Pergamon

SCIENCE DIRECT®

Tetrahedron: *Asymmetry* 14 (2003) 201–215

TETRAHEDRON: *ASYMMETRY*

Synthesis of optically active 1,3-dioxin-4-one derivatives having a hydroxymethyl group at the 2-position and their use for regio-, diastereo-, and enantioselective synthesis of substituted cyclobutanols☆

Masayuki Murakami,[a] Hiroshi Kamaya,[b] Chikara Kaneko[c] and Masayuki Sato[d,*]

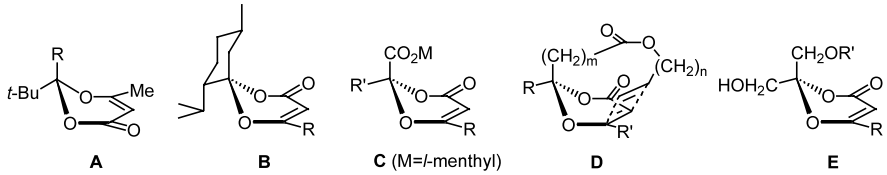
[a]*Process Development Laboratories, Sankyo Co., Ltd., 1-12-1 Shinomiya, Hiratsuka 254-8560, Japan*
[b]*Medicinal Chemistry Department, Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd., 2-2-5-Kawagishi, Toda 335-8505, Japan*
[c]*Emeritus Professor of Tohoku and Kanazawa Universities, 2-35-19 Yagiyama-Honcho, Taihaku-ku, Sendai 982-0801, Japan*
[d]*School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Shizuoka 422-8526, Japan*

Received 18 September 2002; accepted 11 November 2002

Abstract—A new method for preparing optically active 1,3-dioxin-4-one derivatives is presented. A series of prochiral 2,2-bis(hydroxymethyl)-1,3-dioxin-4-ones was synthesized by [4+2]cycloaddition of acylketene to protected 1,3-dihydroxy-2-propanone derivatives followed by deprotection of the hydroxyl groups. Desymmetrization of the prochiral dioxinones by lipase-catalyzed monoacetylation afforded optically active 2-(hydroxymethyl)dioxinones. Intramolecular photo[2+2]cycloaddition of ω-alkenyl esters of these alcohols provided an efficient method for regio-, diastereo-, and enantioselective synthesis of cyclobutanols. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Optically active 1,3-dioxin-4-one derivatives having a stereogenic center at the 2-position (**A**,[1] **B**,[2,3] and **C**[4]) are useful intermediates for the enantioselective synthesis of numerous types of biologically active compounds, since the enone moiety shows excellent diastereofacial selectivity in a variety of addition reactions and the dioxane ring in the addition products can be readily cleaved owing to its acetal structure.[5] So far, these dioxinones have been prepared by a chirality transfer method starting from (*R*)- or (*S*)-3-hydroxybutanoic acid,[1] a diastereomer separation method using chiral ketones[2–4] or resolution of racemic compounds by HPLC with chiral columns.[6] However, it is highly desirable to develop a new and more efficient method for the preparation of enantiomerically pure or enriched dioxinones in view of the synthetic potential of this class of compounds. Previously, we reported a regio- and stereocontrolled synthesis of cyclobutanol derivatives by intramolecular photo[2+2]cycloaddition of dioxinone (**D**: racemic) in which the alkene part is tethered by readily cleavable ester linkage.[7] In this context, our attention was focused on developing a new method for preparing optically active dioxinones having a functional group at the 2-position. Herein, we report the enantioselective synthesis of 2-(hydroxymethyl)dioxinones (**E**) by lipase-catalyzed monoacetylation of prochiral substrates[8] and the use of **E** as chiral enones in the regio-, diastereo-, and enantioselective synthesis of cyclobutanols by intramolecular photo[2+2]-cycloaddition.



☆ Use of 1,3-dioxin-4-ones and related compounds in synthesis, Part 50. Part 49: Sato, M.; Uehara, F.; Sato, K.; Yamaguchi, M.; Kabuto, C. *J. Am. Chem. Soc.* **1999**, *121*, 8270–8276.

* Corresponding authors. Tel./fax: +81-54-264-5754; e-mail: msato@u-shizuoka-ken.ac.jp

0957-4166/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
PII: S0957-4166(02)00760-7

2. Results and discussion

2.1. Synthesis of prochiral dioxinones

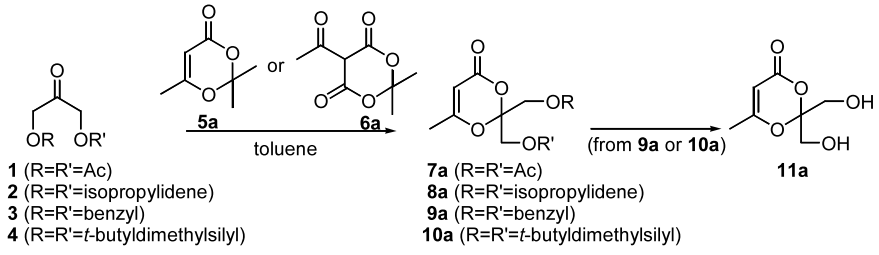
Initially, we examined various protecting groups to synthesize the prochiral 6-methylated dioxinone **11a**. Four protected 1,3-dihydroxy-2-propanones **1**–**4** prepared according to known methods[9–12] were converted to their corresponding dioxinones **7a**–**10a** by reaction with the acetylketene generated from 2,2,6-trimethyl-1,3-dioxin-4-one **5a**[13] or the acetylated Meldrum's acid **6a**[14] in refluxing toluene. The desired dioxinones **7a**–**10a** were obtained in good yields. It was difficult to obtain the requisite alcohol **11a** from **7a** and **8a** because **11a** was unstable under the deprotection conditions (K_2CO_3–methanol or heating in aqueous HCl). The removal of the benzyl and *tert*-butyldimethylsilyl groups in **9a** and **10a** was successful with $H_2/Pd(OH)_2$–C in methanol–chloroform and with trifluoroacetic acid in methanol, respectively, and crystalline **11a** was obtained without further chromatographic purification (Scheme 1).

We next studied the synthesis of the prochiral 6-unsubsituted dioxinone **11b**. The protected 1,3-dihydroxy-2-propanones **3** and **4** were converted to dioxinones **9b** and **10b**, respectively, by the reaction of formylketene generated from formylated Meldrum's acid **6b**[15] in refluxing toluene in good yields. Upon treatment with trifluoroacetic acid in methanol, compound **10b** afforded **11b**. This compound, which is somewhat unstable at room temperature, was purified using a cooled silica gel column. Synthesis of **11b** from dibenzyl derivative **9b** was unsuccessful because the desired hydrogenolytic cleavage of the benzyl groups was accompanied with hydrogenation of the dioxinone C–C double bond also occurred under the hydrogenolysis conditions.

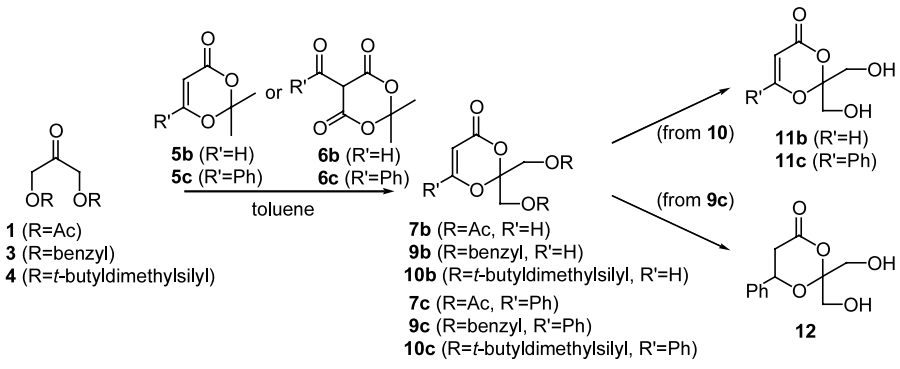
Hydroxyl-protected 6-phenyl dioxinones **9c** and **10c** were prepared by the reaction of the corresponding ketones (**3** or **4**) and benzoylketene generated from the benzoylated Meldrum's acid **6c**[16] or 2,2-dimethyl-6-phenyl-1,3-dioxin-4-one **5c**,[17] respectively. Desilylation of **10c** afforded diol **11c**. Synthesis of **11c** from **9c** by hydrogenolysis was unsuccessful because the initially formed **11c** was again readily hydrogenated to **12**. Thus, it was concluded that *tert*-butyldimethylsilyl group is the best protecting group for the synthesis of bis(hydroxymethyl)-dioxinones **11a**–**c** (Scheme 2).

2.2. Desymmetrization of prochiral dioxinones

Preliminary tests for optimization of the conditions for the desymmetrization of prochiral dioxinones **11a**–**c** with different lipases and solvents were carried out. Lipase A, AY, AK, PS, AH, Pancreatin F (Amano), Lipase MY (Meito), and Toyocheme LIP (Toyobo) were screened as a catalyst. Acetone, acetonitrile, 1,4-



Scheme 1.



Scheme 2.

Table 1. Preliminary tests for acetylation of prochiral dioxinones **11a–c**

Run	R′	Lipase[a] (mg)	Solvent[b] (mL/mL)	Temp. (°C)	Time (h)	HPLC par[c] (%)		E.e.[c] of **13** (*R*/*S*)
						7	**13**	
1	H	AY (20)	A/VA = 1/4	28	11	52	48	59% e.e. (*R*)
2	H	AY (20)	VA = 5	28	63	49	50	82% e.e. (*R*)
3	H	AY (20)	IPE/VA = 1/4	28	19	44	54	70% e.e. (*R*)
4	H	PS (20)	A/VA = 1/4	28	22	40	60	82% e.e. (*S*)
5	H	PS (20)	D/VA = 1/4	28	15	36	64	80% e.e. (*S*)
6	H	AK (20)	D/VA = 1/4	28	16	37	62	80% e.e. (*S*)
7	H	LIP (20)	AN/VA = 1/4	26	12	25	75	99% e.e. (*S*)
8	Me	AY (20)	AN/VA = 1/4	28	10	29	71	97% e.e. (*R*)
9	Me	AY (20)	A/VA = 1/4	28	8	38	62	98% e.e. (*R*)
10	Me	MY (20)	A/VA = 1/4	28	20	25	75	96% e.e. (*R*)
11	Me	PS (40)	D/VA = 1/4	28	25	51	49	82% e.e. (*S*)
12	Me	LIP (10)	AN/VA = 1/4	30	2.5	33	67	96% e.e. (*S*)
13	Me	LIP (5)	D/VA = 1/4	30	20	39	62	95% e.e. (*S*)
14	Me	LIP (5)	VA = 5	30	36	36	64	88% e.e. (*S*)
15	Ph	PS (40)	A/VA = 1/4	30	60	26	74	90% e.e. (*S*)
16	Ph	PS (40)	VA = 5	30	36	20	79	80% e.e. (*S*)
17	Ph	AH (20)	A/VA = 1/4	31	18	43	57	95% e.e. (*S*)
18	Ph	AH (20)	D/VA = 1/4	31	18	48	52	96% e.e. (*S*)
19	Ph	LIP (20)	AN/VA = 1/4	30	7	31	69	88% e.e. (*R*)
20	Ph	LIP (20)	A/VA = 1/4	30	1.5	39	61	88% e.e. (*R*)

[a] AY: Lipase AY, PS: Lipase PS, AH: Lipase AH, MY: Lipase MY, LIP: Toyocheme LIP.

[b] A: acetone, AN: acetonitrile, D: 1,4-dioxane, VA: vinyl acetate, IPE: diisopropyl ether.

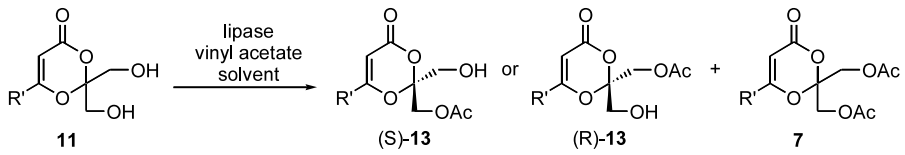
[c] par: peak area ratio. HPLC conditions for R′ = Me, Ph: Chiralpak AS (4.6×250 mm), eluent: *n*-hexane/ethanol = 90/10 (containing 0.1% acetic acid), detection; 254 nm (UV), flow rate: 1.0 mL/min. HPLC conditions for R′ = H: Chiralpak AS (4.6×250 mm), eluent: *n*-hexane/2-propanol = 80/20 (containing 0.1% acetic acid), detection: 254 nm (UV), flow rate: 1.0 mL/min.

dioxane, ethyl acetate, THF, and diisopropyl ether were examined as a reaction solvent. Vinyl acetate was used as an acetyl donor (Scheme 3).

A typical procedure for the reaction involved stirring a mixture of prochiral dioxinones (10 mg), solvent (1 mL), vinyl acetate (4 mL), and lipase (5–40 mg) at room temperature (26–31°C). The reaction was monitored by HPLC analysis using Chiralpak AS (Daicel). Some of the results obtained are summarized in Table 1.

As can be seen from Table 1, monoacetate **13** was obtained with high e.e. In addition, both enantiomers of **13** were obtained by the use of a suitable enzyme and solvent. For example, acetylation of **11a** in the presence of Lipase AY and acetone gave (*R*)-**13a** with 98% e.e. (run 9) and the use of Toyocheme LIP in acetonitrile afforded (*S*)-**13a** with 96% e.e. (run 12). The e.e.s were determined by HPLC analyses with the use of a chiral column and the absolute configuration at the 2-position was determined by the method mentioned in Section 2.3.

Based on the above results, 1–6 mmol of **11a–c** was used to prepare (*R*)- or (*S*)-**13** on a larger scale by asymmetric acetylation. The results are shown in Table 2. Chromatographic purification of the product by silica gel column cooled at −15°C gave **13a–c**.[‡] 6-Substituted compounds **13a** and **13c** were isolated in satisfactory yields. The 6-unsubstituted compound **13b** was isolated in low yields due to some decomposition on the column (runs 1 and 2). (*R*)- and (*S*)-**13c** with high e.e.s were obtained by prolonged reaction, though their yields were lower (runs 7 and 9). A more efficient method to obtain **13c** with high e.e. is purification of **13c** by recrystallization. Only one recrystallization run of (*R*)-**13c** (83% e.e.) obtained in run 8 was enough to afford (*R*)-**13c** (97% e.e.) in 47% yield.



Scheme 3.

[‡] Chromatography at room temperature resulted in significant level of decomposition of (*R*)- and (*S*)-**13a–c**. These compounds were stable for a few months in a refrigerator.

Table 2. Production of (*R*)- or (*S*)-**13** on a larger scale by asymmetric acetylation of **11a–c**

Run[a]	R′	Lipase	Solvent	Temp. (°C)	Time (h)	Isolated yield (%)		E.e.[b] of **13** (*R*/*S*)
						7	**13**	
1	H	LIP	AN/VA = 1/4	25	21	16	50	98% e.e. (*S*)
2	H	AY	VA	27	20 days	28	22	67% e.e. (*R*)
3	Me	AY	A/VA = 1/4	27	24	23	76	96% e.e. (*R*)
4	Me	AY	A/VA = 1/4	27	22	29	68	98% e.e. (*R*)
5	Me	LIP	AN/VA = 1/4	28	2.5	54	46	98% e.e. (*S*)
6	Me	LIP	AN/VA = 1/4	28	9	27	70	94% e.e. (*S*)
7	Ph	LIP	AN/VA = 1/4	29	10	56	26	91% e.e. (*R*)
8	Ph	LIP	AN/VA = 1/4	28	3	27	70	83% e.e. (*R*)
9	Ph	AH	D/VA = 1/4	28	16	44	45	96% e.e. (*S*)
10	Ph	AH	D/VA = 1/4	28	11	34	66	86% e.e. (*S*)

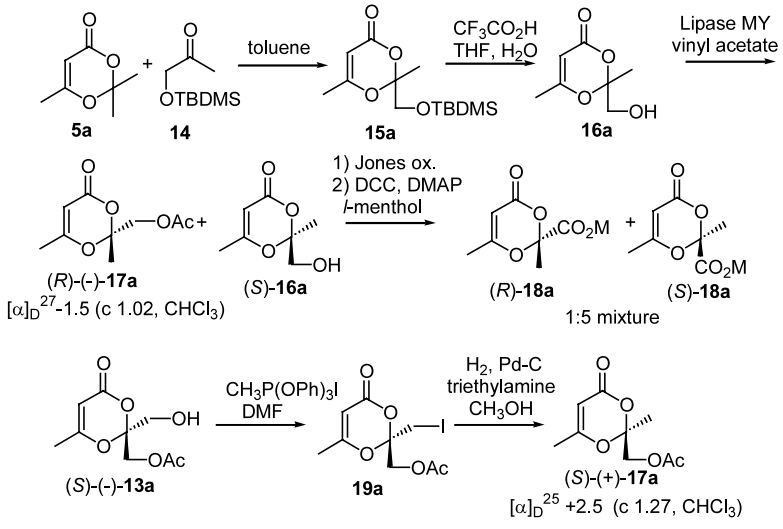
[a] All reactions were carried out using 1–6 mmol of **11**.
[b] E.e.s were determined by HPLC analysis as in Table 1.

2.3. Determination of absolute configuration at the 2-position

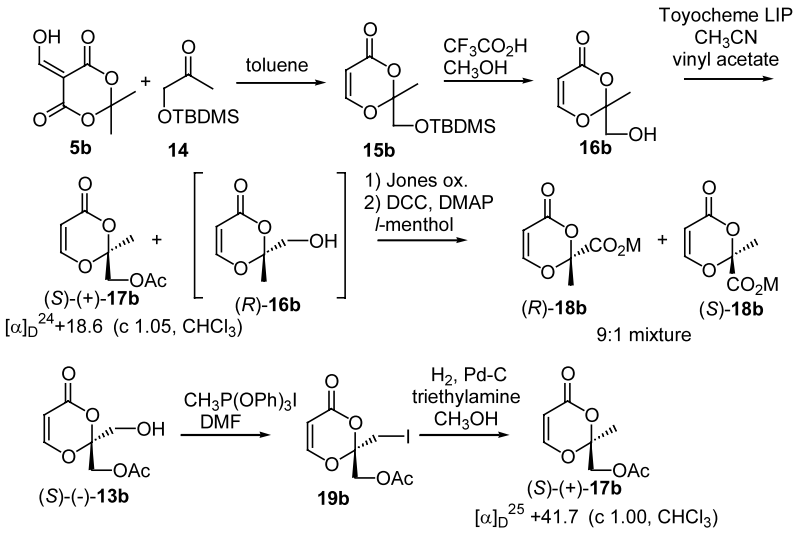
The absolute configuration of the 6-methyl compound **13a** was determined as follows: [4+2]cycloaddition of ketone **14**[18] to the acetylketene generated from **6a** gave dioxinone **15a**, which, upon treatment with trifluoroacetic acid, yielded racemic alcohol **16a**. Kinetic resolution by Lipase MY-catalyzed acetylation of **16a** provided (−)-**17a** and (+)-**16a** in 55 and 42% yields, respectively. Jones' oxidation of (+)-**16a** gave a carboxylic acid, and without purification, this was condensed with *l*-menthol to produce the known compounds (*R*)- and (*S*)-**18a**[4b] in a 1:5 ratio, showing that (+)-**16a** has *S*-configuration. Arbuzov reaction of (−)-**13a** with methyltriphenoxyphosphonium iodide gave iodide **19a**, and hydrogenolysis of **19a** with H_2/Pd–C gave (+)-**17a** in 86% yield. From the positive sign of the specific rotation of this compound, the configuration was determined to be *S*. Therefore, the configuration of (−)-**13a** was assigned as *S* (Scheme 4).

The absolute configuration of the 6-unsubstituted analogue **13b** was determined in the same manner as **13a**. Kinetic resolution via Toyocheme LIP-catalyzed acetylation of racemic alcohol **16b** derived from **5b** and **14** in two steps provided (+)-**17b** and crude optically active **16b** having opposite configuration. Jones' oxidation of **16b** followed by condensation with *l*-menthol yielded diastereomers (*R*)- and (*S*)-**18b** in a 9:1 ratio.[4b] This result shows that alcohol **16b** and therefore (+)-**17b** have *R*-configuration. Next, (−)-**13b** was converted to the iodide **19b** by Arbuzov reaction. Hydrogenolysis of **19b** gave (+)-**17b**. Thus, we could conclude that (−)-**13b** has *S*-configuration at the 2-position (Scheme 5).

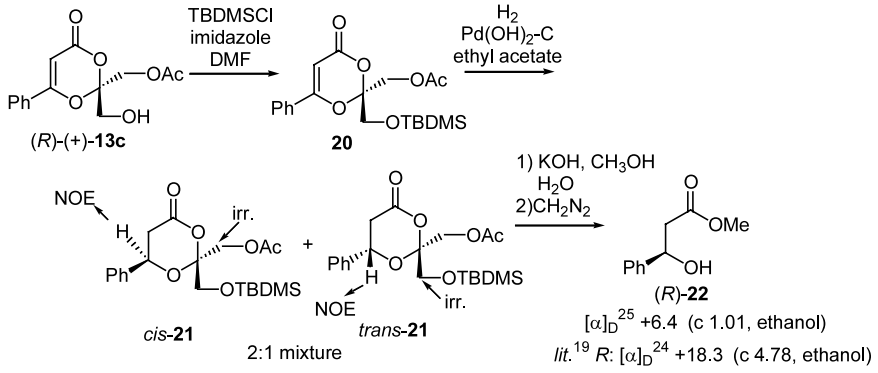
The absolute configuration of the 6-phenyl compound **13c** was determined as follows: (+)-**13c** was transformed into its *tert*-butyldimethylsilyl ether **20**. Hydrogenation of this compound afforded a 2:1 diastereomeric mixture of *cis*- and *trans*-**21**. NOE experiments on this mixture indicated that the major isomer has *cis* configuration. Alkaline-hydrolysis of this mixture followed by



Scheme 4.



Scheme 5.



Scheme 6.

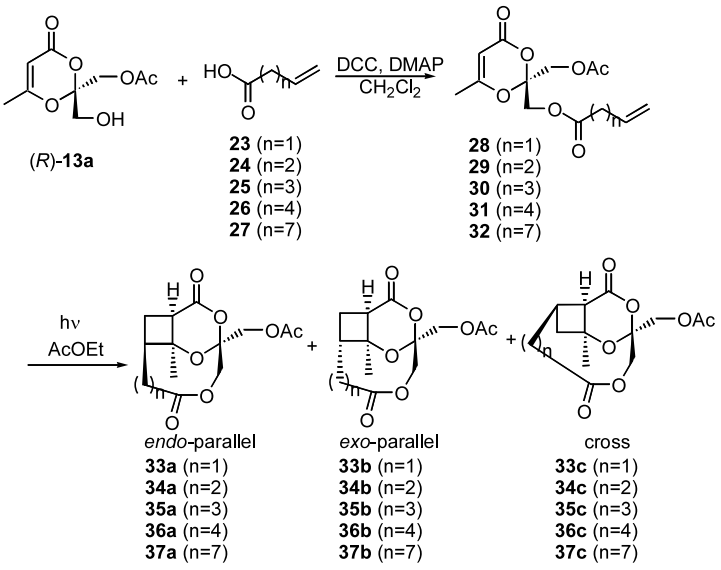
esterification with diazomethane lead to methyl 3-hydroxy-3-phenyl propionate **22** in 79% yield. This compound showed a positive sign for the specific rotation, revealing the configuration to be *R*.[19] Consequently, *cis*-**21** is considered to be the 2*R*,6*R*-diastereomer, and (+)-**13c** is found to have *R*-configuration (Scheme 6).

2.4. Intramolecular photo[2+2]cycloaddition

In order to utilize the optically active dioxinones obtained here, we examined the enantioselective synthesis of cyclobutanols using intramolecular photo[2+2]cycloaddition of dioxinones whose side chain is attached to an appropriate olefin by an ester group. The merits of this strategy are: (1) both the acetal and ester groups in the photoadduct can be cleaved readily; (2) by varying the length of the spacer, it is possible to perform regio- and diastereocontrolled synthesis of cyclobutanols, and (3) because we now have an enantiomerically enriched starting material, it is also possible to achieve enantioselective synthesis of cyclobutanols.

According to this strategy, the enantiomerically enriched dioxinone (*R*)-**13a** was condensed with various commercially available ω-alkenoic acids **23**–**27** by the DCC method to give **28**–**32** in excellent yields (Scheme 7).

Next, intramolecular photo[2+2]cycloaddition reactions of **28**–**32** were examined. A solution of **28**–**32** in ethyl acetate (1–2 mM) was irradiated (300 nm) at room temperature. The results summarized in Table 3 show that parallel adducts were predominantly formed in all cases. A shorter spacer afforded a higher *endo*/*exo* ratio, as determined by ^{1}H NMR analysis of the crude products and photoreaction of **28** gave *endo*-parallel adduct **33a** exclusively. Diastereoselectivities from the photochemical reactions of **29** and **30** were slightly improved when the reaction was conducted at a low temperature (−30°C). Photoreaction of **32** gave unseparable photoadducts. 500 MHz ^{1}H NMR analysis indicated that there are at least three different photoadducts in this mixture. However, the structures were not determined. The stereochemistry of **34a** and **36b** were determined by ^{1}H NMR, ^{1}H–^{1}H COSY, ^{13}C–^{1}H COSY, and NOE experiments. The structures of the other photoadducts were established by systematically comparing their ^{1}H NMR data to those of **34a** and **36b**.

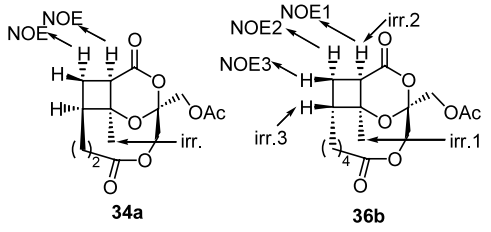


Scheme 7.

Table 3. Intramolecular photo[2+2]cycloaddition of **28**–**32**

n	Substrate	Yield[a] (%) of **33**–**37**			*endo*-Parallel
		endo-Parallel (**a**)	*exo*-Parallel (**b**)	Cross (**c**)	*exo*-parallel
1	**28**	47	0	0	**33a** alone
2	**29**	72	13	0	6 (9 at −30°C)
3	**30**	44	30	0	1.4 (1.5 at −30°C)
4	**31**	25	40	10	0.6
7	**32**	ND[b]	ND[b]	ND[b]	ND[b]

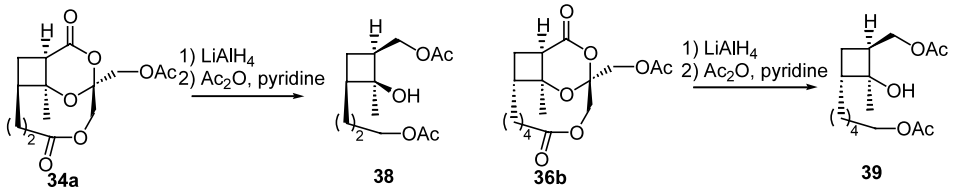
[a] Isolated yield.
[b] ND: not determined.



Finally, the synthesis of cyclobutanols from the intramolecular photoadducts was studied using compounds **34a** and **36b** as representatives. Compounds **34a** and **36b** were treated with excess $LiAlH_4$ and the resulting cyclobutanols were acetylated with acetic anhydride to produce **38** and **39**, respectively (Scheme 8).

3. Conclusions

Optically active dioxinones having a hydroxymethyl group at the 2-position were synthesized by lipase-catalyzed acetylation of prochiral diols. Both enantiomers were obtained with high enantiomeric purity by use of a suitable combination of an appropriate lipase and solvent. The optically active 2-hydroxymethyldioxi-



Scheme 8.

nones thus obtained were transformed into ω-alkenyl carboxylates, whose intramolecular photo[2+2]cycloaddition provided an excellent method for the regio-, diastereo-, and enantioselective synthesis of substituted cyclobutanols.

4. Experimental

4.1. General

All melting points were determined with a Yazawa micro melting point apparatus BY-1 and left uncorrected. Optical rotations were measured on a JASCO DIP-360 digital polarimeter. IR spectra were measured on a JASCO FT/IR-5MP spectrometer, and ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM PMX 60SI or a JEOL JNM-GX 500 spectrometer with tetramethylsilane used as an internal standard. Mass spectra were recorded on a JEOL JMS-DX-303, a JMS-AX-500, a JEOL JMS-SX102, a JEOL JMS-BU20, a JEOL JMS-MS700, a JEOL JMS-700V, or a JEOL JMS-MS700QQ mass spectrometer. High-performance liquid chromatography (HPLC) analyses were carried out on a JASCO LC-800 system (pump, 880-PU; detector, 875-UV; system controller, 802-SC; integrator, Chromato-recorder 12) using Chiralpak AS or Chiralcel OD (Daicel). Merck silica gel 60 was employed for silica gel column chromatography. Merck silica gel 60 F_{254} was employed for thin-layer chromatography (PTLC). Kanto Chemicals silica gel 60N (spherical, neutral) was employed for medium-pressure liquid chromatography (MPLC). A column with a jacket in which cold solvent (ca. −20°C) was circulated was used for the isolation of **11b**, (*R*)- and (*S*)-**13a**–**c**. The ratios of solvent mixtures for chromatography are shown as volume/volume. The photoreactions were carried out in a quartz Rayonet Photochemical Reactor equipped with RPR 3000 Å lamps.

4.2. Synthesis of prochiral dioxinones

4.2.1. 2,2-Bis[(acetoxy)methyl]-6-methyl-4*H*-1,3-dioxin-4-one, 7a. (a) Acetylated Meldrum's acid (**6a**, 5.0 g, 26.9 mmol)[14] was added over a 15 min period to a refluxing solution of 1,3-di(acetoxy)-2-propanone (**1**, 9.35 g, 53.7 mmol)[9] in toluene (400 mL). The solution was heated under reflux for an additional 45 min and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (4:1) gave **7a** (5.84 g, 84%) as a colorless oil. (b) A solution of 2,2,6-trimethyl-1,3-dioxin-4-one (**5a**, 178 mg, 1.25 mmol)[13] and **1** (174 mg, 1.0 mmol) in toluene (5 mL) was heated under reflux for 3 h and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (3:1) gave **7a** (187 mg, 72%) as a colorless oil. HRMS calcd for $C_{11}H_{14}O_7$ (M^+): 258.0740. Found: 258.0760. IR ($CHCl_3$): 1750, 1647 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.01 (3H, s, C_6-CH_3), 2.13 (6H, s, Ac×2), 4.33 and 4.59 (each 2H, d, J=12.0 Hz, CH_2O×2), 5.30 (1H, s, C_5-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.7, 20.6, 61.1, 94.3, 103.2, 158.3, 168.6, 169.9. MS m/z: 258 (M^+).

4.2.2. 4,9,9-Trimethyl-1,5,8,10-tetraoxaspiro[5.5]undec-3-en-2-one, 8a. A solution of **5a** (3.55 g, 25 mmol) and 2,2-dimethyl-1,3-dioxan-5-one (**2**, 2.60 g, 20 mmol)[10] in toluene (50 mL) was heated under reflux for 3 h and then the solvent was evaporated in vacuo. Purification of the residue by recrystallization from hexane–ether gave **8a** (4.29 g, 95%) as colorless prisms having a mp of 97–98°C. Anal. calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.89; H, 6.54%. MS m/z: 215 (MH^+). IR ($CHCl_3$): 1740, 1642 cm^{-1}. ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.40 (6H, s, C_4-CH_3×2), 2.03 (3H, s, C_6-CH_3), 4.00 (4H, s, CH_2O×2), 5.20 (1H, s, C_5-H).

4.2.3. 2,2-Bis[(benzyloxy)methyl]-6-methyl-4*H*-1,3-dioxin-4-one, 9a. (a) Compound **6a** (5.0 g, 26.9 mmol) was added over a 15 min period to a refluxing solution of 1,3-bis(benzyloxy)-2-propanone (**3**, 14.5 g, 53.6 mmol)[11] in toluene (400 mL). The solution was heated under reflux for an additional 45 min and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (7:1) gave **9a** (6.91 g, 73%) as a colorless oil. (b) A solution of **5a** (3.55 g, 25 mmol) and **3** (5.40 g, 20 mmol) in toluene (100 mL) was heated under reflux for 2 h and then the solvent was evaporated in vacuo. Following the same steps as in (a) gave **9a** (5.96 g, 84%). HRMS calcd for $C_{21}H_{23}O_5$ (MH^+): 355.1545. Found: 355.1555. IR ($CHCl_3$): 1736, 1644 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.97 (3H, d, J=1.0 Hz, C_6-CH_3), 3.79 and 3.87 (each 2H, d, J=11.0 Hz, CH_2OCH_2Ph×2), 4.58 and 4.62 (each 2H, d, J=12.0 Hz, CH_2Ph×2), 5.17 (1H, d, J=1.0 Hz, C_5-H), 7.27–735 (10H, m, Ph×2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.8, 68.2, 73.8, 94.0, 105.8, 127.6, 127.8, 128.4, 137.3, 159.5, 168.6.

4.2.4. 2,2-Bis({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-6-methyl-4*H*-1,3-dioxin-4-one, 10a. Compound **6a** (7.0 g, 37.6 mmol) was added to a refluxing solution of 1,3-bis(*tert*-butyldimethylsilyloxy)-2-propanone (**4**, 12.0 g, 37.7 mmol)[12] in toluene (560 mL) over a 0.5 h period. The solution was heated under reflux for an additional 2 h and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (40:1) gave **4** (1.40 g, 12%) and then **10a** (12.33 g, 81%) as a colorless oil. HRMS calcd for $C_{19}H_{38}NaO_5Si_2$ (MNa^+): 425.2155. Found: 425.2148. MS m/z: 403 (MH^+). IR ($CHCl_3$): 1732, 1644 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.03 and 0.04 (each 6H, s, $Si(CH_3)_2$×2), 0.85 (18H, s, *tert*-Bu×2), 1.95 (3H, s, C_6-CH_3), 3.82 and 3.89 (2H, d, J=11.0 Hz, OCH_2×2), 5.121 (1H, s, C_5-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ −5.6, −5.5, 18.1, 19.7, 25.6, 62.0, 93.7, 106.6, 160.0, 168.4.

4.2.5. 2,2-Bis(hydroxymethyl)-6-methyl-4*H*-1,3-dioxin-4-one, 11a. (a) Compound **9a** (354 mg, 1.0 mmol) was hydrogenated in methanol (5 mL) and chloroform (three drops) with 10% $Pd(OH)_2$/C (20 mg) for 4 h. Removal of the catalyst and solvent left crude **11a**.

Recrystallization from acetone–hexane gave **11a** (174 mg, 100%) as colorless needles having a mp of 105–107°C. (b) A solution of **10a** (7.78 g, 19.3 mmol) and trifluoroacetic acid (7.4 mL) in methanol (78 mL) was stirred at room temperature for 45 h and then the solvent was evaporated in vacuo. Recrystallization of the residue gave **11a** (2.12 g, 63%) as colorless needles having a mp of 105–107°C. Anal. calcd for $C_7H_{10}O_5$: C, 48.27; H, 5.79. Found: C, 48.05; H, 5.75%. MS m/z: 175 (MH^+). IR ($CHCl_3$): 3401 (br), 1734, 1644 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.64 (2H, brs, OH×2), 2.06 (3H, d, $J=1.0$ Hz, C_6-CH_3), 3.96 and 4.00 (each 2H, d, $J=12.5$ Hz, CH_2O×2), 5.25 (1H, d, $J=1.0$ Hz, C_5-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.9, 62.0, 94.0, 106.1, 159.5, 169.2.

4.2.6. 2,2-Bis[(acetoxy)methyl]-4*H*-1,3-dioxin-4-one, 7b. Formylated Meldrum's acid (**6b**, 10.0 g, 58.1 mmol)[15] was added to a refluxing solution of **1** (20.0 g, 114.8 mmol) in toluene (400 mL) over a 0.5 h period. The solution was heated under reflux for an additional 0.5 h and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (4:1) gave **1** (13.79 g) as colorless needles and then **7b** (5.87 g, 41%) as a colorless oil. HRMS calcd for $C_{10}H_{13}O_7$ (MH^+): 245.0661. Found: 245.0662. MS m/z: 245 (MH^+). IR ($CHCl_3$): 1750, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.13 (6H, s, Ac×2), 4.40 and 4.55 (each 2H, d, $J=12.5$ Hz, CH_2O×2), 5.48 (1H, d, $J=6.0$ Hz, C_5-H), 7.13 (1H, d, $J=6.0$ Hz, C_6-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.4, 61.0, 97.7, 103.7, 157.2, 157.4, 169.7.

4.2.7. 2,2-Bis[(benzyloxy)methyl]-4*H*-1,3-dioxin-4-one, 9b. Compound **6b** (1.72 g, 9.99 mmol) was added over a 0.5 h period to a refluxing solution of **3** (1.35 g, 4.99 mmol) in toluene (100 mL). The solution was heated under reflux for an additional 0.5 h and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ether (3:1) gave **9b** (0.82 g, 48%) as colorless needles having a mp of 56–57°C (recrystallized from ether–hexane). Anal. calcd for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.52; H, 5.94%. MS m/z: 341 (MH^+). IR ($CHCl_3$): 1742, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.82 and 3.89 (each 2H, d, $J=11.0$ Hz, CH_2OCH_2Ph×2), 4.59 and 4.62 (each 2H, d, $J=12.0$ Hz, CH_2Ph×2), 5.34 (1H, d, $J=6.0$ Hz, C_5-H), 7.10 (1H, d, $J=6.0$ Hz, C_6-H), 7.29–7.35 (10H, m, Ph×2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 68.3, 73.9, 97.5, 106.5, 127.7, 127.9, 128.4, 137.2, 157.6, 158.5.

4.2.8. 2,2-Bis({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-4*H*-1,3-dioxin-4-one, 10b. (a) Compound **6b** (10.0 g, 58.1 mmol) was added to a refluxing solution of **4** (18.5 g, 58.1 mmol) in toluene (400 mL) over a 0.5 h period. The solution was heated under reflux for an additional 2.5 h and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ether (40:1) gave **10b** (10.98 g, 49%) as a colorless oil. (b) A solution of **5b** (256 mg, 2.0 mmol) and **4** (624 mg, 2.0 mmol) in toluene (60 mL) was heated under reflux for 1 h and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (10:1) gave **10b** (467 mg, 60%) as a colorless oil. HRMS calcd for $C_{18}H_{36}NaO_5Si_2$ (MNa^+): 411.1999. Found: 411.1997. MS m/z: 389 (MH^+). IR ($CHCl_3$): 1738, 1620 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ −0.02 and −0.01 (each 6H, s, $SiCH_3$× 4), 0.80 (18H, s, *tert*-Bu×2), 3.80 and 3.85 (2H, d, $J=11.5$ Hz, OCH_2×2), 5.23 (1H, d, $J=6.0$ Hz, C_5-H), 7.03 (1H, d, $J=6.0$ Hz, C_6-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ −5.5, −5.4, 18.2, 25.7, 62.2, 97.1, 107.4, 157.7, 159.0.

4.2.9. 2,2-Bis(hydroxymethyl)-4*H*-1,3-dioxin-4-one, 11b. A solution of **10b** (467 mg, 1.2 mmol) and trifluoroacetic acid (0.5 mL) in methanol (10 mL) was stirred at room temperature for 40 h and then the solvent was evaporated in vacuo. The residue was purified by MPLC with ether (the column temperature was kept at −15 to −20°C) to give **11b** (182 mg, 93%) as a colorless oil. HRMS calcd for $C_6H_8O_5$ (M^+): 160.0371. Found: 160.0381. IR (neat): 3391 (br), 1732, 1618 cm^{-1}. ^1H NMR (500 MHz, acetone-d_6) δ 3.03 (2H, brs, OH×2), 3.84 and 3.93 (2H, d, $J=12.5$ Hz, OCH_2×2), 5.32 (1H, d, $J=5.5$ Hz, C_5-H), 7.36 (1H, d, $J=5.5$ Hz, C_6-H). ^{13}C NMR (125.65 MHz, acetone-d_6) δ 61.4, 97.6, 108.3, 159.3.

4.2.10. 2,2-Bis[(acetoxy)methyl]-6-phenyl-4*H*-1,3-dioxin-4-one, 7c. Benzoylated Meldrum's acid (**6c**, 7.50 g, 30.2 mmol) was added over a 0.5 h period to a refluxing solution of **1** (21.0 g, 120.6 mmol) in toluene (400 mL). The solution was heated under reflux for an additional 45 min and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (4:1) gave the mixture of **7c** and **1**. Methanol (10 mL) and water (40 mL) were added to this mixture. Insoluble crystals were filtered and dried to give **7c** (6.83 g, 71%). Recrystallization from ether–hexane gave an analytical sample as colorless needles having a mp of 76–77°C. Anal. calcd for $C_{16}H_{16}O_7$: C, 60.00; H, 5.04. Found: C, 60.09; H, 5.09%. MS m/z: 321 (MH^+). IR ($CHCl_3$): 1748, 1624 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.13 (6H, s, Ac×2), 4.54 and 4.61 (each 2H, d, $J=12.0$ Hz, CH_2O× 2), 5.94 (1H, s, C_5-H), 7.46–7.68 (5H, m, Ph). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.5, 61.3, 91.4, 103.4, 126.3, 128.9, 129.9, 132.6, 159.1, 164.7, 169.8.

4.2.11. 2,2-Bis[(benzyloxy)methyl]-6-phenyl-4*H*-1,3-dioxin-4-one, 9c. (a) Compound **6c** (5.0 g, 20.1 mmol) was added to a refluxing solution of **3** (10.9 g, 40.3 mmol) in toluene (400 mL) over a 0.5 h period. The solution was heated under reflux for an additional 45 min and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (10:1) gave a mixture of **9c** and **3**. Fractional recrystallization from ether–hexane gave **3** (2.35 g) and **9c** (6.00 g, 72%, colorless needles, mp 66–67°C). (b) A solution of 2,2-dimethyl-6-phenyl-1,3-dioxin-4-one (**5c**, 408 mg, 2.0 mmol) and **3** (540 mg, 2.0 mmol) in toluene (10 mL) was heated under reflux for 1.5 h and then the solvent was evapo-

rated in vacuo. The residue was chromatographed on a silica gel column. Elution with benzene gave **9c** (585 mg, 70%) as colorless needles having a mp of 66–67°C (recrystallized from hexane–ether). Anal. calcd for $C_{26}H_{24}O_5$: C, 74.98; H, 5.81. Found: C, 75.02; H, 5.80%. MS m/z: 417 (MH^+). IR ($CHCl_3$): 1726, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.91 and 4.02 (each 2H, d, $J=11.0$ Hz, $CH_2OCH_2Ph\times2$), 4.60 and 4.65 (each 2H, d, $J=12.0$ Hz, $CH_2Ph\times2$), 5.83 (1H, s, C_5-H), 7.27–771 (15H, m, Ph×3). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 68.1, 73.8, 91.5, 106.0, 126.6, 127.6, 127.8, 128.4, 128.8, 130.6, 132.3, 137.4, 160.4, 164.9.

4.2.12. 2,2-Bis({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-6-phenyl-4*H*-1,3-dioxin-4-one, 10c. Compound **6c** (8.0 g, 32.2 mmol) was added to a refluxing solution of **4** (20.54 g, 64.5 mmol) in toluene (400 mL) over a 0.5 h period. The solution was heated under reflux for an additional hour and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (50:1) gave **4** (10.53 g) and then **10c** (9.66 g, 65%) as colorless needles having a mp of 44–46°C (recrystallized from methanol–water). Anal. calcd for $C_{24}H_{40}O_5Si_2$: C, 62.03; H, 8.68. Found: C, 61.77; H, 8.64%. HRMS calcd for $C_{24}H_{40}NaO_5Si$ (MNa^+): 487.2312. Found: 487.2318. MS m/z: 403 (MH^+). IR ($CHCl_3$): 1721, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 0.00 and 0.02 (each 6H, s, $SiCH_3\times4$), 0.84 (18H, s, *tert*-Bu×2), 3.93 and 4.03 (2H, d, $J=11.0$ Hz, $OCH_2\times2$), 5.78 (1H, s, C_5-H), 7.37–7.67 (5H, m, Ph). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ −5.6, −5.5, 18.1, 25.7, 61.4, 91.3, 106.7, 126.5, 128.7, 130.8, 132.1, 160.7, 164.8.

4.2.13. 2,2-Bis(hydroxymethyl)-6-phenyl-4*H*-1,3-dioxin-4-one, 11c. A solution of **10c** (715 mg, 1.5 mmol) and trifluoroacetic acid (0.6 mL) in methanol (15 mL) was stirred at room temperature for 40 h and then the solvent was evaporated in vacuo. Recrystallization from ethanol–pentane gave **11c** (330 mg, 93%) as colorless needles having a mp of 116–117°C. HRMS calcd for $C_{12}H_{12}O_5$ (M^+): 236.0684. Found: 236.0712. IR ($CHCl_3$): 3385 (br), 1725, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.90 (2H, brs, OH×2), 4.08 and 4.14 (each 2H, d, $J=12.5$ Hz, $OCH_2\times2$), 5.88 (1H, s, C_5-H), 7.45–7.74 (5H, m, Ph). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 61.8, 91.2, 106.2, 126.5, 129.0, 130.3, 132.6, 160.4, 165.4.

4.3. Desymmetrization of prochiral dioxinones

4.3.1. (*S*)-[2-(Hydroxymethyl)-6-methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl]methyl acetate, (*S*)-13a. To a solution of **11a** (400 mg, 2.30 mmol) in acetonitrile (10 mL) was added vinyl acetate (40 mL) and Toyocheme LIP (200 mg) and the whole was stirred at room temperature for 9 h. The mixture was filtered through Celite and the filtrate was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (2:1) (the column temperature was kept at −15 to −20°C) to give first **7a** (160 mg, 27%) and then (*S*)-**13a** (349 mg, 94% e.e., 70%) as colorless oils, respectively. $[\alpha]_D^{27}=-19.7$ (c 1.06, $CHCl_3$). HRMS m/z calcd for $C_9H_{12}O_6$ (M^+): 216.0634. Found: 216.0634. IR ($CHCl_3$): 3420 (br), 1748, 1645 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.03 (3H, d, $J=1.0$ Hz, C_6-CH_3), 2.12 (3H, s, Ac), 3.21 (1H, brs, OH), 3.90 (2H, s, $HOCH_2$), 4.31 and 4.68 (each 1H, d, $J=12.0$ Hz, $AcOCH_2$), 5.27 (1H, d, $J=1.0$ Hz, C_5-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.8, 20.7, 60.2, 62.2, 94.1, 104.9, 159.4, 169.3, 170.4.

4.3.2. (*R*)-[2-(Hydroxymethyl)-6-methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl]methyl acetate, (*R*)-13a. To a solution of **11a** (1.0 g, 5.74 mmol) in acetone (25 mL) was added vinyl acetate (100 mL) and Lipase AY (2.0 g) and the whole was stirred at room temperature for 22 h. The mixture was filtered through Celite and the filtrate was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (2:1) (the column temperature was kept at −15 to −20°C) to give first **7a** (423 mg, 29%) and then (*R*)-**13a** (839 mg, 98% e.e., 68%, $[\alpha]_D^{25}=+20.2$ (c 1.14, $CHCl_3$)) as colorless oils, respectively.

4.3.3. (*S*)-[2-(Hydroxymethyl)-4-*oxo*-4*H*-1,3-dioxin-2-yl]-methyl acetate, (*S*)-13b. To a solution of **11b** (300 mg, 1.87 mmol) in acetonitrile (30 mL) was added vinyl acetate (120 mL) and Toyocheme LIP (600 mg) and the whole was stirred at room temperature for 22 h. The mixture was filtered through Celite and the filtrate was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (3:2) (the column temperature was kept at −15 to −20°C) to give first **7b** (71 mg, 16%) and then (*S*)-**13b** (191 mg, 98% e.e., 50%) as colorless oils, respectively. $[\alpha]_D^{26}=+15.5$ (c 1.07, $CHCl_3$). HRMS calcd for $C_8H_{10}O_6$ (M^+): 202.0477. Found: 202.0492. IR ($CHCl_3$): 3484 (br), 1748, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.13 (3H, s, Ac), 2.83 (1H, brs, OH), 3.90 and 3.94 (each 1H, d, $J=12.5$ Hz, CH_2OH), 4.40 and 4.64 (each 1H, d, $J=12.5$ Hz, CH_2OAc), 5.45 (1H, d, $J=6.0$ Hz, C_5-H), 7.17 (1H, d, $J=6.0$ Hz, C_6-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.6, 60.2, 62.1, 97.6, 105.4, 157.8, 158.1, 170.3.

4.3.4. (*R*)-[2-(Hydroxymethyl)-4-*oxo*-4*H*-1,3-dioxin-2-yl]methyl acetate, (*R*)-13b. To a solution of **11b** (100 mg, 0.62 mmol) in vinyl acetate (50 mL) was added lipase AY (300 mg) and the whole was stirred at room temperature for 20 days. The mixture was filtered through Celite and the filtrate was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (3:2) (the column temperature was kept at −15 to −20°C) to give first **7b** (42 mg, 28%) and then (*R*)-**13b** (28 mg, 67% e.e., 22%, $[\alpha]_D^{26}=-4.1$ (c 0.98, $CHCl_3$)) as colorless oils, respectively.

4.3.5. (*R*)-[2-(Hydroxymethyl)-4-*oxo*-6-phenyl-4*H*-1,3-dioxin-2-yl]methyl acetate, (*R*)-13c. To a solution of **11c** (400 mg, 1.69 mmol) in acetonitrile (10 mL) was added vinyl acetate (40 mL) and Toyocheme LIP (300 mg) and the whole was stirred at room temperature for 3 h. The mixture was filtered through Celite and the filtrate was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (3:1) (the column temperature was kept at −15 to −20°C) to give first **7c**

(144 mg, 27%) as colorless needles having mp of 76–77°C (recrystallized from hexane–ether) and then (*R*)-**13c** (330 mg, 83% e.e., 70%) as crystals. Recrystallization from hexane–ether gave a sample with 97% e.e. (228 mg, 48%) as colorless needles having a mp of 99–100°C. $[\alpha]_D^{25}=+51.9$ (*c* 1.07, $CHCl_3$). Anal. calcd for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07. Found: C, 60.43; H, 5.13%. MS *m*/*z*: 279 (MH^+). IR ($CHCl_3$): 3420 (br), 1732, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.13 (3H, s, Ac), 2.46 (1H, brs, OH), 4.00 and 4.05 (1H, d, $J=12.5$ Hz, $HOCH_2$), 4.52 and 4.70 (1H, d, $J=12.5$ Hz, $AcOCH_2$), 7.46–7.70 (5H, m, Ph). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.6, 60.3, 62.2, 91.4, 104.9, 126.5, 129.0, 130.2, 132.7, 159.7, 165.1, 170.4.

4.3.6. (*S*)-[2-(Hydroxymethyl)-4-*oxo*-6-phenyl-4*H*-1,3-dioxin-2-yl]methyl acetate, (*S*)-13c. To a solution of **11c** (400 mg, 1.69 mmol) in 1,4-dioxane (10 mL) was added vinyl acetate (40 mL) and Lipase AH (400 mg) and the whole was stirred at room temperature for 11 h. The mixture was filtered through Celite and the filtrate was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (3:1) (the column temperature was kept at −15 to −20°C) to give first **7c** (187 mg, 34%) as colorless needles having a mp of 76–77°C (recrystallized from hexane–ether) and then (*S*)-**13c** (310 mg, 87% e.e., 66%) as crystals. Recrystallization from hexane–ether gave 98% e.e. sample (216 mg, 46%, $[\alpha]_D^{26}=-53.6$ (*c* 0.94, $CHCl_3$)) as colorless needles having a mp of 99–100°C.

4.4. Determination of absolute configuration at the 2-position

4.4.1. 2-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2,6-dimethyl-4*H*-1,3-dioxin-4-one, 15a. A solution of **5a** (1.70 g, 12.0 mmol) and 1-*tert*-butyldimethylsilanyloxy-2-propanone (**14**, 2.0 g, 10 mmol) in toluene (40 mL) was heated under reflux for 1.5 h and then the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (20:1) gave **14** (0.75 g) and then **15a** (2.21 g, 86%) as colorless oils, respectively. Anal. calcd for $C_{13}H_{22}O_4Si$: C, 57.74; H, 8.02. Found: C, 57.79; H, 8.25%. MS *m*/*z*: 173 (M^+–*tert*-Bu). IR ($CHCl_3$): 1726, 1642 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 0.00 and 0.01 (each 3H, s, $Si(CH_3)_2$), 0.83 (9H, s, *tert*-Bu), 1.57 (3H, s, C_2-CH_3), 1.92 (3H, d, $J=1.0$ Hz, C_6-CH_3), 3.63 and 3.86 (each 1H, d, $J=11.0$ Hz, $OCH_2\times2$), 5.13 (1H, d, $J=1.0$ Hz, C_5-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ −5.6, 18.0, 19.7, 20.7, 25.6, 65.3, 93.6, 106.7, 160.4, 168.5.

4.4.2. 2-(Hydroxymethyl)-2,6-dimethyl-4*H*-1,3-dioxin-4-one, 16a. A solution of **15a** (2.72 g, 10.0 mmol) in trifluoroacetic acid:water:THF (1:10:10, 10 mL) was stirred for 3 h at room temperature. The reaction mixture was extracted with dichloromethane. The organic layer was washed with brine, dried over $MgSO_4$, and then the solvent was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (1:1) (the column temperature was kept at −30°C) to give **16a** (0.88 g, 56%) as prisms having a mp of 51–52°C (recrystallized from pentane–ether). HRMS calcd for $C_7H_{10}O_4$ (M^+): 158.0579. Found: 158.0598. MS *m*/*z*: 159 (M^++1), 158 (M^+). IR ($CHCl_3$): 3435 (br), 1725, 1642 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.70 (3H, s, C_2-CH_3), 2.07 (3H, s, C_6-CH_3), 3.86 (1H, br s, OH), 3.81 and 3.87 (each 1H, d, $J=12.5$ Hz, CH_2O), 5.28 (1H, s, C_5-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.7, 19.8, 64.7, 93.3, 106.7, 160.9, 169.3.

4.4.3. Kinetic resolution of 16a and conversion of (+)-16a to a mixture of (*R*)- and (*S*)-18a. To a solution of **16a** (370 mg, 2.34 mmol) in vinyl acetate (50 mL) was added Lipase MY (740 mg) and the mixture was shaken for 2 weeks at 27°C. The mixture was filtered through Celite and the filtrate was evaporated under reduced pressure. The residue was purified by MPLC with hexane–ethyl acetate (2:1) (the column temperature was kept under −19°C) to give first (*R*)-(−)-**17a** (257 mg, 55%, $[\alpha]_D^{27}=-1.52$ (*c* 1.02, $CHCl_3$)) as a colorless oil and then (*S*)-(+)-**16a** (157mg, 42%, $[\alpha]_D^{27}=+16.9$ (*c* 1.13, $CHCl_3$)) as crystals. To a solution of (*S*)-(+)-**16a** (144 mg) in acetone (4 mL) was added 2.67 M Jones reagent (1.2 mL) with ice-cooling and the mixture was stirred for 24 h at room temperature. After another addition of 2.67 M Jones reagent (0.6 mL) with ice-cooling, the whole was stirred for 4 h at room temperature. 2-Propanol was added and the mixture was evaporated under reduced pressure. The residue was diluted with water and extracted with ether. The water layer was saturated with NaCl and then extracted with ether. The organic layer was combined, dried over $MgSO_4$, and evaporated to leave crude carboxylic acid as crystals. *N*,*N*′-Dicyclohexylcarbodiimide (DCC, 225 mg, 1.1 mmol) and 4-dimethylaminopyridine (DMAP, 20 mg, 0.28 mmol) were added to a solution of the acid and *l*-menthol (170 mg, 1.1 mmol) in dichloromethane (5 mL), and the whole was stirred for 17 h at room temperature. The mixture was passed through a short column of silica gel and eluted with ether. The solvent was evaporated and the residue was purified by PTLC with dichloromethane to give a 5:1 mixture of (*S*)- and (*R*)-**18a** (137 mg, 49%)[4] as colorless crystals.

4.4.4. (*S*)-(2,6-Dimethyl-4-*oxo*-4*H*-1,3-dioxin-2-yl)-methyl acetate, (*S*)-(+)-17a, from (*S*)-(−)-13a. To a solution of (*S*)-(−)-**13a** (100 mg, 0.46 mmol, 94% e.e.) in DMF (4 mL) was added methyltriphenoxyphosphonium iodide (418 mg, 0.92 mmol). The mixture was stirred at room temperature for 1 h and then at 60°C for an additional hour. After addition of water (10 mL), the product was extracted with benzene (25 mL) and the organic layer was washed with saturated aqueous $Na_2S_2O_3$ (10 mL), water (10 mL) and dried over $MgSO_4$. The residue obtained after evaporation in vacuo was purified by PTLC with hexane–ethyl acetate (2:1) to give iodide **19a**. Compound **19a** was hydrogenated with 5%Pd–C (60 mg) and triethylamine (97 μL, 0.70 mmol) in methanol (8 mL) under 1 atm at room temperature for 2 h. After removal of the catalyst, the solvent was evaporated in vacuo. The residue obtained was chromatographed on a silica gel column. Elution with hexane–ether (2:1) gave (*S*)-(+)-**17a** (80 mg, 86%) as a colorless oil. $[\alpha]_D^{27}=+2.5$ (*c* 1.27, $CHCl_3$).

HRMS calcd for $C_9H_{12}O_5$ (M^+): 200.0685. Found: 200.0677. IR ($CHCl_3$): 1740, 1644 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.70 (3H, s, C_2-CH_3), 2.00 (3H, d, $J=1.0$ Hz, C_6-CH_3), 2.12 (3H, s, Ac), 4.18 and 4.55 (1H, d, $J=12.0$ Hz, CH_2O), 5.27 (1H, d, $J=1.0$ Hz, C_5-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.9, 20.7, 21.7, 63.9, 94.1, 104.8, 159.8, 168.8, 170.1.

4.4.5. 2-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2-methyl-4*H*-1,3-dioxin-4-one, 15b. Compound **5b** (2.85 g, 16.6 mmol) was added to a refluxing solution of **14** (3.12 g, 16.6 mmol) in toluene (120 mL) over a 0.5 h period. The solution was heated under reflux for an additional hour and then evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (50:1) gave **14** (1.08 g, 35%) and **15b** (2.49 g, 58%) as colorless oils, respectively. HRMS calcd for $C_{12}H_{22}NaO_4Si$ (MNa^+): 281.1185. Found: 281.1191. MS m/z: 259 (MH^+). IR ($CHCl_3$): 1738, 1620 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 0.00 and 0.01 (each 3H, s, $SiCH_3\times2$), 0.82 (9H, s, *tert*-Bu), 1.59 (3H, s, C_2-CH_3), 3.65 and 3.88 (1H, d, $J=11.5$ Hz), 5.28 (1H, d, $J=6.0$ Hz, C_5-H), 7.05 (1H, d, $J=6.0$ Hz, C_6-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ −5.6, 18.1, 20.7, 25.6, 65.4, 97.1, 107.5, 157.7, 159.5.

4.4.6. 2-Hydroxymethyl-2-methyl-4*H*-1,3-dioxin-4-one, 16b. A solution of **15b** (1.45 g, 5.61 mmol) and trifluoroacetic acid (2.05 mL, 26.6 mmol) in methanol (14.5 mL) was stirred at room temperature for 23 h and then the solvent was evaporated in vacuo. Recrystallization of the residue from ether gave **16b** (0.43 g, 53%) as colorless prisms having a mp of 53–55°C. The mother liquid was concentrated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (1:1) (the column temperature was kept at −18°C) to give additional **16b** (0.27 g, 33%). Anal. calcd for $C_6H_8O_4$: C, 50.00; H, 5.59. Found: C, 49.93; H, 5.58%. MS m/z: 145 (MH^+). IR ($CHCl_3$): 3445 (br), 1738, 1620 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.70 (3H, s, CH_3), 3.06 (1H, br s, OH), 3.80 and 3.86 (1H, d, $J=12.5$ Hz, CH_2O), 5.41 (1H, d, $J=6.0$ Hz, C_5-H), 7.19 (1H, d, $J=6.0$ Hz, C_6-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.0, 65.2, 97.3, 107.6, 158.3, 159.9.

4.4.7. Kinetic resolution of 16b and conversion of (*R*)-16b to the mixture of (*R*)- and (*S*)-18b. To a solution of **16b** (400 mg, 2.78 mmol) in acetonitrile (40 mL) and vinyl acetate (160 mL) was added Toyocheme LIP (800 mg) and the mixture was shaken for 0.5 h at 25°C. The mixture was filtered through Celite and the filtrate was evaporated in vacuo. The residue was purified by MPLC with hexane–ethyl acetate (3:2) (the column temperature was kept at −18°C) to give first (*S*)-(+)-**17b** (282 mg, 55%, $[\alpha]_D^{24}=+18.6$ (*c* 1.05, $CHCl_3$)) as a colorless oil and then crude (*R*)-**16b** (153 mg) as an oil. To a solution of the crude (*R*)-**16b** (153 mg) in acetone (4 mL) was added 2.67 M Jones reagent (2.0 mL) with ice-cooling and the mixture was stirred for 10 h at room temperature. 2-Propanol (2.0 mL) was added and the whole was evaporated under reduced pressure. The residue was diluted with water and extracted with ether. The water layer was saturated with NaCl and then extracted with ether and ethyl acetate, successively. The organic layers were combined, dried over $MgSO_4$, and evaporated to give a residue. DCC (429 mg, 2.1 mmol) and DMAP (20 mg, 0.28 mmol) was added to a solution of the residue and *l*-menthol (244 mg, 1.6 mmol) in dichloromethane (5 mL), and the whole was stirred for 6 h at room temperature. The mixture was passed through a short column of silica gel and eluted with ether. After evaporation of the solvent, the residue was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (20:1) roughly gave a 9:1 mixture of (*R*)- and (*S*)-**18b** (81 mg, 10%)[4] as colorless crystals.

4.4.8. (*S*)-(+)-(2-Methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl)methyl acetate, (*S*)-(+)-17b, from (*S*)-(−)-13b. To a solution of (*S*)-(−)-**13b** (140 mg, 0.69 mmol, 98% e.e.) in DMF (5 mL) was added methyltriphenoxyphosphonium iodide (626 mg, 1.39 mmol). The mixture was stirred at room temperature for 1 h and then at 60°C for 3 h. After addition of water (10 mL), the product was extracted with benzene (25 mL) and the organic layer was washed with saturated aqueous $Na_2S_2O_3$ (10 mL) and water (10 mL) and dried over $MgSO_4$. The residue obtained after evaporation in vacuo was purified by PTLC with hexane–ethyl acetate (2:1) to give **19b**. Compound **19b** was hydrogenated with 5% Pd–C (60 mg) and triethylamine (145 μL, 1.04 mmol) in methanol (8 mL) under 1 atm at room temperature for 3 h. After removal of the catalyst, the solvent was evaporated in vacuo. The residue was chromatographed on a silica gel column. Elution with hexane–ether (2:1) gave (*S*)-(+)-**17b** (94 mg, 73%) as a colorless oil. $[\alpha]_D^{25}=+41.7$ (*c* 1.00, $CHCl_3$). HRMS calcd for $C_8H_{10}O_5Na$ (MNa^+): 209.0426. Found: 200.0432. MS m/z: 187 (MH^+). IR ($CHCl_3$): 1746, 1620 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.74 (3H, s, C_2-CH_3), 2.13 (3H, s, Ac), 4.27 and 4.49 (each 1H, d, $J=12.0$ Hz, CH_2O), 5.45 (1H, d, $J=5.5$ Hz, C_5-H), 7.16 (1H, d, $J=5.5$ Hz, C_6-H). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.4, 21.2, 63.9, 97.4, 105.3, 157.6, 158.6, 169.8.

4.4.9. (*S*)-2-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-4-*oxo*-6-phenyl-4*H*-1,3-dioxin-2-yl-methyl acetate, 20. To a solution of (*R*)-(+)-**13c** (210 mg, 0.75 mmol) in DMF (5 mL) were added imidazole (206 mg, 3.03 mmol) and *tert*-butylchlorodimethylsilane (228 mg, 1.51 mmol) with ice-cooling and the mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with ether (50 mL), washed with water (20 mL×2) and then with brine (20 mL). The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was chromatographed on a silica gel column (hexane–ethyl acetate, 10:1) to give **20** (297 mg, 100%) as a colorless oil. $[\alpha]_D^{25}=-7.4$ (*c* 1.12, $CHCl_3$). HRMS calcd for $C_{20}H_{28}NaO_6Si$ (MNa^+): 415.1553. Found: 415.1552. MS m/z: 393 (MH^+). IR ($CHCl_3$): 1732, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 0.04 and 0.07 (each 3H, s, $Si(CH_3)_2$), 0.90 (9H, s, *tert*-Bu), 2.11 (3H, s, Ac), 3.94 and 4.14 (1H, d, $J=11.0$ Hz, CH_2OSi), 4.55 and 4.61 (1H, d, $J=11.5$ Hz, CH_2OAc), 5.89 (1H, s, C_5-H), 7.44–7.72 (5H, m, Ph). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ −5.6, 18.1, 20.9, 25.7, 61.5, 61.8, 91.4, 105.2, 126.5, 128.9, 130.4, 132.5, 160.0, 164.8, 170.1.

4.4.10. Methyl (*R*)-3-hydroxy-3-phenylpropanoate, (*R*)-22. Compound **20** (290 mg, 0.74 mmol) was hydrogenated in ethyl acetate (30 mL) with 20% $Pd(OH)_2/C$ (30 mg) for 17 h. Removal of the catalyst and the solvent left a 2:1 mixture of *cis*- and *trans*-**21** as crystals. ^1H NMR (500 MHz, $CDCl_3$) δ 0.09 and 0.11 (each 3H, s, *cis*- and *trans*-**21**-SiMe×2), 0.91 (9H, s, *cis*- and *trans*-**21**-*tert*-Bu), 2.08 (3H, s, *cis*-**21**-Ac), 2.12 (3H, s, *trans*-**21**-Ac), 2.68 (1H, dd, $J=17.5$, 11.0 Hz, *trans*-**21**-C_5-axial H), 2.77 (1H, dd, $J=17.5$, 11.5 Hz, *cis*-**21**-C_5-axial H), 2.85 (1H, dd, $J=17.5$, 3.5 Hz, *cis*- and *trans*-**21**-C_5-equatorial H), 3.80 and 3.84 (each 1H, d, $J=11.5$ Hz, *cis*-**21**-CH_2OSi), 3.95 and 3.98 (each 1H, d, $J=11.0$ Hz, *trans*-**21**-CH_2OSi), 4.24 and 4.37 (each 1H, d, $J=12.0$ Hz, *trans*-**21**-CH_2OAc), 4.26 and 4.64 (each 1H, d, $J=12.0$ Hz, *cis*-**21**-CH_2OAc), 5.24 (1H, dd, $J=11.5$, 3.5 Hz, *cis*-**21**-C_6-H), 5.53 (1H, dd, $J=11.0$, 3.5 Hz, *trans*-**21**-C_6-H), 7.44–7.72 (5H, m, *cis*- and *trans*-**21**-Ph). To a solution of the mixture of *cis*- and *trans*-**21** in methanol (5 mL) was added aqueous (1 mL) KOH (159 mg) and the whole was heated under reflux for 5 min. After evaporation of methanol, the residue was acidified with 10% HCl (4 mL) and extracted with ether (10 mL×2). The organic layer was dried over $MgSO_4$, and treated with ethereal diazomethane. The oily product obtained after evaporation of the solvent was purified by PTLC ($CHCl_3$) to give (*R*)-**22** (105 mg, 79%) as a colorless oil. $[\alpha]_D^{25}=+6.4$ (*c* 1.01, ethanol) [lit.[19] *R*: $[\alpha]_D^{24}=+18.3$ (*c* 4.78, ethanol)].

4.5. Intramolecular photo[2+2]cycloaddition

4.5.1. (*S*)-{2-[(Acetyloxy)methyl]-6-methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl}methyl but-3-enoate, 28. DCC (115 mg, 0.56 mmol) and DMAP (10 mg, 0.08 mmol) were added to a solution of (*R*)-**13a** (100 mg, 0.46 mmol) and 3-butenoic acid (**23**, 48 mg, 0.56 mmol) in dichloromethane (3 mL) at ice-cooling temperature and the mixture was stirred for 4 h with ice-cooling. The whole was passed through a short column of silica gel eluted with ether and then evaporated. Purification of the residue by PTLC with hexane–ethyl acetate (2:1) gave **28** (123 mg, 94%) as a colorless oil. $[\alpha]_D^{26}=+5.8$ (*c* 1.00, $CHCl_3$). HRMS calcd for $C_{13}H_{17}O_7$ (MH^+): 285.0973. Found: 285.0991. IR ($CHCl_3$): 1750, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.00 (3H, d, $J=1.0$ Hz, C_6-CH_3), 2.12 (3H, s, Ac), 3.16 (2H, m, CH_2CO), 4.32 and 4.35 (each 1H, d, $J=6.0$ Hz, CH_2O), 4.57 and 4.64 (each 1H, d, $J=12.0$ Hz, CH_2O), 5.10–5.20 (1H, m, -CH=CH_2(*trans*)), 5.21–5.23 (1H, m, -CH=CH_2(*cis*)), 5.30 (1H, d, $J=1.0$ Hz, C_5-H), 5.86–5.95 (1H, m, -C*H*=CH_2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.8, 20.6, 38.6, 61.2, 94.4, 103.2, 119.3, 129.3, 158.3, 168.7, 169.9, 170.5.

4.5.2. (*S*)-{2-[(Acetyloxy)methyl]-6-methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl}methyl pent-4-enoate, 29. DCC (115 mg, 0.56 mmol) and DMAP (10 mg, 0.08 mmol) were added to a solution of (*R*)-**13a** (100 mg, 0.46 mmol) and 4-pentenoic acid (56 mg, 0.56 mmol) in dichloromethane (3 mL) at ice-cooling temperature and the mixture was stirred for 3 h with ice-cooling. The whole was passed through a short column of silica gel eluted with ether and then evaporated. Purification of the residue by PTLC with hexane–ethyl acetate (2:1) gave **29** (136 mg, 98%) as a colorless oil. $[\alpha]_D^{26}=+1.6$ (*c* 1.02, $CHCl_3$). HRMS calcd for $C_{14}H_{19}O_7$ (MH^+): 299.1131. Found: 299.1120. MS *m*/*z*: 299 (MH^+), 298 (M^+). IR ($CHCl_3$): 1748, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.00 (3H, d, $J=1.0$ Hz, C_6-CH_3), 2.12 (3H, s, Ac), 2.39 and 2.49 (each 2H, m, CH_2CH_2), 4.31 and 4.34 (each 1H, d, $J=4.5$ Hz, CH_2O), 4.57 and 4.63 (each 1H, d, $J=12.0$ Hz, CH_2O), 5.01–5.10 (2H, m, -CH=CH_2), 5.30 (1H, d, $J=1.0$ Hz, C_5-H), 5.82 (1H, m, -C*H*=CH_2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.8, 20.6, 28.6, 33.1, 60.9, 61.3, 94.4, 103.3, 115.9, 136.2, 158.4, 168.7, 169.9, 172.0.

4.5.3. (*S*)-{2-[(Acetyloxy)methyl]-6-methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl}methyl hex-5-enoate, 30. DCC (115 mg, 0.56 mmol) and DMAP (10 mg, 0.08 mmol) were added to a solution of (*R*)-**13a** (100 mg, 0.46 mmol) and 5-hexenoic acid (**25**, 63 mg, 0.55 mmol) in dichloromethane (3 mL) at ice-cooling temperature and the mixture was stirred for 4 h with ice-cooling. The whole was passed through a short column of silica gel eluted with ether and then evaporated. Purification of the residue by PTLC with hexane–ethyl acetate (2:1) gave **30** (133 mg, 92%) as a colorless oil. $[\alpha]_D^{27}=+3.9$ (*c* 1.00, $CHCl_3$). HRMS calcd for $C_{15}H_{20}O_7$ (M^+): 312.1208. Found: 312.1195. IR ($CHCl_3$): 1748, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.74 (2H, m, O=CCH$_2$CH_2CH$_2$), 2.00 (3H, d, $J=1.0$ Hz, C_6-CH_3), 2.10 (2H, m, O=CCH$_2$CH$_2$CH_2), 2.12 (3H, s, Ac), 2.39 (2H, m, O=CCH$_2$CH$_2$CH_2), 4.31 and 4.34 (each 1H, d, $J=3.0$ Hz, CH_2O), 4.56 and 4.62 (each 1H, d, $J=12.5$ Hz, CH_2O), 4.98–5.06 (2H, m, -CH=CH_2), 5.30 (1H, d, $J=1.0$ Hz, C_5-H), 5.77 (1H, m, -C*H*=CH_2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.8, 20.6, 23.9, 32.9, 33.1, 60.9, 61.3, 94.4, 103.3, 115.6, 137.4, 158.4, 168.7, 169.9, 172.5.

4.5.4. (*S*)-{2-[(Acetyloxy)methyl]-6-methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl}methyl hept-6-enoate, 31. DCC (115 mg, 0.56 mmol) and DMAP (10 mg, 0.08 mmol) were added to a solution of (*R*)-**13a** (100 mg, 0.46 mmol) and 6-heptenoic acid (**26**, 71 mg, 0.55 mmol) in dichloromethane (3 mL) at ice-cooling temperature and the whole was stirred for 4 h with ice-cooling. The whole was passed through a short column of silica gel eluted with ether and then evaporated. Purification of the residue by PTLC with hexane–ethyl acetate (2:1) gave **31** (143 mg, 95%) as a colorless oil. $[\alpha]_D^{25}=+3.5$ (*c* 1.24, $CHCl_3$). HRMS calcd for $C_{16}H_{22}O_7$ (M^+): 326.1364. Found: 326.1352. IR ($CHCl_3$): 1748, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.43 and 1.65 (each 2H, m, O=CCH$_2$CH_2CH_2CH$_2$), 2.00 (3H, d, $J=$ 1.0 Hz, C_6-CH_3), 2.07 (2H, m, O=CCH_2CH$_2$CH$_2$CH$_2$), 2.12 (3H, s, Ac), 2.38 (2H, m, O=CCH$_2$CH$_2$CH$_2$CH_2), 4.31 and 4.34 (each 1H, d, $J=5.5$ Hz, CH_2O), 4.57and 4.62 (each 1H, d, $J=12.0$ Hz, CH_2O), 4.94–5.03 (2H, m, -CH=CH_2), 5.30 (1H, d, $J=1.0$ Hz, C_5-H), 5.78 (1H, m, -C*H*=CH_2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.8, 20.6, 24.2, 28.2, 33.3, 33.7, 60.9, 61.3, 94.4, 103.3, 114.8, 138.2, 158.4, 168.7, 169.9, 172.6.

4.5.5. (*S*)-{2-[(Acetyloxy)methyl]-6-methyl-4-*oxo*-4*H*-1,3-dioxin-2-yl}methyl dec-9-enoate, 32. DCC (95 mg, 0.46 mmol) and DMAP (10 mg, 0.08 mmol) were added to a solution of (*R*)-**13a** (83 mg, 0.38 mmol) and 9-decenoic acid (**27**, 79 mg, 0.46 mmol) in dichloromethane (2.5 mL) at ice-cooling temperature and the mixture was stirred for 4 h with ice-cooling. The whole was passed through a short column of silica gel eluted with ether and then evaporated. Purification of the residue by PTLC with hexane–ethyl acetate (2:1) gave **32** (127 mg, 90%) as a colorless oil. $[\alpha]_D^{27}=+1.3$ (*c* 1.39, $CHCl_3$). HRMS calcd for $C_{19}H_{28}O_7$ (M^+): 368.1833. Found: 368.1829. IR ($CHCl_3$): 1748, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.27–1.41 and 1.63 (10H, m, O=CCH$_2$(CH_2)$_5$CH$_2$), 2.00 (3H, d, $J=1.0$ Hz, C_6-CH_3), 2.04 (2H, m, O=CCH_2(CH$_2$)$_5$CH$_2$), 2.12 (3H, s, Ac), 2.37 (2H, m, O=CCH$_2$(CH$_2$)$_5$CH_2), 4.31 and 4.33 (each 1H, d, $J=10.5$ Hz, CH_2O), 4.57 and 4.63 (1H, d, $J=12.0$ Hz, $J=12.0$ Hz, CH_2O), 4.93 (1H, m, -CH=CH_2(*trans*)), 4.99 (1H, m, -CH=CH_2(*cis*)), 5.30 (1H, d, $J=1.0$ Hz, C_5-H), 5.80 (1H, m, -CH=CH$_2$). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.8, 20.6, 24.8, 28.8, 28.9, 28.97, 29.04, 33.7, 33.9, 60.8, 61.3, 94.4, 103.3, 114.2, 139.0, 158.4, 168.7, 169.9, 172.8.

4.5.6. (1*R*,3*R*,6*S*,11*S*)-(11-Methyl-4,9-dioxo-5,8,12-trioxatricyclo[4,4,2,0^{3,11}]dodec-6-yl)methyl acetate, 33a. A solution of **28** (30 mg, 0.11 mmol) in ethyl acetate (70 mL) was irradiated (300 nm) under argon atmosphere for 6 h. The residue obtained after evaporation of the solvent was purified by PTLC with hexane–ethyl acetate (2:1) to give a crystalline product. Recrystallization from hexane–dichloromethane gave **33a** (14 mg, 47%) as colorless needles having a mp of 126–128°C. $[\alpha]_D^{20}=+17.5$ (*c* 1.11, $CHCl_3$). Anal. calcd for $C_{13}H_{16}O_7$: C, 54.93; H, 5.67. Found: C, 54.18; H, 5.60. MS *m*/*z*: 285 (MH^+). IR ($CHCl_3$): 1750 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.49 (3H, s, C_{11}-CH_3), 2.11 (3H, s, Ac), 2.56 (1H, dd, $J=16.0$, 2.5 Hz, C_5-H), 2.58 (1H, dd, $J=12.5$, 7.5 Hz, C_7-H), 2.64 (1H, dt, $J=12.5$, 11.0 Hz,C_7-H), 2.71 (1H, dd, $J=16.0$, 7.0 Hz, C_5-H), 2.82 (1H, m, C_6-H), 3.13 (1H, dd, $J=11.0$, 7.5 Hz, C_8-H), 4.13 and 4.16 (each 1H, d, $J=11.5$ Hz, CH_2O), 4.23 and 4.97 (each 1H, d, $J=12.0$ Hz, CH_2O). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.6, 26.3, 30.5, 33.7, 37.8, 41.9, 66.5, 70.2, 106.0, 167.2, 170.0, 176.1.

4.5.7. (1*S*,7*S*,9*R*,13*S*)-(13-Methyl-4,10-dioxo-3,11,12-trioxatricyclo[5.4.2.0^{9,13}]tridec-1-yl)methyl acetate, 34a and (1*S*,7*R*,9*R*,13*S*)-(13-methyl-4,10-dioxo-3,11,12-trioxatricyclo[5.4.2.0^{9,13}]tridec-1-yl)methyl acetate, 34b. A solution of **29** (11 mg, 0.037 mmol) in ethyl acetate (20 mL) was irradiated (300 nm) under argon atmosphere for 4 h. After evaporation of the solvent, the residue was purified by PTLC with hexane-ethyl acetate (5:1) to give **29** (0.6 mg, 5%), a less polar isomer **34b** (1.4 mg, 13%) as colorless needles having a mp of 117–119°C (crystallized from hexane–ether) and a more polar isomer **34a** (8.0 mg, 72%) as colorless needles having a mp of 151–152°C (recrystallized from pentane-ether). **34a**: $[\alpha]_D^{25}=-54.4$ (*c* 0.95, $CHCl_3$). HRMS calcd for $C_{14}H_{18}O_7$ (M^+): 298.1053. Found: 298.1075. IR ($CHCl_3$): 1752 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.52 (3H, s, C_{13}-CH_3), 1.79 (1H, dt, $J=12.0$, 2.5 Hz, C_8-H), 1.90 (1H, dd, $J=9.5$, 2.0 Hz, C_6-H), 2.09 (3H, s, Ac), 2.25–2.33 (3H, m, C_5-H, C_6-H, and C_7-H), 2.38 (1H, ddd, $J=12.0$, 10.0, 7.5 Hz, C_8-H), 2.69 (1H, dt, $J=14.0$, 7.5 Hz, C_5-H), 2.85 (1H, dt, $J=10.0$, 2.5 Hz, C_9-H), 4.05 (2H, d, $J=11.0$ Hz, CH_2O), 4.14 (1H, d, $J=11.0$ Hz, CHO), 4.93 (1H, d, $J=11.0$ Hz, CHO). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.6, 26.1, 28.0, 29.1, 35.0, 39.7, 47.0, 65.6, 69.1, 104.4, 169.4, 170.4, 175.1. **34b**: $[\alpha]_D^{25}=-105.2$ (*c* 0.26, $CHCl_3$). HRMS calcd for $C_{14}H_{18}O_7$ (M^+): 298.1053. Found: 298.1029. IR ($CHCl_3$): 1752 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.29 (3H, s, C_{13}-CH_3), 1.65–1.72 (2H, m, C_6-H and C_8-H), 1.87 (1H, ddt, $J=14.0$, 7.0, 9.5 Hz, C_6-H), 1.98 (1H, t, $J=10.0$ Hz, C_8-H), 2.07 (3H, s, Ac), 2.40 (1H, ddd, $J=11.5$, 7.0, 2.0 Hz, C_5-H), 2.46 (1H, dt, $J=11.5$, 9.5 Hz, C_5-H), 2.78 (1H, d, $J=7.5$ Hz, C_9-H), 3.69 (1H, m, C_7-H), 3.97 (1H, d, $J=12.0$ Hz, CHO), 4.07 (1H, d, $J=11.5$ Hz, CHO), 4.11 (1H, d, $J=11.5$ Hz, CHO), 4.98 (1H, d, $J=12.0$ Hz, CHO). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 18.8, 20.5, 20.7, 25.8, 33.6, 44.4, 44.5, 65.6, 66.0, 78.6, 104.8, 169.8, 171.1, 172.1.

4.5.8. (1*S*,8*S*,10*R*,14*S*)-(14-Methyl-4,11-dioxo-3,12,13-trioxatricyclo[6.4.2.0^{10,14}]tetradec-1-yl)methyl acetate, 35a and (1*S*,8*R*,10*R*,14*S*)-(14-methyl-4,11-dioxo-3,12,13 - trioxatricyclo[6.4.2.0^{10,14}]tetradec - 1 - yl)methyl acetate, 35b. A solution of **30** (104 mg, 0.33 mmol) in ethyl acetate (310 mL) was irradiated (300 nm) under an argon atmosphere for 10 h. The residue obtained after evaporation of the solvent was purified on a Merck lobar column (hexane–ether (2:1)) to give a less polar isomer **35b** (32 mg, 30%) as colorless prisms having a mp of 132–133°C (crystallized from hexane–dichloromethane) and a more polar isomer **35a** (46 mg, 44%) as colorless needles having a mp of 111–112°C (recrystallized from hexane–dichloromethane). **35a**: $[\alpha]_D^{26}=+5.3$ (*c* 0.53, $CHCl_3$). Anal. calcd for $C_{15}H_{20}O_7$: C, 57.68; H, 6.46. Found: C, 57.69; H, 6.40%. HRMS calcd for $C_{15}H_{20}O_7$ (M^+): 312.1208. Found: 312.1180. IR ($CHCl_3$): 1748 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.32 (1H, dt, $J=8.0$, 13.0 Hz, C_6-H), 1.55 (3H, s, C_{14}-CH_3), 1.66–1.73 (1H, m, C_7-H), 1.74 (1H, dt, $J=12.5$, 2.5 Hz, C_9-H), 1.97 (1H, dt, $J=6.5$, 13.0 Hz, C_7-H), 2.02–2.18 (2H, m, C_7-H and C_8-H), 2.11 (3H, s, Ac), 2.26 (1H, dd, $J=11.0$, 1.5 Hz, C_5-H), 2.34 (1H, dd, $J=11.0$, 6.5 Hz, C_5-H), 2.42 (1H, dt, $J=10.0$, 12.5 Hz, C_9-H), 2.90 (1H, dt, $J=10.0$, 2.5 Hz, C_{10}-H), 3.91 (1H, d, $J=12.0$ Hz, CHO), 4.06 (1H, d, $J=12.0$ Hz, CHO), 4.22 (1H, d, $J=12.0$ Hz, CHO), 5.13 (1H, d, $J=12.0$ Hz, CHO). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.6, 26.07, 26.14, 28.2, 29.2, 35.1, 39.8, 46.8, 64.8, 65.4, 77.2, 103.4, 169.7, 171.2, 176.0. **35b**: $[\alpha]_D^{27}=-33.2$ (*c* 0.30, $CHCl_3$). Anal. calcd for $C_{15}H_{20}O_7$: C, 57.68; H, 6.46. Found: C, 57.69; H, 6.30. HRMS calcd for $C_{15}H_{20}O_7$ (M^+): 312.1208. Found: 312.1201. IR ($CHCl_3$): 1750 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.36 (3H, s, C_{14}-CH_3), 1.49–1.64 (3H, m, C_9-H and C_7-H×2), 1.81 (1H, m, C_6-H), 1.96 (1H, t, $J=9.0$ Hz, C_9-H), 2.00–2.10 (1H, m, C_6-H), 2.07 (3H, s, Ac), 2.29 (1H, dd, $J=12.5$, 10.5 Hz, C_5-H), 2.56 (1H, dd, $J=12.5$, 10.0 Hz, C_5-H), 2.73 (1H, d, $J=9.0$ Hz, C_{10}-H), 3.45 (1H, m, C_8-H), 3.89 (1H, d, $J=12.0$ Hz, CHO), 4.07 (1H, d, $J=12.0$

Hz, CHO), 4.09 (1H, d, $J=12.0$ Hz, CHO), 5.00 (1H, d, $J=12.0$ Hz, CHO). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.4, 20.5, 24.0, 25.9, 29.5, 33.7, 42.8, 43.3, 64.1, 66.3, 78.3, 105.2, 169.5, 171.6, 175.2.

4.5.9. (1*S*,9*S*,11*R*,15*S*)-(15-Methyl-4,12-dioxo-3,13,14-trioxatricyclo[7.4.2.0^{11,15}]pentadec-1-yl)methyl acetate, 36a, (1*S*,9*R*,11*R*,15*S*)-(15-methyl-4,12-dioxo-3,13,14-trioxatricyclo[7.4.2.0^{11,15}]pentadec-1-yl)methyl acetate, 36b, and (1*S*,3*R*,11*S*,13*R*)-(1-methyl-8,13-dioxo-9,12,15-trioxatricyclo[9.3.1.0^{3,14}]pentadec-11-yl)methyl acetate, 36c. A solution of **31** (213 mg, 0.65 mmol) in ethyl acetate (426 mL) was irradiated (300 nm) under an argon atmosphere for 5 h. The residue obtained after evaporation of the solvent was purified on a silica gel column (hexane–ether (2:1)) to give a less polar isomer **36b** (86 mg, 40%) as colorless needles having a mp of 75–76°C (recrystallized from hexane–ether), a more polar isomer **36a** (54 mg, 25%) as colorless needles having a mp of 126–127°C (recrystallized from hexane–ether) and a cross isomer **36c** (23 mg, 11%) as a colorless oil. **36a**: $[\alpha]_D^{27}=+2.0$ (*c* 1.00, $CHCl_3$). Anal. calcd for $C_{16}H_{22}O_7$: C, 58.89; H, 6.79. Found: C, 59.06; H, 6.75%. MS *m*/*z*: 327 (MH^+). IR ($CHCl_3$): 1746 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (1H, ddt, $J=6.0$, 2.5, 13.0 Hz, C_8-H), 1.37 (1H, m, C_7-H), 1.44 (1H, dt, $J=13.0$, 2.5 Hz, C_7-H), 1.50–1.60 (1H, m, C_6-H), 1.54 (3H, s, C_{15}-CH_3), 1.82 (1H, dt, $J=13.0$, 3.0 Hz), 1.86 (1H, dq, $J=13.0$, 2.0 Hz, C_8-H), 1.95 (1H, dddd, $J=16.5$, 13.0, 6.5, 3.5 Hz, C_6-H), 2.07 (1H, m, C_9-H), 2.12 (3H, s, Ac), 2.44–2.52 (2H, m, C_5-H and C_{10}-H), 2.62 (1H, dt, $J=13.0$, 6.5 Hz, C_5-H), 2.91 (1H, ddd, $J=10.5$, 3.0, 1.0 Hz, C_{11}-H), 3.81 (1H, d, $J=12.0$ Hz, CHO), 4.04 (1H, d, $J=12.0$ Hz, CHO), 4.31 (1H, dd, $J=12.0$, 1.5 Hz, CHO), 5.13 (1H, dd, $J=12.0$, 1.5 Hz, CHO). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.5, 23.2, 25.2, 25.7, 28.51, 28.54, 31.7, 38.9, 45.8, 64.0, 64.1, 76.7, 103.0, 169.7, 170.8, 172.9. **36b**: $[\alpha]_D^{27}=-49.3$ (*c* 0.98, $CHCl_3$). Anal. calcd for $C_{16}H_{22}O_7$: C, 58.89; H, 6.79. Found: C, 58.60; H, 6.77. MS *m*/*z*: 327 (MH^+). IR ($CHCl_3$): 1750 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (1H, m, C_7-H), 1.20 (1H, m, C_8-H), 1.33 (3H, s, C_{15}-CH_3), 1.53 (1H, dt, $J=13.0$, 6.5 Hz, C_8-H), 1.64 (1H, dt, $J=9.0$, 11.5 Hz, C_{10}-H), 1.69 (1H, m, $J=11.5$, 7.5 Hz, C_7-H), 1.78 (2H, m, C_6-H), 1.98 (1H, ddd, $J=10.5$, 9.0, 1.0 Hz, C_{10}-H), 2.09 (3H, s, Ac), 2.41 (1H, ddd, $J=15.0$, 9.0, 6.5 Hz, C_5-H), 2.61 (1H, dt, $J=15.0$, 5.5 Hz, C_5-H), 2.80 (1H, dd, $J=9.0$, 1.0 Hz, C_{11}-H), 3.04 (1H, m, C_9-H), 3.75 (1H, d, $J=12.0$ Hz, CHO), 4.07 (1H, d, $J=11.5$ Hz, CHO), 4.11 (1H, d, $J=11.5$ Hz, CHO), 5.06 (1H, d, $J=12.0$ Hz, CHO). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 19.2, 20.4, 22.5, 22.8, 26.0, 27.5, 34.5, 43.0, 44.3, 63.2, 66.4, 78.5, 104.0, 169.3, 171.8, 171.9. **36c**: $[\alpha]_D^{26}=+3.9$ (*c* 2.46, $CHCl_3$). HRMS calcd for $C_{16}H_{23}O_7$: 327.1444. Found: 327.1454. MS *m*/*z*: 327 (MH^+). IR ($CHCl_3$): 1748 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.50 (3H, s, C_1-CH_3), 1.55–1.67 (2H, m, C_6-H×2), 1.70–1.80 (3H, m, C_4-H and C_5-H×2), 1.94 (1H, m, C_4-H), 2.13 (3H, s, Ac), 2.17 (2H, d, $J=6.5$ Hz, C_2-H×2), 2.42 (2H, m, C_7-H), 2.87 (1H, tq, $J=10.0$, 6.5 Hz, C_3-H), 3.16 (1H, d, $J=10.0$ Hz, C_{13}-H), 4.19 (1H, d, $J=12.5$ Hz, CHO), 4.29 (1H, d, $J=12.5$ Hz, CHO), 4.42 (1H, d, $J=12.0$ Hz, CHO), 4.54 (1H, d, $J=12.0$ Hz, CHO). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.6, 23.6, 24.9, 27.2, 28.1, 33.1, 34.2, 38.1, 42.8, 64.8, 77.5, 104.3, 166.5, 169.8, 173.1.

4.5.10. (1*S*, 2*S*, 3*S*)-3-{3-[(Acetyloxy)methyl]-2-hydroxy-2-methylcyclobutyl}propyl acetate, 38. To a suspension of $LiAlH_4$ (46 mg, 1.3 mmol) in dry THF (2 mL) was added a solution of **34a** (60 mg, 0.2 mmol) in dry THF (2 mL) dropwise under an argon atmosphere at ice-cooling temperature. The mixture was stirred for 4 h at room temperature. After decomposition of excess $LiAlH_4$ with 50% aqueous NaOH, the precipitate was removed by filtration through Celite. To the residue obtained after evaporation of the solvent was added acetic anhydride (2 mL) and pyridine (0.5 mL). After stirring for 3 h, the whole was diluted with ether, and washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, successively. The organic layer was dried over $MgSO_4$, and the residue obtained after evaporation of the solvent was chromatographed on a silica gel column. Elution with hexane–ethyl acetate (5:1) gave **38** (36 mg, 69%) as a colorless oil. $[\alpha]_D^{25}=-3.5$ (*c* 0.79, $CHCl_3$). HRMS *m*/*z* calcd for $C_{13}H_{23}O_5$ (MH^+): 259.1544. Found: 259.1533. IR ($CHCl_3$): 3463 (br), 1725 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (3H, s, C_2-CH_3), 1.25–1.44 (2H, m, C_4-H and $C_{1'}$-H), 1.54–1.63 (3H, m, $C_{1'}$-H and $C_{2'}$-H×2), 1.98 (2H, m, C_3-H and C_4-H), 2.05 (3H, s, Ac), 2.06 (3H, s, Ac), 2.24 (1H, ddt, $J=8.0$, 4.0, 10.0 Hz, C_1-H), 2.69 (1H, brs, OH), 3.86 (1H, dd, $J=11.5$, 4.0 Hz, C_1-CH_2), 4.05 (2H, t, $J=6.0$ Hz, $C_{3'}$-H×2), 4.40 (1H, dd, $J=11.5$, 10.0 Hz, C_1-CH_2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 21.0, 21.1, 25.1, 25.4, 26.5, 29.0, 42.0, 42.3, 63.7, 64.7, 75.3, 171.3, 172.1.

4.5.11. (1*R*,2*S*,3*S*)-5-{3-[(Acetyloxy)methyl]-2-hydroxy-2-methylcyclobutyl}pentyl acetate, 39. To a suspension of $LiAlH_4$ (49 mg, 1.3 mmol) in dry THF (3 mL) was added a solution of **36b** (70 mg, 0.21 mmol) in dry THF (2.5 mL) dropwise under an argon atmosphere at ice-cold temperature. The mixture was stirred for 3 h at room temperature. After decomposition of the excess $LiAlH_4$ with 50% aqueous NaOH, the precipitate was removed by filtration through Celite. To the residue obtained after evaporation of the solvent was added acetic anhydride (5 mL) and pyridine (0.5 mL). After stirring for 2 h, the whole was diluted with ether, and washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, successively. The organic layer was dried over $MgSO_4$, and the residue obtained after evaporation of the solvent was chromatographed on a silica gel column. Elution of hexane-ethyl acetate (3:1) gave **39** (45 mg, 73%) as a colorless oil. $[\alpha]_D^{27}=-48.1$ (*c* 1.13, $CHCl_3$). HRMS *m*/*z* calcd for $C_{15}H_{27}O_5$: 287.1859. Found: 287.1862. IR ($CHCl_3$): 3482 (br), 1730 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (3H, s, C_2-CH_3), 1.20–1.28 (3H, m, $C_{1'}$-H and $C_{2'}$-H×2), 1.28–1.39 (3H, m, C_4-H and $C_{3'}$-H×2), 1.51 (1H, m, $C_{1'}$-H), 1.62 (2H, quint, $J=7.0$ Hz, $C_{4'}$-H×2), 1.68 (1H, ddd, $J=12.0$, 9.5, 4.0 Hz, C_4-H), 2.05 (3H, s, Ac), 2.07 (3H, s, Ac), 2.09 (1H, brs, OH), 2.22 (1H, m, C_3-H), 2.28 (1H, m, C_1-H), 4.05 (2H, t, $J=7.0$ Hz, $C_{5'}$-H×2), 4.14 (1H, dd, $J=11.5$, 6.0 Hz, C_1-CH_2), 4.42 (1H, dd, $J=$

11.5, 8.0 Hz, C_1-CH_2). ^{13}C NMR (125.65 MHz, $CDCl_3$) δ 20.9, 21.0, 22.6, 23.4, 26.0, 27.0, 28.5, 29.9, 42.6, 45.3, 64.46, 64.52, 74.6, 171.2, 171.4.

Acknowledgements

The authors thank Dr. Y. Hirose of Amano Enzyme Inc., Japan for the gift of lipases and to Dr. M. Uchida of the School of Pharmaceutical Sciences, University of Shizuoka for the mass spectra measurements. This work was supported in part by Grant-in-Aid for Scientific Research No. 12470484 from the Ministry of Education, Science, Sports, Culture and Technology, Japan.

References

1. Seebach, D.; Zimmermann, J.; Gysel, U.; Ziegler, R.; Ha, T.-K. *J. Am. Chem. Soc.* **1988**, *110*, 4763–4772 and references cited therein.
2. (a) Demuth, M.; Palomer, A.; Sluma, H.-D.; Dey, A. K.; Kruger, C.; Tsay, Y.-H. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1117–1119; (b) Hoffmann, R.; Mattay, J. *Liebigs Ann. Chem.* **1995**, 1455–1461.
3. (a) Sato, M.; Takayama, K.; Furuya, T.; Inukai, N.; Kaneko, C. *Chem. Pharm. Bull.* **1987**, *35*, 3971–3974; (b) Sato, M.; Takayama, K.; Kaneko, C. *Chem. Pharm. Bull.* **1989**, *37*, 2615–2620; (c) Sato, M.; Abe, T.; Takayama, K.; Sekiguchi, K.; Kaneko, C.; Inoue, N.; Furuya, T.; Inukai, N. *J. Heterocycl. Chem.* **1991**, *28*, 241–252.
4. (a) Sato, M.; Murakami, M.; Kaneko, C.; Furuya, T. *Tetrahedron* **1993**, *49*, 8529–8540; (b) Sato, M; Murakami, M.; Sunami, S.; Kaneko, C.; Furuya, T.; Kurihara, H. *J. Am. Chem. Soc.* **1995**, *117*, 4279–4287.
5. For reviews on chiral dioxinones: (a) Kaneko, C.; Sato, M.; Sakaki, J.; Abe, Y. *J. Heterocycl. Chem.* **1990**, *27*, 25–30; (b) Sato, M.; Sunami, S.; Kaneko, C. *Heterocycles* **1996**, *42*, 861–883.
6. Seebach, D.; Muller, S. G.; Gysel, U.; Zimmermann, J. *Helv. Chim. Acta* **1988**, *71*, 1303–1318.
7. (a) Sato, M.; Abe, Y.; Ohuchi, H.; Kaneko, C. *Heterocycles* **1990**, *31*, 2115–2119; (b) Sato, M.; Ohuchi, H.; Abe, Y.; Kaneko, C. *Tetrahedron: Asymmetry* **1992**, *3*, 313–328.
8. Desymmetrization of 2,2-disubstituted-1,3-proopanediol by lipase-catalyzed monoacetylation: (a) Fadel, A.; Arzel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 283–291; (b) Kirihara, M.; Takuwa, T.; Kawasaki, M.; Kakuda, H.; Hirokami, S.; Takahata, H. *Chem. Lett.* **1999**, 405–406; (c) Akai, S.; Naka, T.; Fujita, T.; Takebe, Y.; Tsujino, T.; Kita, Y. *J. Org. Chem.* **2002**, *67*, 411–419.
9. Bentley, P. H.; McCrae, W. *J. Org. Chem.* **1970**, *35*, 2082–2083.
10. Hoppe, D.; Schmincke, H.; Kleemann, H.-W. *Tetrahedron* **1989**, *45*, 687–694.
11. Araki, Y.; Nagasawa, J.; Ishido, Y. *J. Chem. Soc., Perkin Trans. 1* **1981**, 12–23.
12. Sodeoka, M.; Yamada, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1990**, *112*, 4906–4911.
13. (a) Carroll, M. F.; Bader, A. R. *J. Am. Chem. Soc.* **1952**, *74*, 6305; (b) Carroll, M. F.; Bader, A. R. *J. Am. Chem. Soc.* **1953**, *75*, 5400–5402.
14. (a) Sato, M.; Ogasawara, H.; Kato, T. *Chem. Pharm. Bull.* **1984**, *32*, 2602–2608; (b) Oikawa, Y.; Sugano, K.; Yonemitsu, O. *J. Org. Chem.* **1978**, *43*, 2087–2088.
15. Bihlmayer, G. A.; Derflinger, G.; Derkosch, J.; Polansky, O. E. *Monatsh. Chem.* **1967**, *98*, 564–578.
16. Yamamoto, Y.; Watanabe, Y.; Ohnishi, S. *Chem. Pharm. Bull.* **1987**, *35*, 1860–1870.
17. (a) Sato, M.; Sekiguchi, K.; Ogasawara, H.; Kaneko, C. *Synthesis* **1985**, 224–226; (b) Sato, M.; Ogasawara, H.; Oi, K.; Kato, T. *Chem. Pharm. Bull.* **1983**, *31*, 1896–1901.
18. Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1997**, *62*, 8595–8599.
19. Schoepf, C.; Wuest, W. *Justus Liebigs Ann. Chem.* **1959**, *626*, 150–154.