmol) was added to a stirred solution of $Ph_3P^+CH_3Br^-$ (911 mg, 2.55 mmol) in Et_2O (8.5 mL) at 0 °C, and the mixture was stirred at room temperature for 30 min. The 0.27 M solution of $Ph_3P{=}CH_2$ in Et_2O thus obtained (5.1 mL, 1.38 mmol) was added to a solution of aldehyde **5** (354 mg, 0.510 mmol) in Et_2O (5 mL). After stirring for 30 min, the reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the mixture was extracted with AcOEt (15 mL). 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 (403 mg), which was purified by column chromatography (silica gel 10 g, *n*-hexane/AcOEt 10:1) to give alkene **79** (328 mg, 93%) as a colorless oil. $[\alpha]_D^{25}=-10.9$ (c=1.32 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.43 (s, 9H; $CO_2C(CH_3)_3$), 1.45 (s, 9H; $CO_2C(CH_3)_3$), 1.46 (s, 9H; $CO_2C(CH_3)_3$), 1.51 (s, 9H; $OCO_2C(CH_3)_3$), 2.76 (d, J=7.2 Hz, 2H; C1′-H_2), 4.01 (s, 1H; OH), 4.60 (d, J=12.2 Hz, 1H; OCHPh), 4.76 (d, J=12.2 Hz, 1H; OCHPh), 4.79 (brs, 1H; C7-H), 4.81 (s, 1H; C3-H), 5.16 (dd, J=1.3, 10.0 Hz, 1H; =CHH), 5.19 (d, J=1.1 Hz, 1H; C6-H), 5.24 (dd, J=1.3, 17.0 Hz, 1H; =CHH), 5.97 (ddt, J=10.0, 17.0, 7.2 Hz, 1H; C2′-H), 7.28–7.32 (m, 5H; ArH); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=27.7, 27.9, 28.0, 40.4, 71.6, 74.0, 75.5, 77.2, 81.4, 82.6, 83.0, 83.2, 83.4, 84.9, 91.2, 103.8, 119.3, 127.8, 128.2, 128.3, 130.9, 137.2, 152.2, 164.7, 165.7, 168.8; IR (film): $\tilde{\nu}$=3451, 2980, 2934, 1744, 1456, 1370, 1277, 1256, 1157, 1117, 980 cm^{-1}; HR-MS (FAB): m/z: calcd for $C_{36}H_{53}O_{13}$: 693.3486, found: 693.3468 [M^++H].

(3*R*,4*R*)-4-Methyl-5-phenyl-1-penten-3-ol (81): BuLi in *n*-hexane (1.57 M, 5.0 mL, 7.85 mmol) was added to a stirred solution of trimethylsulfonium iodide (1.6 g, 8.04 mmol) in THF (20 mL) at −20 °C. After stirring for 30 min, a solution of epoxide **80**[44] (326 mg, 2.01 mmol) in THF (10 mL) was added. After stirring for another 30 min, the reaction mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was quenched with H_2O (15 mL), and the mixture was extracted with AcOEt (30 mL). The organic extract was washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (420 mg), which was purified by column chromatography (silica gel 15 g, *n*-hexane/AcOEt 20:1) to give allyl alcohol **81** (309 mg, 87%) as a colorless oil. $[\alpha]_D^{21}=+23.4$ (c=0.65 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.87 (d, J=6.8 Hz, 3H; C5′-CH_3), 1.49 (brs, 1H; OH), 1.91 (m, 1H; C5′-H), 2.40 (dd, J=9.0, 13.5 Hz, 1H; C6′-H), 2.86 (dd, J=5.9, 13.5 Hz, 1H; C6′-H), 4.06 (dd, J=4.2, 5.7 Hz, 1H; C4′-H), 5.18 (dd, J=0.8, 10.5 Hz, 1H; =CHH), 5.27 (dd, J=0.8, 17.4 Hz, 1H; =CHH), 5.75 (ddd, J=5.7, 10.5, 17.4 Hz, 1H; C3′-H), 7.17–7.29 (m, 5H; ArH); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=13.8, 39.2, 40.6, 75.5, 77.2, 115.3, 125.8, 128.2, 129.2, 139.7, 141.0; IR (film): $\tilde{\nu}$=3405, 3027, 2967, 1603, 1495, 1454, 1428, 1030, 993, 934 cm^{-1}; HR-MS (EI): m/z: calcd for $C_{12}H_{16}O$: 176.1201, found: 176.1204 [M^+].

(3*R*,4*R*)-4-Methyl-5-phenyl-1-penten-3-yl acetate (82): Acetic anhydride (0.16 mL, 1.70 mmol) was added to a stirred solution of alcohol **81** (150 mg, 0.852 mmol), DMAP (21 mg, 0.17 mmol) and pyridine (0.3 mL, 3.41 mmol) in CH_2Cl_2 (10 mL) at 0 °C. After stirring at room temperature for 1 h, the reaction was quenched by addition of one piece of ice, and the resulting mixture was partitioned between AcOEt (20 mL) and H_2O (5 mL). The organic layer was successively washed with 1 N aqueous HCl (5 mL), saturated aqueous $NaHCO_3$ (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (220 mg), which was purified by column chromatography (silica gel 10 g, *n*-hexane/AcOEt 20:1) to give acetate **82** (178 mg, 96%) as a colorless oil. $[\alpha]_D^{22}=+28.6$ (c=2.06 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.88 (d, J=6.8 Hz, 3H; C5′-CH_3), 2.03 (m, 1H; C5′-H), 2.09 (s, 3H; $COCH_3$), 2.32 (dd, J=9.5, 13.5 Hz, 1H; C6′-H), 2.82 (dd, J=5.2, 13.5 Hz, 1H; C6′-H), 5.22 (dd, J=1.4, 10.1 Hz, 1H; =CHH), 5.24 (m, 1H; C4′-H), 5.25 (dd, J=1.4, 17.2 Hz, 1H; =CHH), 5.81 (ddd, J=6.4, 10.1, 17.2 Hz, 1H; C3′-H), 7.12–7.29 (m, 5H; ArH); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=14.4, 21.1, 38.9, 39.1, 77.6, 117.3, 125.9, 128.3, 129.0, 134.8, 140.4, 170.2; IR (film): $\tilde{\nu}$=3027, 2971, 1740, 1497, 1454, 1372, 1238, 1020, 970, 930 cm^{-1}; HR-MS (EI): m/z: calcd for $C_{14}H_{18}O_2$: 218.1307, found: 218.1300 [M^+]; elemental analysis calcd (%) for $C_{14}H_{18}O_2$ (218.3): C 77.03, H 8.31; found: C 77.01, H 8.30.

Typical procedure for the olefin cross-metathesis: **tri-*tert*-butyl [1*S*,1-(4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-1-(4-acetoxy-5-methyl-6-phenyl-2-hexenyl)-6-benzyloxy-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-2,8-dioxabicyclo[3.2.1]-octane-3,4,5-tricarboxylate (87)**: The Blechert's catalyst (**85**, 51 mg, 0.073 mmol) was added to a stirred solution of alkenes **79** (253 mg, 0.365 mmol) and **82** (159 mg, 0.731 mmol) in benzene (3.7 mL). After stirring at 60 °C for 8 h, the solvent was evaporated in vacuo, and the residue (472 mg) was purified by flash column chromatography (silica gel 10 g, *n*-hexane/AcOEt 20:1 → 6:1) to give cross-coupling products (*E*)-**87** (258 mg, 80%) and (*Z*)-**87** (32.2 mg, 10%) as colorless oils, along with homo-dimer **89** (14.9 mg, 10%) and alkene **92** (4.7 mg, 1.5%) as colorless oils.

Data for (*E*)-**87**: $[\alpha]_D^{19} = -9.27$ ($c = 1.58$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.86$ (d, $J = 6.8$ Hz, 3H; C5′-CH_3), 1.42 (s, 9H; $CO_2C(CH_3)_3$), 1.43 (s, 9H; $CO_2C(CH_3)_3$), 1.45 (s, 9H; $CO_2C(CH_3)_3$), 1.50 (s, 9H; $OCO_2C(CH_3)_3$), 2.03 (s, 3H; $COCH_3$), 2.04 (m, 1H; C5′-*H*), 2.33 (dd, $J =$ 9.5, 13.5 Hz, 1H; C6′-*H*), 2.69 (dd, $J = 7.6$, 14.8 Hz, 1H; C1′-*H*), 2.80 (dd, $J = 6.2$, 14.8 Hz, 1H; C1′-*H*), 2.84 (dd, $J = 5.0$, 13.5 Hz, 1H; C6′-*H*), 4.02 (s, 1H; O*H*), 4.56 (d, $J = 11.9$ Hz, 1H; OC*H*Ph), 4.70 (d, $J = 11.9$ Hz, 1H; OC*H*Ph), 4.80 (s, 1H; C3-*H*), 4.82 (brs, 1H; C7-*H*), 5.17 (d, $J = 1.5$ Hz, 1H; C6-*H*), 5.23 (dd, $J = 5.2$, 6.0 Hz, 1H; C4′-*H*), 5.72 (dd, $J = 6.0$, 15.7 Hz, 1H; C3′-*H*), 5.81 (ddd, $J = 6.2$, 7.6, 15.7 Hz, 1H; C2′-*H*), 7.11–7.16 (m, 3H; Ar*H*), 7.21–7.28 (m, 7H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 14.7$, 21.1, 27.7, 27.9, 27.99, 28.04, 38.3, 38.7, 39.2, 71.9, 74.1, 75.5, 77.2, 81.3, 82.9, 83.1, 83.2, 83.3, 84.9, 91.2, 103.8, 125.5, 125.7, 127.8, 128.1, 128.2, 128.3, 128.4, 129.2, 131.6, 137.2, 140.8, 152.4, 164.7, 165.7, 168.7, 170.2; IR (film): $\tilde{\nu} = 3455$, 2980, 2934, 1732, 1456, 1395, 1372, 1279, 1121, 976, 910, 843 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{48}H_{66}O_{15}Na$: 905.4299, found: 905.4327 [M^++Na].

Data for (*Z*)-**87**: $[\alpha]_D^{21} = -7.22$ ($c = 1.74$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.86$ (d, $J = 6.7$ Hz, 3H; C5′-CH_3), 1.435 (s, 18H; 2×$CO_2C(CH_3)_3$), 1.444 (s, 9H; $CO_2C(CH_3)_3$), 1.50 (s, 9H; $OCO_2C(CH_3)_3$), 2.04 (s, 3H; $COCH_3$), 2.07 (m, 1H; C5′-*H*), 2.29 (dd, $J = 10.1$, 13.4 Hz, 1H; C6′-*H*), 2.85–2.88 (m, 3H; C1′-H_2, C6′-*H*), 3.99 (s, 1H; O*H*), 4.62 (d, $J =$ 11.9 Hz, 1H; OC*H*Ph), 4.78 (brs, 1H; C7-*H*), 4.79 (d, $J = 11.9$ Hz, 1H; OC*H*Ph), 4.82 (s, 1H; C3-*H*), 5.09 (brs, 1H; C6-*H*), 5.49 (dd, $J = 5.6$, 9.6 Hz, 1H; C4′-*H*), 5.59 (dd, $J = 9.6$, 11.0 Hz, 1H; C3′-*H*), 5.90 (dt, $J =$ 11.0, 7.0 Hz, 1H; C2′-*H*), 7.13–7.15 (m, 3H; Ar*H*), 7.23–7.34 (m, 7H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 14.6$, 21.2, 27.5, 27.7, 27.9, 28.0, 28.1, 28.3, 35.0, 38.5, 39.5, 71.8, 73.3, 74.0, 75.6, 77.2, 82.2, 82.7, 82.9, 83.2, 83.4, 84.9, 91.4, 103.6, 125.8, 126.9, 127.8, 128.1, 128.2, 128.3, 128.4, 129.2, 129.3, 137.3, 140.6, 152.2, 164.7, 165.7, 168.7, 170.1; IR (film): $\tilde{\nu} = 3455$, 2978, 2932, 2856, 1738, 1603, 1456, 1395, 1370, 1333, 1254, 1157, 1117, 1030, 980, 910, 843 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{48}H_{66}O_{15}Na$: 905.4299, found: 905.4284 [M^++Na]

Data for **89**: $[\alpha]_D^{22} = -11.5$ ($c = 0.16$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.87$ (d, $J = 6.8$ Hz, 6H; 2×C5′-CH_3), 2.02 (m, 2H; 2×C5′-*H*), 2.08 (s, 6H; 2×$COCH_3$), 2.30 (dd, $J = 9.3$, 13.5 Hz, 2H; 2×C6′-*H*), 2.79 (dd, $J = 5.3$, 13.5 Hz, 2H; 2×C6′-*H*), 5.21 (ddd, $J = 1.6$, 3.5, 4.8 Hz, 2H; 2×C4′-*H*), 5.65 (dd, $J = 1.6$, 3.5 Hz, 2H; 2×C3′-*H*), 7.10–7.20 (m, 6H; Ar*H*), 7.25–7.28 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta =$ 14.6, 21.2, 38.9, 39.3, 76.2, 77.2, 126.0, 128.3, 129.1, 129.9, 140.3, 170.1; IR (film): $\tilde{\nu} = 3027$, 2969, 2932, 1738, 1603, 1495, 1454, 1372, 1236, 1096, 1020, 970, 910 cm^{-1}; HR-MS (EI): *m*/*z*: calcd for $C_{26}H_{32}O_4$: 408.2300, found: 408.2295 [M^+].

Data for **92**: $[\alpha]_D^{21} = -16.4$ ($c = 0.14$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.935$ (d, $J = 6.1$ Hz, 3H; $CHCH_3$), 0.938 (d, $J = 7.0$ Hz, 3H; C5′-CH_3), 0.96 (d, $J = 6.1$ Hz, 3H; $CHCH_3$), 2.12 (s, 3H; $COCH_3$), 2.15 (m, 1H; C5′-*H*), 2.37 (dd, $J = 9.6$, 13.5 Hz, 1H; C6′-*H*), 2.91 (dd, $J = 5.0$, 13.5 Hz, 1H; C6′-*H*), 3.72 (heptet, $J = 6.1$ Hz, 1H; $OCH(CH_3)_2$), 5.42 (dd, $J = 6.0$, 6.8 Hz, 1H; C4′-*H*), 6.19 (dd, $J = 6.8$, 16.0 Hz, 1H; C3′-*H*), 7.02 (d, $J = 16.0$ Hz, 1H; =C*H*Ar), 7.15–7.19 (m, 4H; Ar*H*), 7.23–7.32 (m, 4H; Ar*H*), 7.40 (m, 2H; Ar*H*), 7.49 (m, 1H; Ar*H*), 7.55 (m, 2H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 14.8$, 21.2, 22.0, 39.0, 39.7, 75.9, 76.2, 77.2, 78.0, 123.7, 125.4, 126.0, 126.6, 127.0, 128.1, 128.3, 128.7, 129.1, 129.3, 129.4, 130.7, 131.5, 136.2, 139.3, 140.5, 153.0, 170.2; IR (film): $\tilde{\nu} =$ 3061, 3027, 2973, 2930, 1738, 1497, 1453, 1426, 1372, 1236, 1177, 1138, 1107, 1020, 974 cm^{-1}; HR-MS (EI): *m*/*z*: calcd for $C_{29}H_{32}O_3$: 428.2351, found: 428.2335 [M^+].

Data for **88**: $[\alpha]_D^{22} = +21.3$ ($c = 1.78$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.87$ (d, $J = 6.8$ Hz, 6H; 2×C5′-CH_3), 1.68 (brs, 2H; 2×O*H*), 1.90 (m, 2H; 2×C5′-*H*), 2.38 (dd, $J = 9.0$, 13.4 Hz, 2H; 2×C6′-*H*), 2.85 (dd, $J = 5.9$, 13.4 Hz, 2H; 2×C6′-*H*), 4.06 (m, 2H; 2×C4′-*H*), 5.73 (dd, $J = 1.4$, 3.1 Hz, 2H; 2×C3′-*H*), 7.16–7.20 (m, 6H; Ar*H*), 7.24–7.28 (m, 4H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 14.1$, 39.2, 40.9, 74.9, 125.8, 128.2, 129.1, 132.9, 140.9; IR (film): $\tilde{\nu} = 3385$, 3029, 2967, 2930, 1603, 1495, 1454, 1377, 1265, 1101, 1059, 1017, 974 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{22}H_{27}O_2$: 323.2011, found: 323.2023 [M^+−H].

Data for **91**: $[\alpha]_D^{22} = -18.6$ ($c = 0.79$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.35$ (s, 9H; $CO_2C(CH_3)_3$), 1.42 (s, 9H; $CO_2C(CH_3)_3$), 1.46 (s, 18H; $CO_2C(CH_3)_3$, $OCO_2C(CH_3)_3$), 2.84 (dd, $J = 8.1$, 14.1 Hz, 1H; C1′-*H*), 3.00 (dd, $J = 6.6$, 14.1 Hz, 1H; C1′-*H*), 4.03 (s, 1H; O*H*), 4.59 (d, $J =$ 12.1 Hz, 1H; OC*H*Ph), 4.76 (d, $J = 12.1$ Hz, 1H; OC*H*Ph), 4.78 (brs, 1H; C7-*H*), 4.83 (s, 1H; C3-*H*), 5.21 (brs, 1H; C6-*H*), 6.34 (ddd, $J = 6.6$, 8.1, 15.9 Hz, 1H; C2′-*H*), 6.56 (d, $J = 15.9$ Hz, 1H; =C*H*Ph), 7.19 (m, 1H; Ar*H*), 7.25–7.32 (m, 7H; Ar*H*), 7.36–7.38 (m, 2H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 27.5$, 27.7, 27.9, 28.1, 29.7, 40.0, 71.5, 74.1, 75.7, 81.5, 82.6, 83.0, 83.2, 83.4, 84.9, 91.5, 104.1, 122.8, 126.4, 127.1, 127.8, 128.29, 128.30, 131.0, 133.9, 137.2, 137.5, 152.2, 152.3, 164.7, 165.7, 168.8; IR (film): $\tilde{\nu} = 3455$, 2982, 2934, 1742, 1599, 1497, 1476, 1456, 1395, 1370, 1333, 1275, 1157, 1117, 1032, 978, 905 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{42}H_{56}O_{13}$: 768.3721, found: 768.3734 [M^+].

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 (4): Pd/$BaSO_4$ (5%, 60 mg) was added to a stirred solution of allyl acetate **87** (14.0 mg, 15.9 μmol) in AcOEt (1 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 (14.1 mg), which was used without further purification.

$Pd(OH)_2$ on carbon (20%, 10 mg) was added to a stirred solution of the partially debenzylated mixture of hydrogenation products (crude, 14.1 mg) in AcOEt (1 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. Purification of the residue (14.1 mg) by column chromatography (silica gel 3 g, *n*-hexane/AcOEt 6:1) afforded diol **4** (13.5 mg, 98%) as a colorless oil. $[\alpha]_D^{22} = +29.7$ ($c =$ 0.95 in EtOH) [lit. $[\alpha]_D = +43.3$ ($c = 0.25$ in CH_2Cl_2),[8b] $[\alpha]_D^{21} = +23.8$ ($c =$ 0.59 in EtOH),[12b] $[\alpha]_D^{27} = +25.8$ ($c = 0.47$ in CH_2Cl_2);[13b] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.84$ (d, $J = 6.8$ Hz, 3H; C5′-CH_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; $OCO_2C(CH_3)_3$), 1.59–1.70 (m, 4H; C2′-H_2, C3′-H_2), 1.88–2.04 (m, 3H; C1′-H_2, C5′-*H*), 2.05 (s, 3H; $COCH_3$), 2.31 (dd, $J = 9.6$, 13.5 Hz, 1H; C6′-*H*), 2.76 (dd, $J = 5.0$, 13.5 Hz, 1H; C6′-*H*), 2.79 (d, $J = 2.8$ Hz, 1H; C6-O*H*), 3.92 (s, 1H; C4-O*H*), 4.64 (d, $J = 2.0$ Hz, 1H; C7-*H*), 4.72 (s, 1H; C3-*H*), 4.87 (dt, $J = 6.5$, 4.0 Hz, 1H; C4′-*H*), 5.11 (dd, $J = 2.0$, 2.8 Hz, 1H; C6-*H*), 7.12–7.18 (m, 3H; Ar*H*), 7.24–7.27 (m, 2H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 13.8$, 18.9, 21.2, 27.7, 28.0, 28.05, 28.13, 30.9, 35.5, 37.9, 39.4, 74.1, 75.26, 75.29, 76.8, 76.9, 83.2, 83.8, 83.9, 85.0, 85.5, 90.7, 103.9, 125.8, 128.2, 129.1, 140.7, 153.7, 165.2, 165.8, 168.5, 170.8; IR (film): $\tilde{\nu} = 3461$, 2932, 1732, 1603, 1456, 1370, 1277, 1155, 966, 916, 845 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{41}H_{63}O_{15}$: 795.4167, found: 795.4190 [M^++H].

Tri-*tert*-butyl [1*S*,1(2*E*,4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-6-benzyloxy-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-1-(4-hydroxy-5-methyl-6-phenyl-2-hexenyl)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (86): DIBALH in toluene (0.10 M, 1.0 mL, 0.10 mmol) was added dropwise over a 30 min period to a stirred solution of acetate (*E*)-**87** (20 mg, 0.023 mmol) in toluene (0.4 mL)/CH_2Cl_2 (0.4 mL) at −78 °C. After stirring for 30 min, the reaction was quenched by addition of MeOH (50 μL) followed by 15% aqueous potassium sodium tartrate (5 mL). After stirring at room temperature for 1 h, the mixture was extracted with AcOEt (15 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (19.0 mg), which was purified by column chromatography (silica gel 3 g, *n*-hexane/AcOEt 3:1) to give diol **86** (16.2 mg, 84%) as a colorless oil. $[\alpha]_D^{27} = +3.93$ ($c = 1.45$ in EtOH); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.85$ (d, $J = 6.8$ Hz, 3H; C5′-CH_3), 1.44 (s, 27H; 3×$CO_2C(CH_3)_3$), 1.50 (s, 9H; $OCO_2C(CH_3)_3$), 1.79 (brs, 1H; C4′-O*H*), 1.90 (m, 1H; C5′-*H*), 2.37 (dd, $J = 9.1$, 13.3 Hz, 1H; C6′-*H*), 2.72 (dd, $J = 6.7$, 14.1 Hz, 1H; C1′-*H*), 2.80 (dd, $J = 4.9$, 14.1 Hz, 1H; C1′-*H*), 2.87 (dd, $J = 5.7$, 13.3 Hz, 1H; C6′-*H*), 4.04 (dd, $J = 5.1$, 9.4 Hz, 1H; C4′-*H*), 4.06 (s, 1H; C4-O*H*), 4.57 (d, $J =$ 12.0 Hz, 1H; OC*H*Ph), 4.72 (d, $J = 12.0$ Hz, 1H; OC*H*Ph), 4.80 (s, 1H; C3-*H*), 4.81 (brs, 1H; C7-*H*), 5.16 (d, $J = 1.4$ Hz, 1H; C6-*H*), 5.76 (dd, $J = 5.1$, 15.7 Hz, 1H; C3′-*H*), 5.81 (ddd, $J = 4.9$, 6.7, 15.7 Hz, 1H; C2′-*H*), 7.14–7.18 (m, 3H; Ar*H*), 7.23–7.30 (m, 7H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 14.1$, 27.7, 27.9, 28.0, 28.1, 38.6, 39.0, 40.7, 71.8, 74.0, 75.0, 75.5, 77.2, 81.5, 82.6, 83.28, 83.34, 83.5, 85.1, 91.2, 103.8, 123.9, 125.6,

127.9, 128.1, 128.2, 128.3, 129.3, 136.7, 137.1, 141.3, 152.3, 164.7, 165.7, 168.7; IR (film): $\tilde{\nu}$ = 3455, 2980, 2934, 1742, 1495, 1456, 1395, 1370, 1256, 1154, 1117, 1030, 978 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{46}H_{64}O_{14}Na$: 863.4194, found: 863.4186 [M^++Na].

Tri-*tert*-butyl [1*S*,1(2*E*,4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-6-benzyloxy-1-[4-[(bromomethyl)dimethylsilyl]oxy-5-methyl-6-phenyl-2-hexenyl]-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (94): (Bromomethyl)chlorodimethylsilane (11 mg, 0.06 mmol) was added to a stirred solution of diol **86** (42.1 mg, 0.05 mmol), Et_3N (14 μL, 0.10 mmol) and DMAP (0.6 mg, 5.0 μmol) in CH_2Cl_2 (1 mL) at 0 °C. After stirring for 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL), and the mixture was extracted with AcOEt (15 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (29 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 8:1) to give silyl ether **94** (47.4 mg, 96 %) as a colorless oil. $[\alpha]_D^{24} = -5.33$ (*c* = 0.92 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.24 (s, 3H; Si(*CH*$_3$)), 0.25 (s, 3H; Si(*CH*$_3$)), 0.79 (d, *J* = 6.7 Hz, 3H; C5′-(*CH*$_3$)), 1.42 (s, 18H; 2 × $CO_2C(CH_3)_3$), 1.43 (s, 9H; $CO_2C(CH_3)_3$), 1.50 (s, 9H; $OCO_2C(CH_3)_3$), 1.83 (m, 1H; C5′-*H*), 2.26 (dd, *J* = 9.9, 13.3 Hz, 1H; C6′-*H*), 2.48 (d, *J* = 16.5 Hz, 1H; one of Si(*CH*$_2$)Br), 2.51 (d, *J* = 16.5 Hz, 1H; one of Si(*CH*$_2$)Br), 2.68 (dd, *J* = 6.5, 14.5 Hz, 1H; C1′-*H*), 2.80 (dd, *J* = 3.9, 14.5 Hz, 1H; C1′-*H*), 2.86 (dd, *J* = 4.6, 13.3 Hz, 1H; C6′-*H*), 3.98 (s, 1H; C4-O*H*), 4.08 (dd, *J* = 4.1, 4.3 Hz, 1H; C4′-*H*), 4.57 (d, *J* = 11.9 Hz, 1H; OC*H*Ph), 4.71 (d, *J* = 11.9 Hz, 1H; OC*H*Ph), 4.78 (s, 1H; C3-*H*), 4.83 (brs, 1H; C7-*H*), 5.14 (d, *J* = 1.2 Hz, 1H; C6-*H*), 5.72 (ddd, *J* = 3.9, 6.5, 16.3 Hz, 1H; C2′-*H*), 5.75 (dd, *J* = 4.1, 16.3 Hz, 1H; C3′-*H*), 7.13–7.15 (m, 3H; Ar*H*), 7.22–7.28 (m, 7H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = −2.5, 14.2, 17.0, 27.7, 27.9, 28.0, 28.1, 38.3, 38.8, 41.8, 72.1, 74.1, 75.5, 77.3, 81.7, 83.0, 83.2, 83.3, 84.9, 91.2, 103.8, 123.7, 125.5, 127.8, 128.0, 128.2, 128.3, 129.2, 136.0, 137.2, 141.5, 152.4, 164.8, 165.7, 168.8; IR (film): $\tilde{\nu}$ = 3457, 2978, 2934, 2870, 1742, 1495, 1456, 1395, 1370, 1256, 1156, 1119, 1030, 976 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{49}H_{71}BrO_{14}SiNa$: 1013.3694, found: 1013.3688 [M^++Na].

Tri-*tert*-butyl [1*S*,1(3*R*,4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-6-benzyloxy-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-1-[4-hydroxy-3-(hydroxymethyl)-5-methyl-6-phenylhexyl]-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (96): A solution of Bu_3SnH (60 mg, 0.206 mmol) and AIBN (1.1 mg, 7.0 μmol) in degassed benzene (6 mL) was added dropwise over 3 h to a refluxing solution of silyl ether **94** (136 mg, 0.137 mmol) in degassed benzene (6 mL), and the mixture was stirred for 1 h. After cooling, the mixture was evaporated in vacuo to provide a crude product (201 mg), which was used without further purification.

To a stirred mixture of the crude cyclic siloxane **95** (201 mg), $NaHCO_3$ (12 mg, 0.143 mmol) and KF (16 mg, 0.275 mmol) in THF (3 mL)/MeOH (3 mL) was added 35 % aqueous H_2O_2 (44 μL, 0.45 mmol), and the mixture was stirred for 24 h. The reaction mixture was poured into a two-layer mixture of Et_2O (5 mL) and 50 % aqueous $Na_2S_2O_3$ (10 mL). The resulting mixture was filtered through a Celite pad, and the filtrate was extracted with AcOEt (20 mL). 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 (150 mg), which was purified by column chromatography (silica gel 10 g, *n*-hexane/AcOEt 3:2) to give triol **96** (102 mg, 85 %) as a colorless oil. $[\alpha]_D^{24} = -6.09$ (*c* = 1.39 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.6 Hz, 3H; C5′-*CH*$_3$), 1.44 (s, 18H; 2 × $CO_2C(CH_3)_3$), 1.46 (s, 9H; $CO_2C(CH_3)_3$), 1.51 (s, 9H; $OCO_2C(CH_3)_3$), 1.60 (m, 2H; C2′-*H*$_2$), 1.83 (m, 1H; C5′-*H*), 1.93 (ddd, *J* = 5.5, 9.2, 14.5 Hz, 1H; C1′-*H*), 2.00 (ddd, *J* = 5.5, 9.2, 14.5 Hz, 1H; C1′-*H*), 2.06 (m, 1H; C3′-*H*), 2.47 (dd, *J* = 8.7, 13.4 Hz, 1H; C6′-*H*), 2.74 (dd, *J* = 6.0, 13.4 Hz, 1H; C6′-*H*), 2.95 (brs, 2H; C4′-O*H*, C3′-CH$_2$O*H*), 3.52 (dd, *J* = 3.9, 7.4 Hz, 1H; C4′-*H*), 3.75 (dd, *J* = 5.8, 11.4 Hz, 1H; C14′-*H*), 3.97 (dd, *J* = 2.8, 11.4 Hz, 1H; C14′-*H*), 4.03 (s, 1H; C4-O*H*), 4.59 (d, *J* = 11.9 Hz, 1H; OC*H*Ph), 4.74 (d, *J* = 11.9 Hz, 1H; OC*H*Ph), 4.78 (s, 1H; C3-*H*), 4.83 (brs, 1H; C7-*H*), 5.09 (d, *J* = 1.6 Hz, 1H; C6-*H*), 7.15–7.18 (m, 3H; Ar*H*), 7.23–7.32 (m, 7H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.1, 21.0, 27.7, 27.9, 28.0, 28.1, 32.8, 37.4, 40.4, 41.9, 63.8, 72.1, 73.9, 75.3, 77.8, 82.8, 83.46, 83.54, 83.6, 85.2, 91.1, 104.2, 125.7, 127.9, 128.2, 128.4, 129.2, 137.1, 141.1, 152.6, 164.8, 165.9, 168.8; IR (film): $\tilde{\nu}$ = 3457, 2976, 2930, 2857, 1742, 1456, 1395, 1370, 1277, 1258, 1155, 1119, 1076 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{47}H_{68}O_{15}Na$: 895.4456, found: 895.4452 [M^++Na].

Tri-*tert*-butyl (1*S*,1{2,[4*S*,4(2*R*),5*R*]},3*S*,4*S*,5*R*,6*R*,7*R*)-6-benzyloxy-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-1-[2-[2,2-dimethyl-4-(1-phenylpropan-2-yl)-1,3-dioxan-5-yl]ethyl]-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (97): *p*-Toluenesulfonic acid monohydrate (0.1 mg, 0.5 μmol) was added to a stirred solution of triol **96** (9.0 mg, 9.2 μmol) in 2,2-dimethoxypropane (1.0 mL). After stirring for 1 h, the reaction was quenched with Et_3N (0.1 mL), and the volatile elements were removed in vacuo. Purification of the residue by column chromatography (silica gel 3 g, *n*-hexane/AcOEt 4:1) afforded acetonide **97** (8.0 mg, 85 %) as a colorless oil. $[\alpha]_D^{21} = -17.0$ (*c* = 0.40 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.8 Hz, 3H; C5′-*CH*$_3$), 1.31 (s, 3H; acetonide *CH*$_3$), 1.38 (s, 3H; acetonide *CH*$_3$), 1.43 (s, 9H; $CO_2C(CH_3)_3$), 1.45 (s, 18H; 2 × $CO_2C(CH_3)_3$), 1.50 (s, 9H; $OCO_2C(CH_3)_3$), 1.55 (m, 1H; C2′-*H*), 1.65 (m, 1H; C2′-*H*), 1.80 (m, 1H; C5′-*H*), 1.85 (t, *J* = 8.6 Hz, 2H; C1′-*H*$_2$), 2.07 (m, 1H; C3′-*H*), 2.56 (dd, *J* = 7.5, 13.5 Hz, 1H; C6′-*H*), 2.63 (dd, *J* = 7.8, 13.5 Hz, 1H; C6′-*H*), 3.44 (dd, *J* = 1.8, 10.4 Hz, 1H; C4′-*H*), 3.52 (dd, *J* = 11.4, 11.5 Hz, 1H; C14′-*H*$_{ax}$), 3.82 (dd, *J* = 5.0, 11.5 Hz, 1H; C14′-*H*$_{eq}$), 4.02 (s, 1H; C4-O*H*), 4.59 (d, *J* = 12.0 Hz, 1H; OC*H*Ph), 4.74 (d, *J* = 12.0 Hz, 1H; OC*H*Ph), 4.77 (s, 1H; C3-*H*), 4.81 (brs, 1H; C7-*H*), 5.04 (d, *J* = 1.1 Hz, 1H; C6-*H*), 7.14–7.15 (m, 3H; Ar*H*), 7.21–7.32 (m, 7H; Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 12.7, 19.2, 20.3, 27.7, 27.9, 27.98, 28.03, 29.6, 29.7, 32.8, 35.1, 35.3, 40.1, 64.3, 71.9, 73.87, 73.91, 75.5, 76.8, 77.2, 77.8, 82.4, 82.7, 83.2, 83.3, 83.5, 85.1, 91.2, 97.9, 103.9, 125.6, 127.9, 128.1, 128.3, 128.4, 129.3, 137.1, 141.3, 152.5, 164.7, 165.8, 168.9; IR ($CHCl_3$): $\tilde{\nu}$ = 3021, 2928, 2855, 1728, 1464, 1281, 1221, 1017, 918, 851, 760 cm^{-1}; HR-MS (ESI): *m*/*z*: calcd for $C_{50}H_{72}O_{15}Na$: 935.4769, found: 935.4775 [M^++Na].

Tri-*tert*-butyl [1*S*,1(3*R*,4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-7-(*tert*-butoxycarbonyl)-oxy-4,6-dihydroxy-1-[4-hydroxy-3-(hydroxymethyl)-5-methyl-6-phenylhexyl]-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (98): $Pd(OH)_2$ on carbon (20 %, 82 mg) was added to a stirred solution of benzyl ether **96** (82.0 mg, 0.094 mmol) in AcOEt (3 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 13 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. Purification of the residue (80 mg) by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 1:1) afforded tetraol **98** (69.7 mg, 95 %) as a colorless oil. $[\alpha]_D^{22} = +16.6$ (*c* = 1.02 in EtOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.7 Hz, 3H; C5′-*CH*$_3$), 1.45 (s, 9H; $CO_2C(CH_3)_3$), 1.48 (s, 9H; $CO_2C(CH_3)_3$), 1.50 (s, 9H; $CO_2C(CH_3)_3$), 1.58 (s, 9H; $OCO_2C(CH_3)_3$), 1.60–1.76 (m, 2H; C2′-*H*$_2$), 1.83 (m, 1H; C5′-*H*), 1.89 (dt, *J* = 9.2, 6.3 Hz, 1H; C1′-*H*), 1.99 (dt, *J* = 9.2, 6.3 Hz, 1H; C1′-*H*), 2.06 (m, 1H; C3′-*H*), 2.48 (dd, *J* = 8.7, 13.4 Hz, 1H; C6′-*H*), 2.74 (dd, *J* = 6.1, 13.4 Hz, 1H; C6′-*H*), 2.87 (brs, 1H; O*H*), 2.95 (brs, 1H; O*H*), 3.52 (dd, *J* = 4.0, 7.3 Hz, 1H; C4′-*H*), 3.75 (dd, *J* = 5.8, 11.3 Hz, 1H; C14′-*H*), 3.95 (dd, *J* = 2.9, 11.3 Hz, 1H; C14′-*H*), 3.99 (s, 1H; C4-O*H*), 4.68 (d, *J* = 1.9 Hz, 1H; C7-*H*), 4.72 (s, 1H; C3-*H*), 5.13 (brs, 1H; C6-*H*), 7.15–7.19 (m, 3H; Ar*H*), 7.27 (m, 2H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.3, 21.0, 27.7, 28.0, 28.1, 28.2, 32.6, 37.5, 40.4, 41.9, 63.8, 74.0, 75.1, 77.2, 77.7, 83.6, 84.0, 84.2, 85.3, 85.7, 90.8, 103.9, 125.8, 128.3, 129.2, 141.0, 153.6, 165.2, 165.8, 168.5; IR (film): $\tilde{\nu}$ = 3455, 2978, 2932, 1732, 1289, 1117, 986, 845, 795 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{40}H_{63}O_{15}$: 783.4167, found: 783.4184 [M^++H].

Tri-*tert*-butyl [1*S*,1(3*S*,4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-7-(*tert*-butoxycarbonyl)-oxy-4,6-dihydroxy-1-[4-hydroxy-5-methyl-3-[(2-nitrophenylseleno)methyl]-6-phenylhexyl]-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (99): Bu_3P (10.7 mg, 53 μmol) was added to a stirred solution of tetraol **98** (8.0 mg, 10.2 μmol) and 2-nitrophenyl selenocyanate (12.0 mg, 53 μmol) in THF (0.5 mL). After stirring for 30 min, the solvent was removed in vacuo, and the yellow residue (35 mg) was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 3:1) to give selenide **99** (6.1 mg, 62 %) as a yellow oil. $[\alpha]_D^{22} = -10.5$ (*c* = 1.22 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.7 Hz, 3H; C5′-*CH*$_3$), 1.45 (s, 9H; $CO_2C(CH_3)_3$), 1.48 (s, 9H; $CO_2C(CH_3)_3$), 1.50 (s, 9H; $CO_2C(CH_3)_3$), 1.58 (s, 9H; $OCO_2C(CH_3)_3$), 1.80–2.00 (m, 3H; C2′-*H*$_2$, C5′-*H*), 2.04–2.14 (m, 3H; C1′-*H*$_2$, C3′-*H*), 2.46 (dd, *J* = 8.5, 13.5 Hz, 1H; C6′-*H*), 2.75 (dd, *J* =

7.4, 13.5 Hz, 1H; C6′-*H*), 2.82 (d, *J* = 3.4 Hz, 1H; C6-O*H*), 2.96 (dd, *J* = 7.1, 11.2 Hz, 1H; C14′-*H*), 3.23 (dd, *J* = 4.1, 11.2 Hz, 1H; C14′-*H*), 3.53 (m, 1H; C4′-*H*), 3.96 (s, 1H; C4-O*H*), 4.61 (d, *J* = 1.9 Hz, 1H; C7-*H*), 4.72 (s, 1H; C3-*H*), 5.13 (dd, *J* = 1.9, 3.4 Hz, 1H; C6-*H*), 7.16–7.30 (m, 6H; Ar*H*), 7.49 (m, 1H; Ar*H*), 7.61 (m, 1H; Ar*H*), 8.25 (m, 1H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6, 23.8, 27.5, 27.7, 28.0, 28.1, 28.2, 32.1, 36.9, 40.1, 40.5, 74.0, 75.2, 76.8, 83.5, 84.0, 84.1, 85.3, 90.7, 103.9, 125.2, 126.0, 126.3, 128.4, 129.2, 129.7, 133.5, 134.4, 140.6, 147.0, 153.7, 165.1, 165.8, 168.6; IR (film): $\tilde{\nu}$ = 3457, 2978, 2934, 1738, 1591, 1566, 1514, 1456, 1395, 1370, 1333, 1279, 1256, 1155, 1119, 986 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{46}H_{65}NO_{16}NaSe$: 990.3366, found: 990.3367 [*M*$^+$+Na].

Tri-*tert*-butyl [1*S*,1(3*S*,4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-6-acetoxy-1-[4-acetoxy-5-methyl-3-[(2-nitrophenylseleno)methyl]-6-phenylhexyl]-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (100): Acetic anhydride (19 mg, 0.19 mmol) was added to a stirred solution of triol **99** (42.5 mg, 0.044 mmol) and DMAP (46 mg, 0.37 mmol) in CH_2Cl_2 (1 mL) at 0 °C. After stirring for 30 min, the reaction was quenched with 1 N aqueous KH_2PO_4 (5 mL), and the mixture was extracted with AcOEt (15 mL). The organic extract was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (51 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 5:1) to give diacetate **100** (45.3 mg, 98 %) as a yellow oil. $[\alpha]_D^{22} = -12.0$ (*c* = 1.14 in benzene); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.7 Hz, 3H; C5′-C*H*$_3$), 1.43 (s, 9H; $CO_2C(CH_3)_3$), 1.46 (s, 18H; 2 × $CO_2C(CH_3)_3$), 1.62 (s, 9H; $OCO_2C(CH_3)_3$), 1.80–1.90 (m, 3H; C2′-*H*$_2$, C5′-*H*), 2.01 (m, 1H; C3′-*H*), 2.10 (s, 3H; COC*H*$_3$), 2.16 (s, 3H; COC*H*$_3$), 2.30 (m, 2H; C1′-*H*$_2$), 2.38 (dd, *J* = 8.5, 13.5 Hz, 1H; C6′-*H*), 2.69 (dd, *J* = 6.0, 13.5 Hz, 1H; C6′-*H*), 2.87 (dd, *J* = 6.0, 11.4 Hz, 1H; C14′-*H*), 2.96 (dd, *J* = 5.5, 11.4 Hz, 1H; C14′-*H*), 4.07 (s, 1H; O*H*), 4.80 (d, *J* = 1.8 Hz, 1H; C7-*H*), 4.89 (s, 1H; C3-*H*), 5.00 (dd, *J* = 4.1, 7.5 Hz, 1H; C4′-*H*), 6.40 (d, *J* = 1.8 Hz, 1H; C6-*H*), 7.16–7.31 (m, 6H; Ar*H*), 7.51 (m, 2H; Ar*H*), 8.26 (m, 1H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.8, 20.7, 21.3, 24.6, 27.3, 27.6, 27.86, 27.94, 28.1, 32.1, 36.4, 38.6, 40.3, 73.9, 75.3, 76.3, 77.7, 83.2, 83.4, 83.7, 84.0, 86.2, 89.9, 103.5, 125.2, 126.0, 126.3, 128.3, 129.35, 129.39, 133.6, 134.6, 140.1, 146.9, 152.3, 164.0, 165.4, 168.4, 168.6, 170.9; IR (film): $\tilde{\nu}$ = 3453, 2980, 2934, 1746, 1591, 1566, 1516, 1456, 1372, 1333, 1279, 1155, 1119, 1038, 905 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{50}H_{69}NO_{18}NaSe$: 1074.3577, found: 1074.3568 [*M*$^+$+Na].

Tri-*tert*-butyl [1*S*,1(4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-6-acetoxy-1-(4-acetoxy-5-methyl-3-methylene-6-phenylhexyl)-7-(*tert*-butoxycarbonyl)oxy-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (101): 35 % Aqueous H_2O_2 (21 μL, 0.22 mmol) was added at 0 °C to a solution of selenide **100** (45.3 mg, 0.043 mmol) in THF (1 mL), and the mixture was stirred at room temperature for 4 h. The reaction mixture was partitioned between AcOEt (15 mL) and saturated aqueous $NaHCO_3$ (5 mL). 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 (46 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 5:1) to give alkene **101** (34.1 mg, 93 %) as a colorless oil. $[\alpha]_D^{22} = +14.2$ (*c* = 1.71 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.80 (d, *J* = 6.7 Hz, 3H; C5′-C*H*$_3$), 1.46 (s, 9H; $CO_2C(CH_3)_3$), 1.470 (s, 9H; $CO_2C(CH_3)_3$), 1.471 (s, 9H; $CO_2C(CH_3)_3$), 1.63 (s, 9H; $OCO_2C(CH_3)_3$), 2.085 (s, 3H; COC*H*$_3$), 2.091 (s, 3H; COC*H*$_3$), 2.11–2.14 (m, 3H; C1′-*H*$_2$, C5′-*H*), 2.33 (dd, *J* = 9.7, 13.4 Hz, 1H; C6′-*H*), 2.40 (m, 2H; C2′-*H*$_2$), 2.73 (dd, *J* = 5.0, 13.4 Hz, 1H; C6′-*H*), 4.10 (s, 1H; O*H*), 4.87 (d, *J* = 1.8 Hz, 1H; C7-*H*), 4.93 (s, 1H; C3-*H*), 4.98 (brs, 2H; C14′-*H*$_2$), 5.14 (d, *J* = 5.1 Hz, 1H; C4′-*H*), 6.42 (d, *J* = 1.8 Hz, 1H; C6-*H*), 7.15–7.28 (m, 5H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6, 20.7, 21.1, 25.3, 27.6, 27.86, 27.92, 28.1, 34.4, 36.6, 40.0, 73.9, 75.3, 76.2, 77.2, 79.3, 83.2, 83.3, 83.5, 84.0, 86.2, 89.9, 103.5, 111.5, 125.9, 128.2, 129.2, 140.4, 145.6, 152.3, 164.0, 165.5, 168.4, 168.6, 170.1; IR (film): $\tilde{\nu}$ = 3453, 2932, 2857, 1740, 1651, 1603, 1456, 1372, 1279, 1157, 1119, 1038, 936, 905, 843 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{44}H_{64}O_{16}Na$: 871.4092, found: 871.4086 [*M*$^+$+Na].

Tri-*tert*-butyl [1*S*,1(4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-1-(4-acetoxy-5-methyl-3-methylene-6-phenylhexyl)-7-(*tert*-butoxycarbonyl)oxy-4,6-dihydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (3): A 0.2 % solution of potassium carbonate in MeOH (1.0 mL) was added to diacetate **101** (34 mg, 0.04 mmol) at 0 °C. After stirring at room temperature for 1 h, the reaction was quenched with 0.3 N aqueous KH_2PO_4 (5 mL), and the mixture was partitioned between AcOEt (15 mL) and brine (5 mL). 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 (32 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 4:1) to give diol **3** (26.0 mg, 80 %) as a white foam. $[\alpha]_D^{22} = +3.86$ (*c* = 1.30 in $CHCl_3$) [lit. $[\alpha]_D^{27} = +1.6$ (*c* = 0.83 in $CHCl_3$);[14] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.81 (d, *J* = 6.7 Hz, 3H; C5′-C*H*$_3$), 1.45 (s, 9H; $CO_2C(CH_3)_3$), 1.50 (s, 18H; 2 × $CO_2C(CH_3)_3$), 1.59 (s, 9H; $OCO_2C(CH_3)_3$), 2.00–2.17 (m, 3H; C1′-*H*$_2$, C5′-*H*), 2.09 (s, 3H; COC*H*$_3$), 2.30–2.45 (m, 2H; C2′-*H*$_2$), 2.35 (dd, *J* = 9.4, 13.5 Hz, 1H; C6′-*H*), 2.72 (dd, *J* = 5.2, 13.5 Hz, 1H; C6′-*H*), 2.84 (d, *J* = 3.5 Hz, 1H; C6-O*H*), 3.97 (s, 1H; C4-O*H*), 4.65 (d, *J* = 1.9 Hz, 1H; C7-*H*), 4.73 (s, 1H; C3-*H*), 4.97 (brs, 2H; C14′-*H*$_2$), 5.12–5.14 (m, 2H; C6-*H*, C4′-*H*), 7.14–7.18 (m, 3H; Ar*H*), 7.24–7.27 (m, 2H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.6, 21.1, 25.4, 27.6, 27.97, 28.04, 28.1, 29.7, 33.9, 36.6, 40.0, 74.0, 75.3, 76.8, 77.2, 79.2, 83.2, 83.8, 83.9, 85.1, 85.6, 90.8, 103.6, 111.3, 125.9, 128.3, 129.2, 140.4, 145.6, 153.6, 165.1, 165.8, 168.5, 170.2; IR (film): $\tilde{\nu}$ = 3461, 2980, 2932, 1732, 1456, 1395, 1372, 1279, 1157, 1036, 990, 916, 845 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{42}H_{62}O_{15}Na$: 829.3986, found: 829.3979 [*M*$^+$+Na].

Tri-*tert*-butyl [1*S*,1(4*S*,5*R*),3*S*,4*S*,5*R*,6*R*,6(2*E*,4*S*,6*S*),7*R*]-1-(4-acetoxy-5-methyl-3-methylene-6-phenylhexyl)-7-(*tert*-butoxycarbonyl)oxy-6-(4,6-dimethyl-2-octenoyl)oxy-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (103): DCC (66 mg, 0.320 mmol) was added to a stirred solution of carboxylic acid **102** (55 mg, 0.320 mmol) in CH_2Cl_2 (1.5 mL), and the mixture was stirred for 30 min. The solution of DCC–carboxylic acid **102** in CH_2Cl_2 (0.5 mL) was added to a stirred solution of diol **3** (13.7 mg, 0.017 mmol) and DMAP (31 mg, 0.256 mmol) in CH_2Cl_2 (2 mL). After stirring for 5 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (6 mL), and the mixture was extracted with Et_2O/*n*-hexane 3:1 (15 mL). The organic extract was successively washed with saturated aqueous $NaHCO_3$ (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (52 mg), which was purified by column chromatography (silica gel 5 g, *n*-hexane/AcOEt 5:1) to give ester **103** (14.6 mg, 90 %) as a colorless oil. $[\alpha]_D^{22} = +29.9$ (*c* = 0.73 in $CHCl_3$) [lit. $[\alpha]_D^{25} = +38$ (*c* = 0.43 in $CHCl_3$);[14] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.80 (d, *J* = 6.7 Hz, 3H; C5′-C*H*$_3$), 0.82–0.89 (m, 6H; C8″-*H*$_3$, C6″-C*H*$_3$), 1.02 (d, *J* = 6.7 Hz, 3H; C4″-C*H*$_3$), 1.08–1.14 (m, 2H; C6″-*H*, C7″-*H*), 1.26–1.39 (m, 3H; C5″-*H*$_2$, C7″-*H*), 1.42 (s, 9H; $CO_2C(CH_3)_3$), 1.46 (s, 9H; $CO_2C(CH_3)_3$), 1.47 (s, 9H; $CO_2C(CH_3)_3$), 1.65 (s, 9H; $OCO_2C(CH_3)_3$), 2.09 (s, 3H; COC*H*$_3$), 2.11–2.16 (m, 3H; C1′-*H*$_2$, C5′-*H*), 2.33 (dd, *J* = 9.7, 13.4 Hz, 1H; C6′-*H*), 2.28–2.48 (m, 3H; C2′-*H*$_2$, C4″-*H*), 2.74 (dd, *J* = 4.9, 13.4 Hz, 1H; C6′-*H*), 4.08 (brs, 1H; O*H*), 4.92 (d, *J* = 1.7 Hz, 1H; C7-*H*), 4.98 (brs, 2H; C14′-*H*$_2$), 4.99 (s, 1H; C3-*H*), 5.15 (d, *J* = 5.1 Hz, 1H; C4′-*H*), 5.79 (d, *J* = 15.7 Hz, 1H; C2″-*H*), 6.51 (d, *J* = 1.7 Hz, 1H; C6-*H*), 6.91 (dd, *J* = 8.1, 15.7 Hz, 1H; C3″-*H*), 7.15–7.18 (m, 3H; Ar*H*), 7.24–7.27 (m, 2H; Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 11.1, 13.6, 18.9, 19.2, 20.0, 21.1, 25.2, 27.6, 27.9, 27.96, 27.99, 28.1, 29.6, 31.6, 31.7, 32.7, 34.3, 34.7, 36.6, 40.0, 43.3, 73.8, 74.0, 75.4, 75.8, 79.5, 83.25, 83.29, 83.31, 83.5, 84.1, 86.2, 90.1, 103.5, 111.5, 118.7, 125.9, 128.2, 129.2, 140.4, 145.7, 152.1, 156.5, 163.6, 164.3, 165.6, 168.7, 170.1; IR (film): $\tilde{\nu}$ = 3455, 2975, 2934, 2876, 1740, 1651, 1456, 1395, 1372, 1279, 1256, 1159, 1119, 1032, 992, 949, 912 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{52}H_{78}O_{16}Na$: 981.5188, found: 981.5197 [*M*$^+$+Na].

Zaragozic acid A (1): Trifluoroacetic acid (2.2 mL) was added to a stirred solution of fully protected zaragozic acid A **103** (13.9 mg, 14.5 μmol) in CH_2Cl_2 (6.5 mL). After stirring 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 A (**1**, 9.0 mg, 90 %) as a white film. $[\alpha]_D^{22} = +33.9$ (*c* = 0.45 in MeOH) [lit. $[\alpha]_D^{25} = +37$ (*c* = 1.29 in MeOH),[3c,d] $[\alpha]_D^{20} = +10.7$ (*c* = 1.0 in $CHCl_3$),[4a] $[\alpha]_D^{22} = +18.3$ (*c* = 0.60 in $CHCl_3$),[9d] $[\alpha]_D^{25} = +36$ (*c* = 0.28 in MeOH);[14] ^{1}H NMR (400 MHz, CD_3OD): δ = 0.82–0.91 (m, 9H; C5′-C*H*$_3$, C8″-*H*$_3$, C6″-C*H*$_3$), 1.02 (d, *J* = 6.8 Hz, 3H; C4″-C*H*$_3$), 1.06–1.15 (m, 2H; C5″-*H*, C7″-*H*), 1.28–1.41 (m, 3H; C5″-*H*, C6″-*H*, C7″-*H*), 2.02 (m, 2H; C1′-*H*$_2$), 2.09 (s, 3H; COC*H*$_3$), 2.23 (m,

1H; C5′-*H*), 2.43 (dd, $J=8.7$, 13.4 Hz, 1H; C6′-*H*), 2.34–2.45 (m, 3H; C2′-H_2, C4″-*H*), 2.66 (dd, $J=6.1$, 13.4 Hz, 1H; C6′-*H*), 4.03 (d, $J=1.9$ Hz, 1H; C7-*H*), 4.96 (brs, 1H; C14′-*H*), 5.01 (brs, 1H; C14′-*H*), 5.07 (d, $J=$ 4.5 Hz, 1H; C4′-*H*), 5.26 (s, 1H; C3-*H*), 5.79 (d, $J=15.8$ Hz, 1H; C2″-*H*), 6.30 (d, $J=1.9$ Hz, 1H; C6-*H*), 6.84 (dd, $J=8.1$, 15.8 Hz, 1H; C3″-*H*), 7.11–7.26 (m, 5H; Ar*H*); ^{13}C NMR (100.6 MHz, CD_3OD): $\delta=11.6$, 14.3, 19.3, 20.6, 21.0, 26.6, 30.9, 33.3, 35.1, 35.7, 37.8, 41.0, 44.5, 75.6, 76.6, 80.1, 81.1, 82.6, 91.2, 106.8, 111.5, 119.9, 126.9, 129.3, 130.1, 141.6, 147.7, 157.4, 166.5, 168.5, 170.2, 172.0, 172.5; IR (film): $\tilde{\nu}=3443$, 2962, 2928, 1736, 1649, 1456, 1372, 1254, 1144, 1022, 841, 747, 700 cm^{-1}; HR-MS (FAB): *m*/*z*: calcd for $C_{35}H_{45}O_{14}$: 689.2809, found: 689.2833 [M^+–H].

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[1] For reviews, see: a) J. D. Bergstrom, C. Dufresne, G. F. Bills, M. Nallin-Omstead, K. Byrne, *Annu. Rev. Microbiol.* **1995**, *49*, 607–639; b) S. A. Biller, K. Neuenschwander, M. M. Ponpipom, C. D. Poulter, *Curr. Pharm. Des.* **1996**, *2*, 1–40; c) N. S. Watson, P. A. Procopiou, *Prog. Med. Chem.* **1996**, *36*, 331–378.

[2] a) J. B. Gibbs, D. L. Pompliano, S. D. Mosser, E. Rands, R. B. Lingham, S. B. Singh, E. M. Scolnick, N. E. Kohl, A. Oliff, *J. Biol. Chem.* **1993**, *268*, 7617–7620; b) C. Dufresne, K. E. Wilson, S. B. Singh, D. L. Zink, J. D. Bergstrom, D. Rew, J. D. Polishook, M. Meinz, L. Huang, K. C. Silverman, R. B. Lingham, M. Mojena, C. Cascales, F. Pelaéz, J. B. Gibbs, *J. Nat. Prod.* **1993**, *56*, 1923–1929.

[3] a) K. E. Wilson, R. M. Burk, T. Biftu, R. G. Ball, K. Hoogsteen, *J. Org. Chem.* **1992**, *57*, 7151–7158; b) C. Dufresne, K. E. Wilson, D. Zink, J. Smith, J. D. Bergstrom, M. Kurtz, D. Rew, M. Nallin, R. Jenkins, K. Bartizal, C. Trainor, G. Bills, M. Meinz, L. Huang, J. Onishi, J. Milligan, M. Mojena, F. Pelaez, *Tetrahedron* **1992**, *48*, 10221–10226; c) J. D. Bergstrom, M. M. Kurtz, D. J. Rew, A. M. Amend, J. D. Karkas, R. G. Bostedor, V. S. Bansal, C. Dufresne, F. L. VanMiddlesworth, O. D. Hensens, J. M. Liesch, D. L. Zink, K. E. Wilson, J. Onishi, J. A. Milligan, G. Bills, L. Kaplan, M. Nallin Omstead, R. G. Jenkins, L. Huang, M. S. Meinz, L. Quinn, R. W. Burg, Y. L. Kong, S. Mochales, M. Mojena, I. Martin, F. Pelaez, M. T. Diez, A. W. Alberts, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 80–84; d) O. D. Hensens, C. Dufresne, J. M. Liesch, D. L. Zink, R. A. Reamer, F. VanMiddlesworth, *Tetrahedron Lett.* **1993**, *34*, 399–402; e) C. Santini, R. G. Ball, G. D. Berger, *J. Org. Chem.* **1994**, *59*, 2261–2266.

[4] a) M. J. Dawson, J. E. Farthing, P. S. Marshall, R. F. Middleton, M. J. O'Neill, A. Shuttleworth, C. Stylli, R. M. Tait, P. M. Taylor, H. G. Wildman, A. D. Buss, D. Langley, M. V. Hayes, *J. Antibiot.* **1992**, *45*, 639–647; b) P. J. Sidebottom, R. M. Highcock, S. J. Lane, P. A. Procopiou, N. S. Watson, *J. Antibiot.* **1992**, *45*, 648–658; c) W. M. Blows, G. Foster, S. J. Lane, D. Noble, J. E. Piercey, P. J. Sidebottom, G. Webb, *J. Antibiot.* **1994**, *47*, 740–754.

[5] K. Hasumi, K. Tachikawa, K. Sakai, S. Murakawa, N. Yoshikawa, S. Kumazawa, A. Endo, *J. Antibiot.* **1993**, *46*, 689–691.

[6] For reviews, see: a) U. Koert, *Angew. Chem.* **1995**, *107*, 849–855; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 773–778; b) A. Nadin, K. C. Nicolaou, *Angew. Chem.* **1996**, *108*, 1732–1766; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1622–1656; c) N. Jotterand, P. Vogel, *Curr. Org. Chem.* **2001**, *5*, 637–661; d) A. Armstrong, T. J. Blench, *Tetrahedron* **2002**, *58*, 9321–9349.

[7] a) H. Abdel-Rahman, J. P. Adams, A. L. Boyes, M. J. Kelly, D. J. Mansfield, P. A. Procopiou, S. M. Roberts, D. H. Slee, N. S. Watson, *J. Chem. Soc. Chem. Commun.* **1993**, 1839–1841; b) H. Abdel-Rahman, J. P. Adams, A. L. Boyes, M. J. Kelly, D. J. Mansfield, P. A. Procopiou, S. M. Roberts, D. H. Slee, P. J. Sidebottom, V. Sik, N. S. Watson, *J. Chem. Soc. Chem. Commun.* **1993**, 1841–1843; c) V. K. Aggarwal, M. F. Wang, A. Zaparucha, *J. Chem. Soc. Chem. Commun.* **1994**, 87–88; d) L. M. McVinish, M. A. Rizzacasa, *Tetrahedron Lett.* **1994**, *35*, 923–926; e) R. W. Gable, L. M. McVinish, M. A. Rizzacasa, *Aust. J. Chem.* **1994**, *47*, 1537–1544; f) H. Abdel-Rahman, J. P. Adams, A. L. Boyes, M. J. Kelly, R. B. Lamont, D. J. Mansfield, P. A. Procopiou, S. M. Roberts, D. H. Slee, N. S. Watson, *J. Chem. Soc. Perkin Trans. 1* **1994**, 1259–1261; g) H. Koyama, R. G. Ball, G. D. Berger, *Tetrahedron Lett.* **1994**, *35*, 9185–9188; h) G. A. Kraus, H. Maeda, *J. Org. Chem.* **1995**, *60*, 2–3; i) S. Caron, A. I. McDonald, C. H. Heathcock, *J. Org. Chem.* **1995**, *60*, 2780–2785; j) M. K. Gurjar, S. K. Das, K. S. Sadalapure, *Tetrahedron Lett.* **1995**, *36*, 1933–1936; k) M. K. Gurjar, S. K. Das, A. C. Kunwar, *Tetrahedron Lett.* **1995**, *36*, 1937–1940; l) R. H. Schlessinger, X.-H. Wu, T. R. R. Pettus, *Synlett* **1995**, 536–538; m) A. Armstrong, P. A. Barsanti, *Synlett* **1995**, 903–906; n) A. Shimizu, K. Ohmori, S. Ohba, S. Nishiyama, S. Yamamura, *Carbohydr. Lett.* **1996**, *1*, 433–440; o) D. M. Hodgson, J. M. Bailey, T. Harrison, *Tetrahedron Lett.* **1996**, *37*, 4623–4626; p) N. Maezaki, H. J. M. Gijsen, L.-Q. Sun, L. A. Paquette, *J. Org. Chem.* **1996**, *61*, 6685–6692; q) K. D. Freeman-Cook, R. L. Halcomb, *Tetrahedron Lett.* **1996**, *37*, 4883–4886; r) I. Paterson, K. Feßner, M. R. V. Finlay, M. F. Jacobs, *Tetrahedron Lett.* **1996**, *37*, 8803–8806; s) Y. Xu, C. R. Johnson, *Tetrahedron Lett.* **1997**, *38*, 1117–1120; t) I. Paterson, K. Feßner, M. R. V. Finlay, *Tetrahedron Lett.* **1997**, *38*, 4301–4304; u) S. G. Hegde, D. C. Myles, *Tetrahedron* **1997**, *53*, 11179–11190; v) S. G. Hegde, D. C. Myles, *Tetrahedron Lett.* **1997**, *38*, 4329–4332; w) H. Ito, M. Matsumoto, T. Yoshizawa, K. Takao, S. Kobayashi, *Tetrahedron Lett.* **1997**, *38*, 9009–9012; x) J. B. Brogan, C. K. Zercher, *Tetrahedron Lett.* **1998**, *39*, 1691–1694; y) R. K. Mann, J. G. Parsons, M. A. Rizzacasa, *J. Chem. Soc. Perkin Trans. 1* **1998**, 1283–1293; z) A. M. Reid, P. G. Steel, *J. Chem. Soc. Perkin Trans. 1* **1998**, 2795–2801; aa) P. Fraisse, I. Hanna, J.-Y. Lallemand, *Tetrahedron Lett.* **1998**, *39*, 7853–7856; ab) K. D. Freeman-Cook, R. L. Halcomb, *Tetrahedron Lett.* **1998**, *39*, 8567–8570; ac) M. Tsubuki, H. Okita, T. Honda, *Synlett* **1998**, 1417–1419; ad) M. A. Calter, P. M. Sugathapala, *Tetrahedron Lett.* **1998**, *39*, 8813–8816; ae) K. Tomooka, M. Kikuchi, K. Igawa, P.-H. Keong, T. Nakai, *Tetrahedron Lett.* **1999**, *40*, 1917–1920; af) H. Koshimizu, T. Baba, T. Yoshimitsu, H. Nagaoka, *Tetrahedron Lett.* **1999**, *40*, 2777–2780; ag) C. Taillefumier, M. Lakhrissi, Y. Chapleur, *Synlett* **1999**, 697–700; ah) P. J. Parsons, T. Montagnon, M. Giles, P. Hitchcock, *Synlett* **1999**, 1407–1408; ai) P. Fraisse, I. Hanna, J.-Y. Lallemand, T. Prangé, L. Ricard, *Tetrahedron* **1999**, *55*, 11819–11832; aj) G. D. Fallon, E. D. Jones, P. Perlmutter, W. Selajarern, *Tetrahedron Lett.* **1999**, *40*, 7435–7438; ak) P. Perlmutter, W. Selajarern, *Aust. J. Chem.* **2000**, *53*, 349–353; al) D. M. Hodgson, C. Villalonga-Barber, *Tetrahedron Lett.* **2000**, *41*, 5597–5600; am) K. D. Freeman-Cook, R. L. Halcomb, *J. Org. Chem.* **2000**, *65*, 6153–6159; an) D. M. Hodgson, J. M. Bailey, C. Villalonga-Barber, M. G. B. Drew, T. Harrison, *J. Chem. Soc. Perkin Trans. 1* **2000**, 3432–3443; ao) D. J. Wardrop, A. I. Velter, R. E. Forslund, *Org. Lett.* **2001**, *3*, 2261–2264; ap) M. A. Calter, C. Zhu, R. J. Lachicotte, *Org. Lett.* **2002**, *4*, 209–212; aq) A. Armstrong, P. A. Barsanti, T. J. Blench, R. Ogilvie, *Tetrahedron* **2003**, *59*, 367–375; ar) A. Bierstedt, J. Roels, J. Zhang, Y. Wang, R. Fröhlich, P. Metz, *Tetrahedron Lett.* **2003**, *44*, 7867–7870; as) P. Perlmutter, W. Selajerern, F. Vounatsos, *Org. Biomol. Chem.* **2004**, *2*, 2220–2228; at) M. Tsubuki, H. Okita, T. Honda, *Heterocycles* **2006**, *67*, 731–748.

[8] a) E. M. Carreira, J. Du Bois, *J. Am. Chem. Soc.* **1994**, *116*, 10825–10826; b) E. M. Carreira, J. Du Bois, *J. Am. Chem. Soc.* **1995**, *117*, 8106–8125.

[9] a) K. C. Nicolaou, E. W. Yue, Y. Naniwa, F. De Riccardis, A. Nadin, J. E. Leresche, S. La Greca, Z. Yang, *Angew. Chem.* **1994**, *106*, 2306–2309; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2184–2187;

b) K. C. Nicolaou, A. Nadin, J. E. Leresche, S. La Greca, T. Tsuri, E. W. Yue, Z. Yang, *Angew. Chem.* **1994**, *106*, 2309–2312; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2187–2190; c) K. C. Nicolaou, A. Nadin, J. E. Leresche, E. W. Yue, S. La Greca, *Angew. Chem.* **1994**, *106*, 2312–2313; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2190–2191; d) K. C. Nicolaou, E. W. Yue, S. La Greca, A. Nadin, Z. Yang, J. E. Leresche, T. Tsuri, Y. Naniwa, F. De Riccardis, *Chem. Eur. J.* **1995**, *1*, 467–494.

[10] D. A. Evans, J. C. Barrow, J. L. Leighton, A. J. Robichaud, M. Sefkow, *J. Am. Chem. Soc.* **1994**, *116*, 12111–12112.

[11] a) D. Stoermer, S. Caron, C. H. Heathcock, *J. Org. Chem.* **1996**, *61*, 9115–9125; b) S. Caron, D. Stoermer, A. K. Mapp, C. H. Heathcock, *J. Org. Chem.* **1996**, *61*, 9126–9134.

[12] a) H. Sato, S. Nakamura, N. Watanabe, S. Hashimoto, *Synlett* **1997**, 451–454; b) S. Nakamura, H. Sato, Y. Hirata, N. Watanabe, S. Hashimoto, *Tetrahedron* **2005**, *61*, 11078–11106.

[13] a) A. Armstrong, L. H. Jones, P. A. Barsanti, *Tetrahedron Lett.* **1998**, *39*, 3337–3340; b) A. Armstrong, P. A. Barsanti, L. H. Jones, G. Ahmed, *J. Org. Chem.* **2000**, *65*, 7020–7032.

[14] K. Tomooka, M. Kikuchi, K. Igawa, M. Suzuki, P.-H. Keong, T. Nakai, *Angew. Chem.* **2000**, *112*, 4676–4679; *Angew. Chem. Int. Ed.* **2000**, *39*, 4502–4505.

[15] 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: a) S. F. Martin, S. Naito, *J. Org. Chem.* **1998**, *63*, 7592–7593; b) S. Naito, M. Escobar, P. R. Kym, S. Liras, S. F. Martin, *J. Org. Chem.* **2002**, *67*, 4200–4208.

[16] For reviews, see: a) A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, *96*, 223–269; b) M. C. McMills, D. Wright, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry toward Heterocycles and Natural Products* (Eds.: A. Padwa, W. H. Pearson), Wiley, New York, **2002**, pp. 253–314; c) G. Mehta, S. Muthusamy, *Tetrahedron* **2002**, *58*, 9477–9504; d) A. Padwa, *Helv. Chim. Acta* **2005**, *88*, 1357–1374.

[17] K. Ueda, T. Ibata, M. Takebayashi, *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2779–2782.

[18] A. Padwa, G. E. Fryxell, L. Zhi, *J. Am. Chem. Soc.* **1990**, *112*, 3100–3109.

[19] For recent studies on the synthesis of bioactive molecules via a carbonyl ylide cycloaddition strategy, see: a) A. Padwa, M. A. Brodney, J. P. Marino, Jr., S. M. Sheehan, *J. Org. Chem.* **1997**, *62*, 78–87; b) B. Jauk, F. Belaj, C. O. Kappe, *J. Chem. Soc. Perkin Trans. 1* **1999**, 307–314; c) C. S. Straub, A. Padwa, *Org. Lett.* **1999**, *1*, 83–85; d) J. E. Baldwin, A. V. W. Mayweg, K. Neumann, G. J. Pritchard, *Org. Lett.* **1999**, *1*, 1933–1935; e) J. L. Wood, B. D. Thompson, N. Yusuff, D. A. Pflum, M. S. P. Matthäus, *J. Am. Chem. Soc.* **2001**, *123*, 2097–2098; f) F. Liu, D. J. Austin, *Org. Lett.* **2001**, *3*, 2273–2276; g) T. Graening, W. Friedrichsen, J. Lex, H.-G. Schmalz, *Angew. Chem.* **2002**, *114*, 1594–1597; *Angew. Chem. Int. Ed.* **2002**, *41*, 1524–1526; h) D. M. Hodgson, T. D. Avery, A. C. Donohue, *Org. Lett.* **2002**, *4*, 1809–1811; i) B. Chen, R. Y. Y. Ko, M. S. M. Yuen, K.-F. Cheng, P. Chiu, *J. Org. Chem.* **2003**, *68*, 4195–4205; j) D. M. Hodgson, F. Le Strat, T. D. Avery, A. C. Donohue, T. Brückl, *J. Org. Chem.* **2004**, *69*, 8796–8803; k) T. Graening, V. Bette, J. Neudorfl, J. Lex, H.-G. Schmalz, *Org. Lett.* **2005**, *7*, 4317–4320; l) H. Oguri, S. L. Schreiber, *Org. Lett.* **2005**, *7*, 47–50; m) J. M. Mejía-Oneto, A. Padwa, *Org. Lett.* **2006**, *8*, 3275–3278; n) Z. Geng, B. Chen, P. Chiu, *Angew. Chem.* **2006**, *118*, 6343–6347; *Angew. Chem. Int. Ed.* **2006**, *45*, 6197–6201; o) S. Nakamura, Y. Sugano, F. Kikuchi, S. Hashimoto, *Angew. Chem.* **2006**, *118*, 6682–6685; *Angew. Chem. Int. Ed.* **2006**, *45*, 6532–6535.

[20] For preliminary communications on the carbonyl ylide cycloaddition approach to zaragozic acid C, see: a) O. Kataoka, S. Kitagaki, N. Watanabe, J. Kobayashi, S. Nakamura, M. Shiro, S. Hashimoto, *Tetrahedron Lett.* **1998**, *39*, 2371–2374; b) S. Nakamura, Y. Hirata, T. Kurosaki, M. Anada, O. Kataoka, S. Kitagaki, S. Hashimoto, *Angew. Chem.* **2003**, *115*, 5509–5513; *Angew. Chem. Int. Ed.* **2003**, *42*, 5351–5355.

[21] Independent of our study, the two groups of Koyama[7g] and Hodgson[7o,al,an] pursued carbonyl ylide cycloaddition-based strategies en route to this class of natural products.

[22] After the publication of our preliminary communication,[20a] reports on the use of α-diazo esters as carbonyl ylide precursors emerged from the Padwa laboratory: A. Padwa, Z. J. Zhang, L. Zhi, *J. Org. Chem.* **2000**, *65*, 5223–5232.

[23] A. Padwa, S. F. Hornbuckle, G. E. Fryxell, P. D. Stull, *J. Org. Chem.* **1989**, *54*, 817–824.

[24] E. Abushanab, P. Vemishetti, R. W. Leiby, H. K. Singh, A. B. Mikkilineni, D. C.-J. Wu, R. Saibaba, R. P. Panzica, *J. Org. Chem.* **1988**, *53*, 2598–2602.

[25] a) N. Nakajima, K. Horita, R. Abe, O. Yonemitsu, *Tetrahedron Lett.* **1988**, *29*, 4139–4142; b) K. K. Reddy, M. Saady, J. R. Falck, G. Whited, *J. Org. Chem.* **1995**, *60*, 3385–3390.

[26] Carboxylic acid **16** was prepared in 52% yield from methyl 3-hydroxypropionate[27] by the following two-step sequence: 1) $H_2C(OMe)_2$, P_2O_5, $CHCl_3$, 10 h;[28] 2) LiOH, THF/H_2O 2:1, 2 h.

[27] T. Ogawa, A. Nakazato, M. Sato, K. Hatayama, *Synthesis* **1990**, 459–460.

[28] K. Fuji, S. Nakano, E. Fujita, *Synthesis* **1975**, 276–277.

[29] a) Y. Oikawa, T. Yoshioka, O. Yonemitsu, *Tetrahedron Lett.* **1982**, *23*, 885–888; b) K. Horita, T. Yoshioka, T. Tanaka, Y. Oikawa, O. Yonemitsu, *Tetrahedron* **1986**, *42*, 3021–3028.

[30] a) D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155–4156; b) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287.

[31] a) E. Wenkert, C. A. McPherson, *J. Am. Chem. Soc.* **1972**, *94*, 8084–8090; b) U. Schöllkopf, B. Bánhidai, H. Frasnelli, R. Meyer, H. Beckhaus, *Liebigs Ann. Chem.* **1974**, 1767–1783.

[32] J. Mulzer, B. Schöllhorn, *Angew. Chem.* **1990**, *102*, 433–435; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 431–432.

[33] For a review, see: G. R. Krow, *Org. React.* **1993**, *43*, 251–798.

[34] Molecular orbital calculations were performed by the CAChe Worksystem after geometry optimization using MM2 (molecular mechanics) followed by MOPAC with AM1 parameters.

[35] G. Uray, W. Lindner, *Tetrahedron* **1988**, *44*, 4357–4362.

[36] a) N. Nagashima, M. Ohno, *Chem. Lett.* **1987**, 141–144; b) N. Nagashima, M. Ohno, *Chem. Pharm. Bull.* **1991**, *39*, 1972–1982.

[37] In this case it would be preferable to obtain 1,2-diol **51**; however, reduction of **48** under the Saito conditions ($BH_3{\cdot}SMe_2$, $NaBH_4$, THF) did not work: a) S. Saito, T. Hasegawa, M. Inaba, R. Nishida, T. Fujii, S. Nomizu, T. Moriwake, *Chem. Lett.* **1984**, 1389–1392; b) S. Saito, T. Ishikawa, A. Kuroda, K. Koga, T. Moriwake, *Tetrahedron* **1992**, *48*, 4067–4086.

[38] The reaction of α-diazo ester **8** with 3-butyn-2-one (**40**) in refluxing benzene in the absence of rhodium(II) catalyst proceeded to completion within 10 h to provide pyrazole **61** in 82% yield.

[39] a) G. A. Kraus, M. J. Taschner, *J. Org. Chem.* **1980**, *45*, 1175–1176; b) B. S. Bal, W. E. Childers, Jr., H. W. Pinnick, *Tetrahedron* **1981**, *37*, 2091–2096.

[40] L. J. Mathias, *Synthesis* **1979**, 561–576.

[41] S. Hanessian, D. Delorme, Y. Dufresne, *Tetrahedron Lett.* **1984**, *25*, 2515–2518.

[42] P. R. Blakemore, W. J. Cole, P. J. Kocienski, A. Morley, *Synlett* **1998**, 26–28. For a review, see: P. R. Blakemore, *J. Chem. Soc. Perkin Trans. 1* **2002**, 2563–2585.

[43] H. E. Blackwell, D. J. O'Leary, A. K. Chatterjee, R. A. Washenfelder, D. A. Bussmann, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 58–71. For reviews, see: a) S. J. Connon, S. Blechert, *Angew. Chem.* **2003**, *115*, 1944–1968; *Angew. Chem. Int. Ed.* **2003**, *42*, 1900–1923; b) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem.* **2005**, *117*, 4564–4601; *Angew. Chem. Int. Ed.* **2005**, *44*, 4490–4527.

[44] H. Sato, J. Kitaguchi, S. Nakamura, S. Hashimoto, *Chem. Pharm. Bull.* **1998**, *46*, 1816–1819.

[45] L. Alcaraz, J. J. Harnett, C. Mioskowski, J. P. Martel, T. Le Gall, D.-S. Shin, J. R. Falck, *Tetrahedron Lett.* **1994**, *35*, 5449–5452.

[46] S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

[47] H. Wakamatsu, S. Blechert, *Angew. Chem.* **2002**, *114*, 2509–2511; *Angew. Chem. Int. Ed.* **2002**, *41*, 2403–2405.

[48] Grubbs and co-workers proposed a categorization of olefins based on relative rates of homodimerization: A. K. Chatterjee, T.-L. Choi, D. P. Sanders, R. H. Grubbs, *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370. Given the reluctance of **79** to undergo homodimerization, **79** is undoubtedly a Type III olefin. On the other hand, the formation of homodimers **88** and **89** that did not undergo secondary metathesis revealed that alkenes **81** and **82** would be categorized as type II.

[49] a) H. Nishiyama, T. Kitajima, M. Matsumoto, K. Itoh, *J. Org. Chem.* **1984**, *49*, 2298–2300; b) G. Stork, M. Kahn, *J. Am. Chem. Soc.* **1985**, *107*, 500–501; For a review on intramolecular reactions of silicon-tethered molecules, see: L. Fensterbank, M. Malacria, S. M. Sieburth, *Synthesis* **1997**, 813–854.

[50] a) K. Tamao, N. Ishida, M. Kumada, *J. Org. Chem.* **1983**, *48*, 2120–2122; b) K. Tamao, N. Ishida, T. Tanaka, M. Kumada, *Organometallics* **1983**, *2*, 1694–1696; c) K. Tamao, N. Ishida, *J. Organomet. Chem.* **1984**, *269*, C37–C39; for a review on oxidation of the C–Si bond, see: G. R. Jones, Y. Landais, *Tetrahedron* **1996**, *52*, 7599–7662.

[51] P. A. Grieco, S. Gilman, M. Nishizawa, *J. Org. Chem.* **1976**, *41*, 1485–1486.

[52] S. Nakamura, J. Inagaki, J. Kitaguchi, K. Tatani, S. Hashimoto, *Chem. Pharm. Bull.* **1999**, *47*, 1330–1333.

[53] After submission of this manuscript, a formal synthesis of zaragozic acid C was published: J. O. Bunte, A. N. Cuzzupe, A. M. Daly, M. A. Rizzacasa, *Angew. Chem.* **2006**, *118*, 6524–6528; *Angew. Chem. Int. Ed.* **2006**, *45*, 6376–6380.

[54] R. E. Ireland, L. Liu, *J. Org. Chem.* **1993**, *58*, 2899.

[55] J. Levisalles, *Bull. Soc. Chim. Fr.* **1957**, 997–1003.

[56] M. Yamaura, T. Suzuki, H. Hashimoto, J. Yoshimura, T. Okamoto, C. Shin, *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1413–1420.

[57] M. Regitz, J. Hocker, A. Liedhegener, *Org. Synth.* **1968**, *48*, 36–40.

[58] A. Pelter, K. Smith, H. C. Brown, *Borane Reagents*, Academic Press, London, **1988**, pp. 413–414.

[59] a) H. Bauer, *Ber.* **1913**, *46*, 92–98; b) K. B. Sharpless, M. W. Young, *J. Org. Chem.* **1975**, *40*, 947–949.

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