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Stereospecific Annulation of Hydroxy Vinyl Ethers. Synthetic Application to Polyfunctionalized Cyclic Compounds

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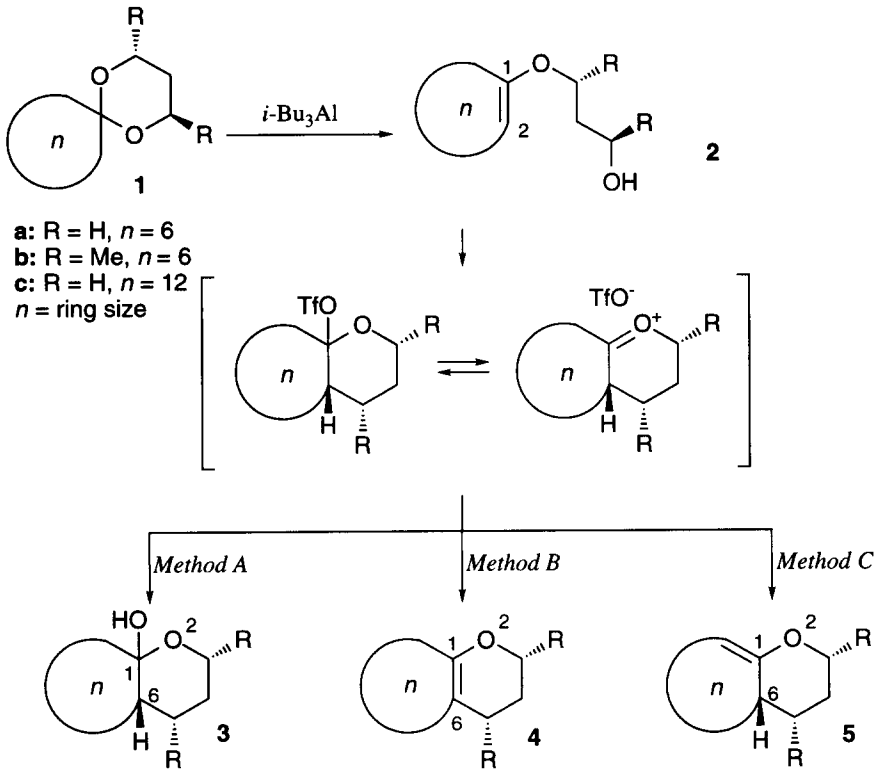
Abstract: Stereospecific annulation of hydroxy vinyl ethers in the presence of triflic anhydride and tertiary amines and its synthetic application are described. Each 1-hydroxy-2-oxabicyclo[n.4.0]alkane, 2-oxabicyclo[n.4.0]alk-1(6)-ene and 2-oxabicyclo[n.4.0]alk-1(6+n)-ene is stereoselectively synthesized from the same hydroxy vinyl ether depending on the choice of the reaction conditions (temperature, solvent and tertiaryamine). These compounds lead to polyfunctionalized cyclic compounds and some natural products. We propose that this annulation reaction proceeds through a pure S_N2-like mechanism.

Introduction

A remarkable number of medium- and large-size cyclic ether formation reactions have been reported[2] and successfully applied to total synthesis of some natural products containing cyclic ether moieties, as recent examples, Brevetoxin B,[3] Lonomycin A,[4] and (+)-Laurencin.[5] While studying diastereoselective cleavages of chiral acetals, our group found that triisobutylaluminum was an outstanding reagent for the transformation of acetal **1** to hydroxy vinyl ether **2**,[6] and also that the kinetic resolution of chiral acetals derived from racemic cyclic ketones[6] and the asymmetrization of chiral acetals derived from *meso*-cyclic ketones[7] were observed by acetal cleavages using triisobutylaluminum. We expected that hydroxy vinyl ether **2** would have the possibility of ring formation by an intramolecular substitution reaction of a double bond to the terminal hydroxy group. Now we describe novel methods for stereoselective formation of cyclic ether derivatives and synthetic application to polyfunctionalized cyclic compounds.[8]

Results and Discussion

The deprotonation and ether cleavage reaction of acetal **1** with 4 equiv of triisobutylaluminum in dichloromethane at 0 °C gives the corresponding hydroxy vinyl ether **2** in excellent yield.[6,7] In our preliminary study, the crude **2** was treated with triflic anhydride in the presence of excess *N,N*-diisopropylethylamine at -78 °C for 3 h, quenched with aqueous sodium hydrogen carbonate, then warmed to room temperature (*Method A*) to give the cyclic hemiacetal **3** in high yield (Scheme 1).[9] Some of the results are summarized in Table 1.



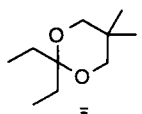
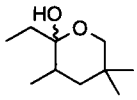
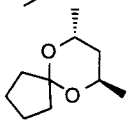
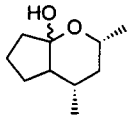
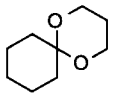
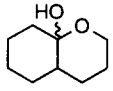
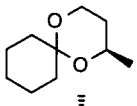
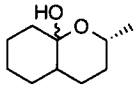
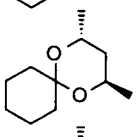
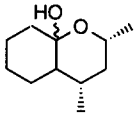
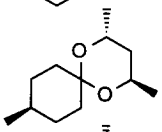
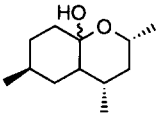
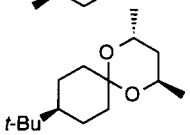
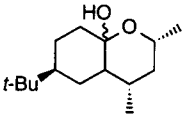
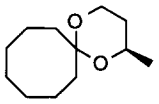
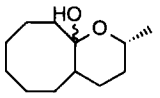
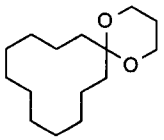
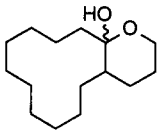
Method A: 1) Tf_2O (1.2 equiv), *i*-Pr_2EtN, CH_2Cl_2 -78 °C; 2) aq. $NaHCO_3$; 3) warm to 25 °C
Method B: Tf_2O (1.2 equiv), *i*-Pr_2EtN, toluene -78 to 25 °C
Method C: Tf_2O (1.2 equiv), *i*-Pr_2EtN, CH_2Cl_2 -78 to 25 °C

Scheme 1. Regio- and Stereo-selective Annulation-Elimination Reactions of Hydroxy Vinyl Ether **2**

The consecutive reactions using *Method A* smoothly proceeded when not only spiroacetals but also acetals derived from acyclic ketones were used (entry 1). For spiroacetals, we draw attention to the fact that in elimination of chiral acetals derived from ketones and (-)-(2*R*,4*R*)-2,4-pentanediol with triisobutylaluminum, an asymmetric deprotonation reaction takes place (selectivity: >9 : 1),[6] leading to optically pure hemiacetal after the cyclization process (entry 6). After one recrystallization of the crude product, all chiral centers of the molecule were found to be homogeneous (see also entry 7).

Table 1. Stereospecific Annulation of Hydroxy Vinyl Ethers Using *Method A*

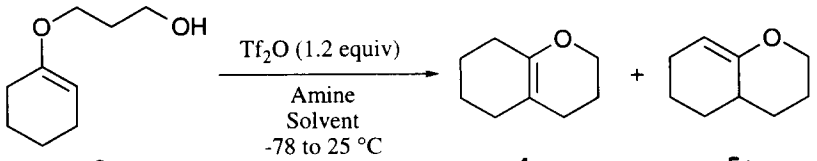
1 —(1) *i*-Bu_3Al, (2) *Method A*→ **3**

Entry	Acetal **1**	Hemiacetal **3** [a]	Yield (%)
1			79
2			68
3	 **1a**	 **3a**	75
4			87
5	 **1b**	 **3b**	>95
6			>95
7			87
8			85
9	 **1c**		83

[a] A mixture of anomers.

In a second study, while investigating in further detail the annulation reaction of 1-cyclohexyl-3-hydroxypropyl ether (**2a**) derived from 1,5-dioxaspiro[5.5]undecane (**1a**), we found that a mixture of 2-oxobicyclo[4.4.0]dec-1(6)-ene (**4a**) and 2-oxabicyclo[4.4.0]-dec-1(10)-ene (**5a**) was obtained by warming to 25 °C, without quenching, the reaction solution of **2a** in the presence of triflic anhydride and tertiary amine (Scheme 1).[10] Proceeding of the reaction was monitored by ^{1}H NMR analysis of the reaction solution because the products **4a** and **5a** were highly acid sensitive compounds. Therefore, the reaction gradually proceeded above 0 ℃ and was completed by stirring for over 12 h at 25 °C. Taking both experimental results into consideration, it was suggested that the reaction intermediate, a bicyclic triflate, which was produced in the reaction of **2a** with triflic anhydride at -78 °C, was hydrolyzed by warming to 25 ℃ after adding water at -78 ℃ to give **3a**, while its intermediate was transformed to the triflic acid-eliminated compounds **4a** and **5a** by warming to 25 °C under anhydrous conditions.

Table 2. Effects of Amines and Solvents for the Regioselectivity



2a **4a** **5a**

Entry	Amine [mL per 1mmol of **2a**]	Solvent [mL per 1 mmol of **2a**]	Ratio [a] **4a** : **5a**
1	*c*-Hex_2MeN, 1	CH_2Cl_2, 5	10 : 90
2[b]	*i*-Pr_2EtN, 2	CH_2Cl_2, 5	11 : 89
3	*c*-$HexEt_2N$, 1	CH_2Cl_2, 5	14 : 86
4	*i*-Pr_2EtN, 1	CH_2Cl_2, 5	16 : 84
5	*c*-Hex_2EtN, 1	CH_2Cl_2, 5	17 : 83
6	*i*-Pr_2EtN, 1	CH_2Cl_2, 10	18 : 82
7	*i*-Bu_3N, 1	CH_2Cl_2, 5	91 : 9
8	*i*-Pr_2EtN, 1	Toluene, 5	91 : 9
9[c]	*i*-Pr_2EtN, 1	Toluene, 10	97 : 3

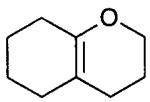
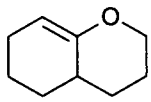
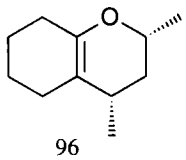
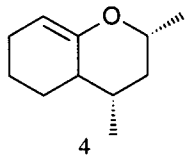
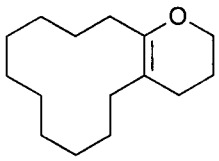
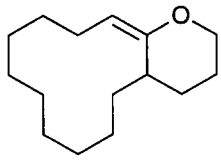
[a] The ration was determined by ^{1}H NMR analysis of the crude products.
[b] *Method C*: entry 2. [c] *Method B*: entry 9;

The substantial difference in **4a** and **5a** prompted us to examine the regioselective annulation-elimination reaction of **2a**. The ratio of **4a** and **5a** was determined by ^{1}H NMR analysis of crude products to check the real selectivity. A variety of tertiary amines were first screened to investigate the regioselectivity in the elimination reaction of **2a**. Some of the results are summarized in Table 2; they strongly suggest a crucial role for the steric hindrance of tertiary amines. The use of sterically hindered tertiary amines in dichloromethane gave **5a** in good regioselectivity (entries 1, 2, 3 and 5). In contrast, the use of non-nucleophilic and relatively less hindered tertiary amine, triisobutylamine, in dichloromethane gave **4a** in good regioselectivity (entry 7). These results can be understood on the basis that the direction of the elimination of the cationic intermediate in dichloromethane is governed by the degree of steric hindrance to the approach of amine to the β-proton under kinetic control. The regioselectivity and the mechanistic consideration presented above is consistent with Gassman's regioselective vinyl ether formation from acetal in dichloromethane in the presence of trimethylsilyl triflate and *N,N*-diisopropylethylamine.[11]

Solvent effect is also an important factor in the regioselectivity: the use of *N,N*-diisopropylethylamine in toluene gave **4a** as a major isomer (entry 4 vs. entry 8). This result was understandable based on the direction of the elimination in toluene governed by thermodynamic control. Thus, the product composition of the vinyl ethers favors the more substituted, and therefore more stable, vinyl ether **4** regardless of the steric factor of tertiary amine. These mechanistic considerations confirm that the ratio of **4a** vs. **5a** is changed by the concentration of tertiary amine: high concentration of tertiary amine favors **5a** (entry 2 vs. entries 4 and 6) while high dilution of tertiary amine favors **4a** (entry 8 vs. entry 9). Thus, the procedures used in the reactions of entry 9 (*Method B*)[12] and entry 2 (*Method C*) were established as representative of the regioselective annulation-elimination reaction of **2a**.

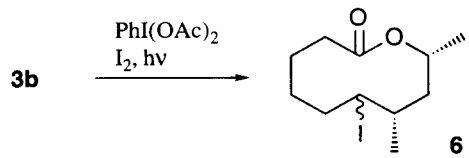
The generality and scope of the annulation were explored by examining *Method B* and *Method C* for the reaction of hydroxy vinyl ethers **2** derived from several structurally diverse acetals **1** (Table 3). Both methods gave **4** and **5**, respectively, in good yields and with good regioselectivity. *To our knowledge, the regioselective annulation-elimination reaction using Method C is the first examples of a practicable synthesis of* **5**.[12] Using these three methods, we were able to get three kinds of cyclic ethers from the same acetal. The applications to useful polyfunctionalized compounds are the following.

Table 3. Regioselective Synthesis of Bicyclic Vinyl Ethers **4** and **5** from Spiroacetal **1** [a]

Spiroacetal	*Method* [b]	**4** : **5** [c]	
1a			
	B	97	3
	C	13	87
1b			
	B	96	4
	C	31	69
1c			
	B	87	13
	C	9	91

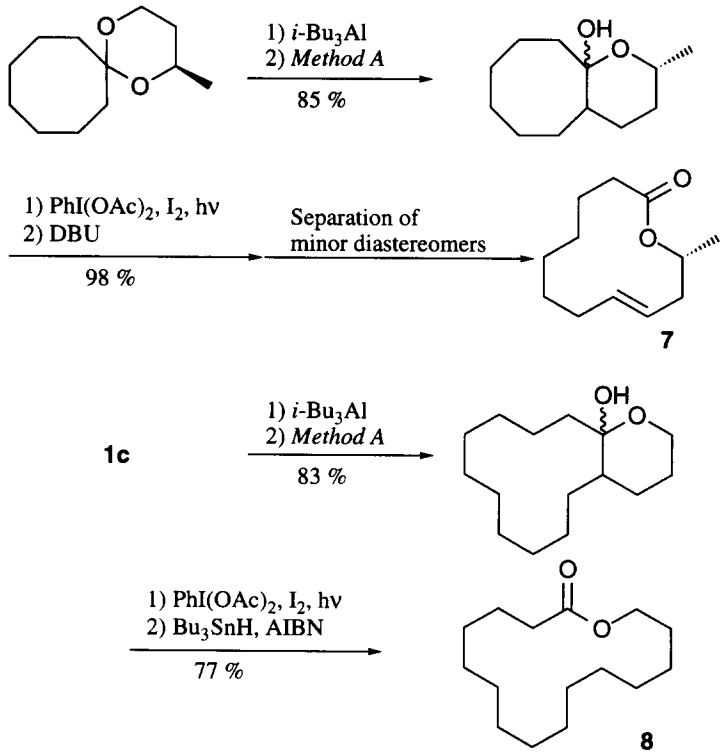
[a] The crude product **2**, which was prepared from **1** using *i*-Bu_3Al, was immidiately used. [b] *Method B*: entry 9 in Table 2; *Method C*: entry 2 in Table 2. [c] The ratio was determined by ^1H NMR analysis of the crude products.

The hemiacetals **3** using *Method A* were easily converted to lactones by the method of Suarez's,[13] Suginome's[14] or Nagao's[15] group. For example, hemiacetal **3b** was quantitatively transformed to the medium ring iodolactone **6**[13] (Scheme 2).



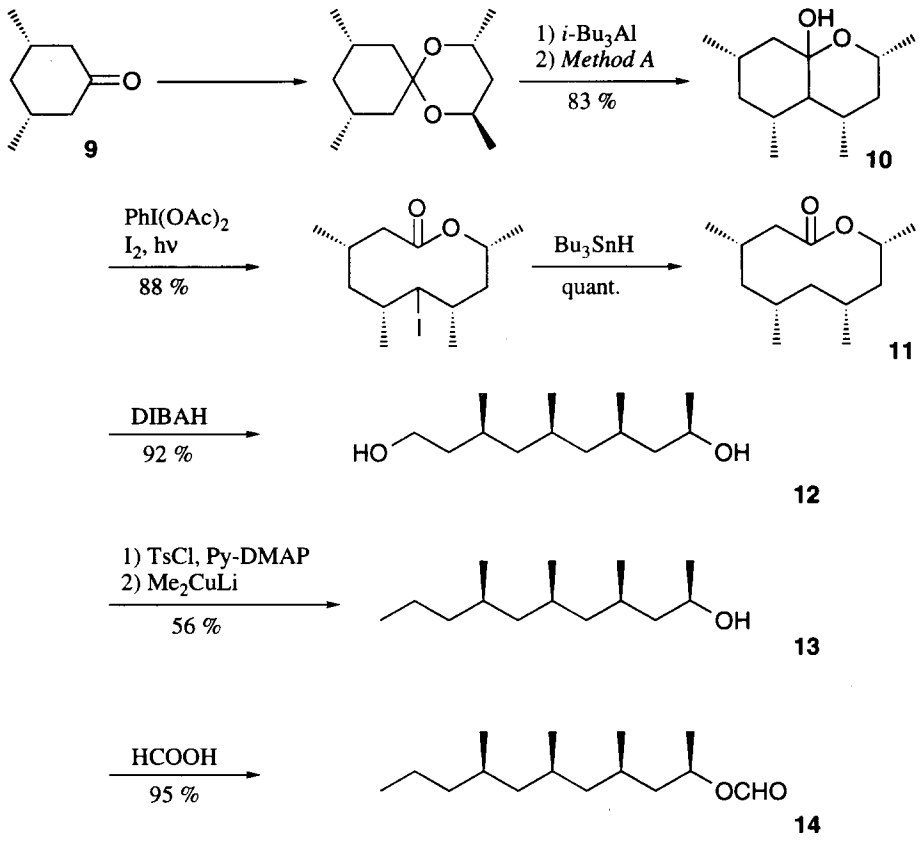
Scheme 2. Conversion of Hemiacetal **3** to Iodolactone **6**

The method thus provides a facile route to large and medium ring lactones in a stereospecific way, as demonstrated by the synthesis of (+)-recifeiolide (**7**)[16] and exaltolide (15-pentadecanolide (**8**))[17] in short steps (Scheme 3).



Scheme 3. Facile Syntheses of (+)-Recifeiolide **7** and Exaltolide **8**

We demonstrate the effectiveness of *Method A* approach starting with simple ketone **9**[18] that can be transformed in short steps into (-)-Lardolure (**14**),[19] the aggregation pheromone of the acarid mite, *Lardoglyphus Konoi*. Under standard cyclization conditions the hemiacetal **10** was obtained in 83% yield, mp 78-80 °C after one recrystallization. Ring opening with iodobenzene diacetate gave the iodolactone, which was further transformed to lactone **11** quantitatively with tributyltin hydride. Addition of an excess of DIBAH at -78 °C produced the diol **12**. Selective monotosylation followed by exposure of the monotosylate to excess dimethyl copper lithium in ether gave **13** with the desired carbon framework and desired stereochemistry. Formylation of **13** then led to pheromone **14**,[19] which was identical to the authentic material kindly provided by Professor Kenji Mori. The synthesis of **14** described herein is straightforward with full stereocontrol; its brevity stems from the effective dovetailing of the new annulation process.

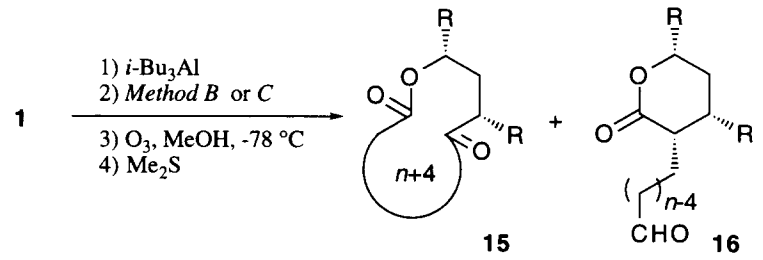


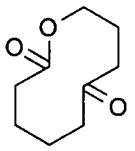
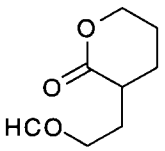
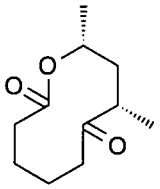
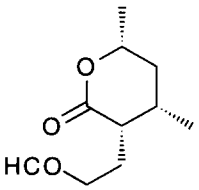
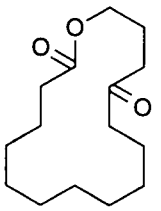
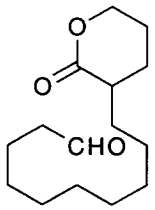
Scheme 4. Facile Synthesis of (-)-Lardolure **14**

The synthetic utility of the unstable compounds **4** and **5** via *Method B* and *Method C* is clear from oxidative transformations to four useful synthetic intermediates **15**, **16**, **17** and **18**. Ozonolysis of **4** and **5** gave (2+n)-oxolactones (**15**)[20] and 2-substituted-5-pentanolides (**16**), respectively. These results are summarized in Table 4. Hydroboration of **5** using BH_3•THF or 9-BBN gave (6+n)-hydroxy-2-oxabicyclo[n.4.0]alkanes (**17**) or (**18**) with high stereoselectivity. Because **4** did not react under the same conditions, the oxidation products derived from **4** were undefined. These results are summarized in Table 5.

For each case, product stereochemistry was confirmed by ^{1}H NMR and ^{13}C NMR analyses. The structural assignment of **17a** and **18a** was based on comparison with the special values of *cis*- and *trans*-2-oxabicyclo[4.4.0]decanes reported in the literature.[21] In addition, for product **18b**, the *cis* structure and absolute configuration was determined by single-crystal X-ray crystallographic analysis of the *p*-nitrobenzoate (Figure 1).[22] The absolute stereochemistry of **15b** and **16b** was analogized from the X-ray structure of the *p*-nitrobenzoate. The structure of **17c** and **18c** could not be determined by NMR analyses, but the diastereomeric ratio was found by capillary GLC analysis.

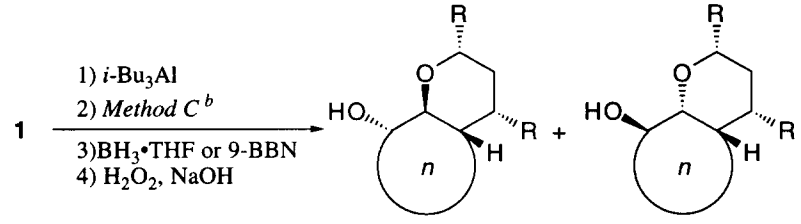
Table 4. Ozonolysis of Bicyclic Vinyl Ethers Derived from **1**



Spiroacetal	*Method* [b]	Yield (%) [c]	**15** : **16** [d]	
1a				
	B	58	88	: 12
	C	61	22	: 78
1b				
	B	52	97	: 3
	C	54	35	: 65
1c				
	B	43	79	: 21
	C	77	24	: 76

[a] Ozonolysis was carried out in methanol at -78 °C. [b] *Method B*: entry 9 in Table 2; *Method C*: entry 2 in Table 2. [c] Overall yield from **1**. [d] The ratio was determined by ^{1}H NMR analysis.

Table 5. Stereoselective Hydroboration of Bicyclic Vinyl Ethers Derived from **1** [a]



Spiroacetal	Yield (%) [c]	**17** : **18** [d]
1a	48 [e]	94 : 6
	(89) [e,f]	93 : 7
	(<95) [f]	75 : 25
1b	53	<1 : >99
1c	65	(70 : 30) [g]

[a] Hydroboration was carried out in THF using 1.5 equiv of BH_3•THF at 25 °C. [b] *Method C*: entry 2 in Table 2. [c] Overall yield from **1**. [d] The ratio was determined by capillary GLC analysis. [e] 9-BBN was used in place of BH_3•THF. [f] **5** purified by column chromatography was used. [g] The stereochemistries of diastereomers **17c** and **18c** were not determined.

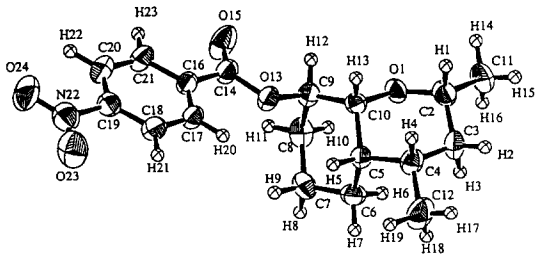
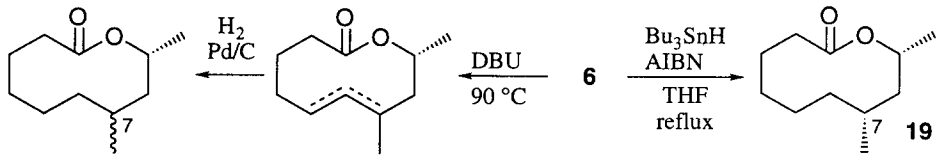
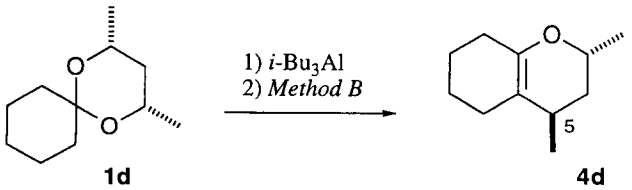


Figure 1. ORTEP structure of the *p*-nitrobenzoate of **18b** as determined by X-ray crystallographic analysis.

It is presumed that the specific annulation of **2b** into **3b**, **4b** or **5b** proceeds through a pure S_N2-like mechanism, namely, the inversion of stereochemistry at hydroxy function. Evidence for the mechanism was based upon the following experimental results: (1) Iodolactone **6**, prepared from the annulation reaction of **2b** by *Method A* and photoiodolactonization, was treated with DBU at 90 °C to eliminate iodine and hydrogenation on Pd/C. In this case, it was assumed that hydrogenation should give a mixture of diastereomers. Indeed, the crude reaction mixture from hydrogenation revealed two peaks on GLC analysis, *i.e.*, each stereoisomer at C(7), while exposure of the iodolactone with tributyltin hydride-AIBN in THF under reflux furnished quantitatively lactone **19** as a sole product (Scheme 5). (2) The X-ray structure of *p*-nitrobenzoate of **18b** indicates that the annulation-elimination reaction of **2b** proceeds with complete inversion of stereochemistry at the triflate function and by stereospecific attack to *re*-face of vinyl ether carbon. (3) The annulation-elimination reaction of the acetal **1d** derived from cyclohexanone and *meso*-2,4-pentanediol by *Method B* gave the (4*RS*,5*RS*)-3,5-dimethyl-2-oxabicyclo[4.4.0]dec-1(6)-ene (**4d**), another diastereomer of **4b**, *i.e.*, another stereochemistry on C(5), determined as a unique product by GLC analysis (Scheme 6).

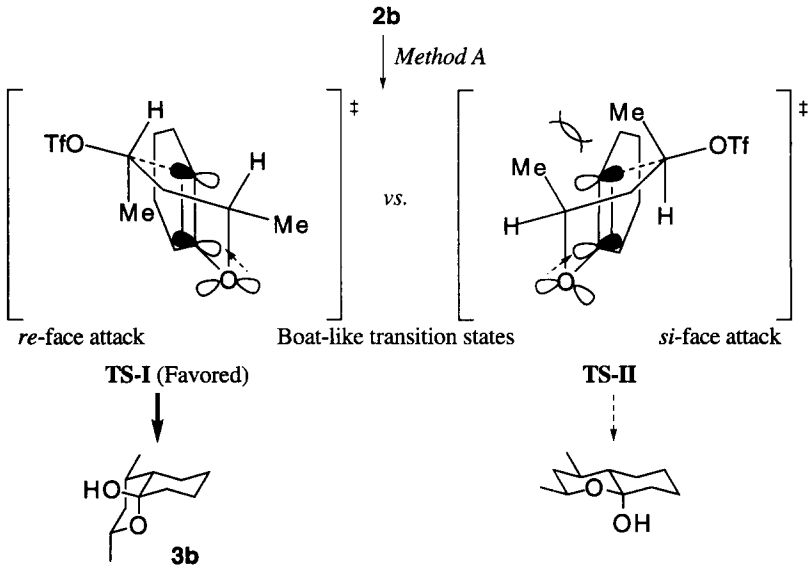


Scheme 5. Deiodinations of Iodolactone **6**

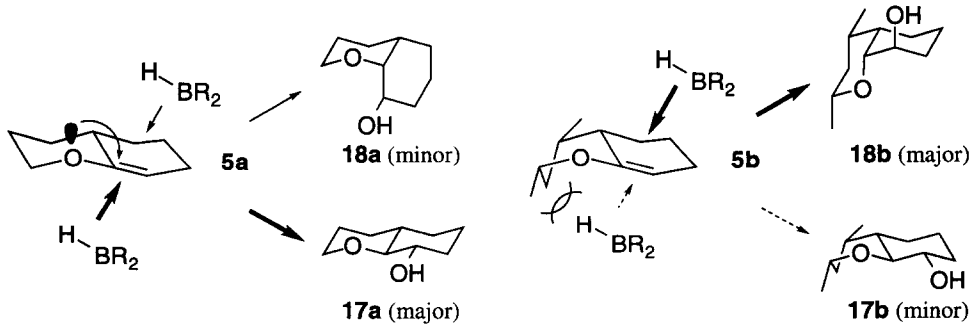


Scheme 6. Stereospecific Annulation-Elimination Reaction Using *Method B*

The observed intramolecular stereospecific attack of the hydroxy group-attached carbon of **2b** to the *re*-face on vinyl ether carbon was predicted on the basis of a boat-like transition state in order to fulfill the stereoelectronic requirement: one electron pair on the ether oxygen atom is parallel to the π system of the double bond to give a delocalized oxocarbenium ion.[23] The preference for **TS-I** (*re*-face attack on vinyl ether carbon) over **TS-II** (*si*-face attack) is believed to have a steric origin, with the latter destabilized by 1,3-diaxial repulsion between two methyl groups (Scheme 7).



Scheme 7. Proposed Mechanism for Stereospecific Cyclization of **2b**



Scheme 8. Stereoselectivity on the Hydroboration of Bicyclic Vinyl Ethers **5a** and **5b**

Hydroboration reaction on vinyl ether double bond using **5** is highly stereo- and regio-selective.[24] The hetero atom directs the addition of diborane nearly exclusively to the β-position to give β-hydroxy ether. The observed relative stereochemical preferences for the formation of **17** or **18** are consistent with the pathway shown in Scheme 8. In the hydroboration of **5a**, borane reagent stereoselectively approaches the antiperiplanar side of the axial lone pair on ether oxygen by anomeric interaction between π orbital on olefin and its lone pair, to afford **17a** as major product. In the reaction of **5b**, in contrast, borane reagent stereoselectively approaches the less hindered side of the olefin, to afford **18b** as a major product, since the antiperiplanar arrangement of lone pairs on ether oxygen and π orbital of olefin is obstructed by steric hindrance of the two dimethyl groups.

In summary, this paper describes novel methods of cyclic ether preparation through stereoselective- and regioselective annulation-elimination reactions. These products are easily transformed to polyfunctionalized cyclic compounds and applied to some natural product syntheses. Also, the annulation reaction of hydroxy vinyl ether proceeds through a complete S_N2-like mechanism.

Experimental Section

General. Melting points were taken on a Shimadzu MM-2 apparatus or a Yanaco MP-J3 and are uncorrected. Infrared (IR) were recorded on a Shimadzu FTIR-8100 or a Hitachi 260-10 spectrometers. ^{1}H NMR spectra were measured on a Varian Gemini 200 (200 MHz), a Varian Gemini 300 (300 MHz) and a VXR 500 (500 MHz) spectrometers. Chemical shifts of ^{1}H NMR are expressed in parts per million downfield relative to internal tetramethylsilane (δ=0) or chloroform (δ=7.26). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; br, broad peak. ^{13}C NMR spectra were measured on a VXR 500 (160 MHz) spectrometer. Chemical shifts of ^{13}C NMR are expressed in parts per million downfield relative to internal chloroform (δ=77.07 ppm). Optical rotations were measured on a Jasco DIP 140 polarimeter. Analytical gas-liquid phase chromatography (GLC) was performed on a Gasukuro Kogyo Model 370 or a Shimadzu Model 8A instrument with a flame-ionization detector and a capillary column of PEG-20M Bonded (0.25 mm × 25 m), PEG-HT Bonded (0.25 mm × 25 m), or OV-101 (0.25 mm × 25 m) using nitrogen as carrier gas. GC/MS analyses were done on a Shimadzu GC-17A gas chromatograph and a Shimadzu Parvum (QP-5000) mass spectrometer. The column used was a 30 m × 0.25 mm TC-1 (GL Sciences Inc.) with a film thickness of 0.1 μm. The molecular ion is indicated by M^+. For thin layer chromatographic (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel 60 E. Merck Art 9385 and ICN Alumina B, Akt. I. Microanalyses were accomplished at the School of Agriculture of Nagoya University. Reactions involving air- or moisture- sensitive compounds were conducted in appropriate round-bottomed flasks with magnetic stirring bars under an atmosphere of dry argon. The ozone was generated by electric discharge in an oxygen stream, using a Nippon Ozone Co. Ltd., QOT-31R-2 ozonator.

In experiments requiring dry solvents, dichloromethane and toluene were distilled from calcium hydride. Tertiary amines were also distilled from calcium hydride. (-)-(2*R*,4*R*)-2,4-Pentanediol was purchased from Wako Pure Chemical Industries, Ltd. and ,after checking the optical purity; $[\alpha]^{23}_D$=-41.2° (*c* 9.99, $CHCl_3$). (-)-(3*R*)-1,3-Butanediol was purchased from Aldrich Chemical Company, Inc. and ,after checking the optical purity; $[\alpha]^{24}_D$=-29.6° (*c* 1.00, EtOH). Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. *Triflic anhydride used was purchased from either Tokyo Chemical or Merck. When that from Aldrich was used in the regioselective annulation-elimination reaction of* **2**,

thermodynamic bicyclic vinyl ether **4** *was obtained as a major product regardless of whether Method B or Method C was employed. It was ascertained by* ^{19}F *NMR analysis that unknown impurities were included in the triflic anhydride purchased from Aldrich.*

Preparation of Acetals. Acetals were prepared in excellent yield from the corresponding ketones and 1,3-diols in the presence of a catalytic quantity of *p*-toluenesulfonic acid or pyridinium *p*-toluenesulfonate.

2,2-Diethyl-5,5-dimethyl-1,3-dioxane: TLC, R_f=0.61 (hexane-EtOAc, 5 : 2); IR (film) 2950, 2880, 1470, 1460, 1160, 1140, 1105, 960, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, *J*=7.6 Hz, 6H, $2CH_2CH_3$), 0.97 (s, 6H, $2CH_3$), 1.73 (q, *J*=7.6 Hz, 4H, $2CH_2CH_3$), 3.49 (s, 4H, $2CH_2O$).

(7*R*,9*R*)-7,9-Dimethyl-6,10-dioxaspiro[4.5]decane: TLC, R_f=0.53 (hexane-EtOAc, 10 : 3); IR (film) 2990, 2960, 2900, 1385, 1355, 1335, 1200, 1155, 1130, 1110, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (d, *J*=6.4 Hz, 6H, $2CH_3$), 1.58-1.96 (m, 10H), 3.98 (septet, *J*=6.6 Hz, 2H, 2C*H*O).

1,5-Dioxaspiro[5.5]undecane (1a): TLC, R_f=0.47 (hexane-EtOAc, 5 : 2); IR (film) 2970, 2900, 1180, 1160, 1120, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35-1.95 (m, 12H, $(CH_2)_5$ and CH_2), 3.92 (t, *J*=5.6 Hz, 4H, $2CH_2O$).

2-Methyl-1,5-dioxaspiro[5.5]undecane: TLC, R_f=0.47 (hexane-EtOAc, 10 : 3); IR (film) 2950, 2880, 2370, 2340, 1450, 1370, 1170, 1160, 1115, 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, *J*=6.2 Hz, 3H, CH_3), 1.30-2.06 (m, 12H, $(CH_2)_5$ and CH_2), 3.79 (ddd, *J*=1.7, 5.5, 11.5 Hz, 1H, C*H*HO), 3.98 (dt, *J*=3.1, 11.5 Hz, 1H, CH*H*O), 3.94-4.12 (m, 1H, C*H*O).

(2*R*,4*R*)-2,4-Dimethyl-1,5-dioxaspiro[5.5]undecane (1b): TLC, R_f=0.58 (hexane-EtOAc, 10 : 3); IR (film) 2980, 2950, 2880, 2380, 2340, 1540, 1160, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, *J*=6.4 Hz, 6H, $2CH_3$), 1.30-1.73 (m, 12H, $(CH_2)_5$ and CH_2), 3.99 (septet, *J*=6.4 Hz, 2H, 2C*H*O).

(2*R*,4*R*)-2,4,9-Trimethyl-1,5-dioxaspiro[5.5]undecane: Physical properties were identical with those of reported.[7b]

(2*R*,4*R*)-2,4-Dimethyl-9-(1,1-dimethylethyl)1,5-dioxaspiro[5.5]undecane: Physical properties were identical with those of reported.[7b]

(2*R*)-2-Methyl-1,5-dioxaspiro[5.7]tridecane: 82% yield. TLC, R_f=0.50 (hexane-EtOAc, 5 : 2); IR (film) 3000, 2950, 2890, 1480, 1460, 1395, 1175, 1155, 1120, 990, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, *J*=6.0 Hz, 3H, CH_3), 1.36-1.70 (m, 12H, $6CH_2$), 1.76-1.86 (m, 2H, CH_2), 1.92-2.18 (m, 2H, CH_2), 3.79 (ddd, *J*=1.8, 5.6, 11.7 Hz, 1H, OC*H*H), 3.97 (dt, *J*=3.4, 11.7 Hz, 1H, OCH*H*), 3.93-4.08 (m, 1H, C*H*Me); Anal. Found: C, 72.63; H, 11.19. $C_{12}H_{22}O_2$ calcd.: C, 72.68; H, 11.18%.

1,5-Dioxaspiro[5.11]heptadecane (1c): 88% yield. TLC, R_f=0.53 (hexane-EtOAc, 5 : 2); IR (film) 2950, 2880, 1470, 1120, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23-1.50 (m, 18H, $(CH_2)_9$), 1.65-1.85 (m, 6H, $3CH_2$), 3.90 (t, *J*=5.7 Hz, 4H, $2CH_2O$); Anal. Found: C, 75.05; H, 11.84. $C_{15}H_{28}O_2$ calcd.: C, 74.95; H, 11.74%.

(2*R*,4*R*)-2,4,8,10-Tetramethyl-1,5-dioxaspiro[5.5]undecane: Physical properties were identical with those of reported.[7b]

(2*RS*,4*SR*)-2,4-Dimethyl-1,5-dioxaspiro[5.5]undecane (1d): TLC, R_f=0.63 (hexane-EtOAc, 5 : 2); IR (film) 2936, 2865, 1447, 1379, 1366, 1175, 1121, 1082, 990, 978 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (d, *J*=6.1 Hz, 3H, $2CH_3$), 1.34-1.94 (m, 12H, $6CH_2$), 3.99 (ddq, *J*=2.6, 6.1, 12.2 Hz, 2H, 2C*H*O).

Preparation of Hydroxy Vinyl Ethers (2). Hydroxy vinyl ethers **2** were prepared in excellent yield by deprotonation and ether cleavage of the corresponding spiroacetals using triisobutylaluminum.[6]

General Procedure for Stereoselective Annulation Reaction of Hydroxy Vinyl Ethers 2 (*Method A*). A crude product of hydroxy vinyl ether **2**, which was prepared from the corresponding acetal **1** (1 mmol) by the method reported in the literature,[6] was diluted in dichloromethane (10 mL) and *N*,*N*-diisopropylethylamine (1 mL). After cooling to -78 °C, triflic anhydride (1.2 mmol, 210 μL) was slowly added dropwise to this solution. After stirring for 3 h, the resulting mixture was poured into saturated aqueous sodium hydrogen carbonate (50 mL), and extracted with ether for three times (20 mL × 3). The combined ether extracts were washed successively with 1 *N* sodium hydrogen sulfate and concentrated *in vacuo* afforded a crude product, which was diluted in 50 % aqueous acetic acid (1.2 mL) and acetone (15 mL). After stirring at ambient temperature overnight, the solution was diluted with water (30 mL), and extracted with ether (30 mL × 3). The combined ether extracts were washed with sat. aqueous sodium hydrogen carbonate and brine, dried over sodium sulfate-potassium carbonate, concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to give a colorless solid or oil, which can be recrystallized from petroleum ether.

2-Ethyl-2-hydroxy-3,5,5-trimethyltetrahydropyran: TLC, R_f=0.45 (hexane-EtOAc, 5 : 2); IR (film) 3700-3200 (br), 2980, 2900, 1475, 1468, 1080, 1065, 1005, 955 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (s, 3H, CH_3); 0.90 (d, *J*=6.8 Hz, 3H, CH_3), 0.97 (t, *J*=7.6 Hz, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.05-2.00 (m, 6H, $CH_2C(OH)C(3)HC(4)H_2$), 3.12 (dd, *J*=2.6, 10.8 Hz, 1H, OC*H*H), 3.65 (d, *J*=10.8 Hz, 1H, OCH*H*).

(3*R*,5*S*)-3,5-Dimethyl-1-hydroxy-2-oxabicyclo[4.3.0]nonane: TLC, R_f=0.23 (hexane-EtOAc, 10 : 3); IR (film) 3700-3150 (br), 2990, 2950, 2380, 1120, 1070, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, *J*=6.8 Hz, 3H, CH_3), 0.99-2.16 (m, 10H), 1.16 (d, *J*=6.4 Hz, 3H, CH_3), 2.28-2.29 (br, 1H, O*H*), 3.89-4.05 (m, 1H, OC*H*); $[\alpha]^{26}_D$=-3.58° (*c* 1.00, ether).

1-Hydroxy-2-oxabicyclo[4.4.0]decane: Physical properties were identical with those of reported.[14,25]

1-Hydroxy-3-methyl-2-oxabicyclo[4.4.0]decane:[14,25] TLC, R_f=0.31 (hexane-EtOAc, 10 : 3); IR (CCl_4) 3610, 3000, 2950, 2930, 2890, 2370, 2350, 1560, 1550, 1530, 1080, 1070, 1060, 990, 980 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14-2.01 (m, 10H), 1.16 and 1.20 (d and d, *J*=6.2 and 6.4 Hz, 3H, CH_3), 1.90 (s, 1H, O*H*), 2.01-2.46 (m, 3H, $CH_2C(OH)CH$), 3.69-3.78 and 4.03-4.18 (m and m, 1H, OC*H*Me).

(3*R*,5*S*)-3,5-Dimethyl-1-hydroxy-2-oxabicyclo[4.4.0]decane (3b): TLC, R_f=0.30 (hexane-EtOAc, 4 : 1); mp: 52-53 °C; IR (nujol mull) 3600-3300 (br), 1460, 1380, 1215, 1105, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (d, *J*=6.5 Hz, 3H, CH_3), 1.40 (d, *J*=6.3 Hz, 3H, $OCHCH_3$), 0.90-1.78 (13H), 4.06-4.19 (m, 1H, MeC*H*O); $[\alpha]^{23}_D$=+37.2° (*c* 1.00, ether).

(3*R*,5*S*,8*S*)-1-Hydroxy-3,5,8-trimethyl-2-oxabicyclo[4.4.0]decane: TLC, R_f=0.28 (hexane-EtOAc, 4 : 1); mp: 97-98 °C; IR (nujol mull) 3550-3300 (br), 1740, 1465, 1380, 980 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (d, *J*=6.4 Hz, 3H, CH_3), 0.93 (d, *J*=6.0 Hz, 3H, CH_3), 1.14 (d, *J*=6.3 Hz, 3H, $OCHCH_3$), 0.90-1.79 (12H), 4.09-4.19 (m, 1H, MeC*H*O); $[\alpha]^{23}_D$=+27.5° (*c* 1.01, ether).

(3*R*,5*S*,8*S*)-3,5-Dimethyl-8-(1,1-dimethylethyl)-1-hydroxy-2-oxabicyclo[4.4.0}decane: TLC, R_f=0.20 (hexane-EtOAc, 4 : 1); mp: 90-91 °C; IR (nujol mull) 3600-3300 (br), 1460, 1385, 1220, 1160, 1090, 985, 935 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86-0.95 (complex of d and s, 12H, CH_3, and $(CH_3)_3C$), 0.90-2.40 (12H), 1.15 (d, *J*=6.2 Hz, 3H, CH_3CHO), 4.10-4.20 (m, 1H, MeC*H*O); $[\alpha]^{23}_D$=+55.4° (*c* 1.07, ether).

(3*R*,5*S*,7*R*,9*S*)-1-Hydroxy-3,5,7,9-tetramethyl-2-oxabicyclo[4.4.0]decane (10): TLC, R_f=0.45 (hexane-EtOAc, 4 : 1); mp: 78-80 °C; IR (CCl_4) 3640, 2980, 2950, 2900, 2400, 2360, 1565, 1550, 1260, 1205, 1170, 1100, 1000, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.71-1.33 (m, 4H), 0.88 (d, *J*=6.6 Hz, 3H, CH_3), 1.05 (d, *J*=6.6 Hz, 3H, CH_3), 1.06 (d, *J*=6.4 Hz, 3H, CH_3), 1.12 (d, *J*=6.4 Hz, 3H, CH_3), 1.45-1.99 (m, 7H), 4.04-4.20 (m, 1H, OC*H*); Anal. Found: C, 73.45; H, 11.54. $C_{13}H_{24}O_2$ calcd.: C, 73.52; H, 11.41%.

(11*R*)-1-Hydroxy-11-methyl-12-oxabicyclo[6.4.0]dodecane: TLC, R_f=0.12 (hexane-EtOAc, 5 : 2); IR (film) 3460, 2950, 2880, 1710, 1475, 1460, 1385, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, *J*=6.2 Hz, 3H, CH_3), 1.10-2.15 (m, 15H, C(3)H_2C(4)H_2C(5)H_2C(6)H_2C(7)H_2, C(9)H_2C(10)H_2 and O*H*), 2.25-2.70 (m, 3H, C(2)H_2 and C(8)*H*), 3.60-3.85 (m, 1H, C*H*Me); Anal. Found: C, 72.44; H, 11.35. $C_{12}H_{22}O_2$ calcd.: C, 72.68; H, 11.18%.

1-Hydroxy-16-oxabicyclo[10.4.0]octadecane: TLC, R_f=0.11 (hexane-EtOAc, 5 : 2); IR (film) 3450, 2950, 2900, 1720, 1480, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12-1.86 (m, 23H, $(CH_2)_2CH(CH_2)_9$ and O*H*), 2.42 (ddd, *J*=4.6, 7.6, 17.0 Hz, 1H, CC*H*H), 2.51-2.66 (m, 1H, C*H*), 2.63 (ddd, *J*=4.6, 7.6, 17.0 Hz, 1H, CCH*H*), 3.54-3.72 (m, 2H, OCH_2); Anal. Found: C, 75.04; H, 11.94. $C_{15}H_{28}O_2$ calcd.: C, 74.95; H, 11.74%.

General Procedure for Regio- and Stereoselective Annulation-Elimination Reaction of Hydroxy Vinyl Ethers 2 (*Method B* and *Method C*). A crude product of hydroxy vinyl ether **2**, which was prepared from the corresponding acetal **1** (1 mmol) by the method reported in the literature,[6] was diluted in toluene (10 mL, *Method B*) or dichloromethane (5 mL, *Method C*) and *N*,*N*-diisopropylethylamine (1 mL, *Method B*; 2 mL, *Method C*). After cooling to -78 °C, triflic anhydride (1.2 mmol, 210 μL) was slowly added dropwise to this solution. The reaction mixture was stirred at the same temperature for 5 h and then warmed to 0 °C. Further, the reaction mixture was gradually warmed to ambient temperature over 1 h and stirred for 12 h. After complete conversion, the solution was poured into saturated aqueous sodium hydrogen carbonate (10 mL), extracted with hexane (10 mL), and washed with brine (10 mL × 3). The combined hexane extracts were dried over potassium carbonate and magnesium carbonate, and concentrated *in vacuo*. The ratio of **4** to **5** was determined by ^1H NMR analysis of the crude mixture. These products were immediately used for the next step without further purification since **5** was highly acid sensitive. In general, **5** is easily isomerized to **4** through column chromatography on silica gel. Nevertheless, the crude mixture of **4a** and **5a** could be purified and separated by column chromatography on basic alumina.

2-Oxabicyclo[4.4.0]dec-1(6)-ene (4a):[26] TLC, R_f=0.69 (hexane-EtOAc, 5 : 2); ^1H NMR ($CDCl_3$) δ 1.50-2.05 (m, 12H), 3.92 (t, *J*=4.8 Hz, 2H, OCH_2).

2-Oxabicyclo[4.4.0]dec-1(10)-ene (5a): TLC, R_f=0.69 (hexane-EtOAc, 5 : 2); ^1H NMR ($CDCl_3$) δ 1.16-2.24 (m, 11H, $(CH_2)_3CH(CH_2)_2$), 3.51 (dt, *J*=2.5, 11.3 Hz, 1H, OC*H*H), 4.02-4.09 (m, 1H, OCH*H*), 5.06 (t, *J*=2.0 Hz, 1H, C*H*=CO).

(3*R*,5*S*)-3,5-Dimethyl-2-oxabicyclo[4.4.0]dec-1(6)-ene (4b): TLC, R_f=0.72 (hexane-EtOAc, 5 : 2); ^1H NMR ($CDCl_3$) δ 0.95 (d, *J*=6.8 Hz, 3H, CH_3CH), 1.10-2.30 (m, 11H, $(CH_2)_4CCHCH_2$), 1.24 (d, *J*=6.3 Hz, 3H, CH_3CHO), 3.85 (ddq, *J*=1.6, 6.3, 17.4 Hz, 1H, MeC*H*O).

(3*RS*,5*RS*)-3,5-Dimethyl-2-oxabicyclo[4.4.0]dec-1(6)-ene (4d): TLC, R_f=0.72 (hexane-EtOAc, 5 : 2); ^1H NMR ($CDCl_3$) δ 1.02 (d, *J*=7.0 Hz, 3H, CH_3CH), 1.10-2.23 (m, 10H, $(CH_2)_3(CH)_2CH_2$), 1.26 (d, *J*=6.5 Hz, 3H, CH_3CHO), 3.92 (ddq, *J*=2.2, 6.3 and 10.7 Hz, 1H, MeC*H*O).

(3*R*,5*S*)-3,5-Dimethyl-2-oxabicyclo[4.4.0]dec-1(10)-ene (5b): TLC, R_f=0.72 (hexane-EtOAc, 5 : 2); ^{1}H NMR ($CDCl_3$) δ 0.80-2.70 (m, 10H, $(CH_2)_3(CH)_2CH_2$), 0.94 (d, *J*=7.0 Hz, 3H, CH_3CH), 1.19 (d, *J*=6.1 Hz, 3H, CH_3CHO), 4.07 (ddq, *J*=1.5, 6.1, 16.0 Hz, 1H, MeC*H*O), 4.96 (t, *J*=4.9 Hz, 1H, C*H*=CO).

2-Oxabicyclo[10.4.0]hexadec-1(6)-ene (4c):[27] TLC, R_f=0.75 (hexane-EtOAc, 5 : 2); ^{1}H NMR ($CDCl_3$) δ 1.10–2.20 (m, 24H), 3.88 (t, *J*=5.1 Hz, 2H, CH_2O).

2-Oxabicyclo[10.4.0]hexadec-1(16)-ene (5c): TLC, R_f=0.75 (hexane-EtOAc, 5 : 2); ^{1}H NMR ($CDCl_3$) δ 1.00-2.65 (m, 23H, $(CH_2)_9CH(CH_2)_2$), 3.55 (dt, *J*=2.5, 11.7 Hz, 1H, C*H*HO), 4.12 (ddd, *J*=2.5, 4.7, 10.6 Hz, 1H, CH*H*O), 4.56 (dd, *J*=4.5, 11.0 Hz, 1H, C*H*=CO).

General Procedure for the Iodolactonization of Bicyclic Hemiacetals 3. The following procedure was modified upon the basis of Suarez's method[13] for the synthesis of medium-sized lactones. A solution of hemiacetal (1.0 mmol), iodobenzene diacetate (98%, 360 mg, 1.1 mmol), and iodine (250 mg, 1.0 mmol) in cyclohexane (20 mL) was irradiated with stirring by 250 W tungsten filament lamp for 90 min. The resulting solution was poured into aqueous sodium sulfite (30 mL), and extracted with ether (20 mL × 3). The combined organic layers were washed with aqueous sat. sodium hydrogen carbonate (30 mL) and brine (30 mL), dried over magnesium sulfate, concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluent: first with hexane, then hexane-EtOAc) to give a colorless oil of the corresponding iodolactone.

(7*S*,9*R*)-6-Iodo-7,9-dimethylnonanolide (6): TLC, R_f=0.48 (hexane-EtOAc, 10 : 3); IR (film) 2965, 2940, 2880, 2360, 2350, 1740, 1460, 1260, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.18 (d, *J*=6.6 Hz, 3H, CH_3); 1.29 (d, *J*=5.2 Hz, 3H, CH_3), 1.43-2.25 (m, 8H, $(CH_2)_3CHI$ and $MeCHCH_2$), 4.70-4.79 (m, 1H, C*H*I), 5.10-5.17 (m, 1H, OC*H*), 2.25-2.36 (m, 1H, C*H*HCO_2), 2.58 (dt, *J*=15.6, 4.6 Hz, 1H, CH*H*CO_2).

(3*S*,5*R*,7*S*,9*R*)-6-Iodo-3,5,7,9-tetramethylnonanolide: TLC, R_f=0.35 (hexane-EtOAc, 10:1); IR (CCl_4) 2970, 2930, 2355, 2340, 1725, 1560, 1540, 1520, 1510, 1455, 1230, 1110, 1000, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80-1.99 (m, 6H), 0.99 (d, *J*=6.4 Hz, 3H, CH_3), 1.00 (d, *J*=6.2 Hz, 3H, CH_3), 1.22 (d, *J*=6.2 Hz, 3H, CH_3), 1.22 (d, *J*=6.2 Hz, 3H, CH_3), 1.30 (d, *J*=6.6 Hz, 3H, CH_3), 2.04-2.40 (m, 3H), 4.91 (m, 1H, C*H*I), 5.19-5.29 (m, 1H, OC*H*); Anal. Found: C, 46.17; H, 6.96. $C_{13}H_{23}O_2I$ calcd.: C, 46.16; H, 6.87%.

(11*R*)-8-Iodo-11-methyl-11-undecanolide: TLC, R_f=0.58 (hexane-EtOAc, 5 : 2); IR (film) 2960, 2900, 1750, 1465, 1265, 1240, 1215, 1160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25 (d, *J*=6.4 Hz, 3H, CH_3 (major isomer)), 1.26 (d, *J*=6.2 Hz, 3H, CH_3 (minor isomer)), 1.10-2.57 (m, 16H, $8CH_2$), 4.16-4.32 (m, 1H, C*H*I (minor isomer)), 4.48 (quintet, *J*=6.4 Hz, 1H, C*H*I (major isomer)), 4.92-5.09 (m, 1H, C*H*Me (minor isomer)), 5.23 (dquintet, *J*=3.0, 6.4 Hz, 1H, C*H*Me (major isomer)); Anal. Found: C, 44.48; H, 6.61. $C_{12}H_{21}O_2I$ calcd.: C, 44.46; H, 6.53%.

12-Iodo-15-pentadecanolide: TLC, R_f=0.59 (hexane-EtOAc, 5 : 2), IR (film) 2950, 2900, 1750, 1470, 1460, 1250, 1190 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.18-2.12 (m, 22H, $(CH_2)_2CHI(CH_2)_9$), 2.35 (t, *J*=7.0Hz, 2H, CH_2C=O), 4.03-4.31 (m, 3H, OCH_2 and C*H*I); Anal. Found C, 49.20; H, 7.53. $C_{15}H_{27}O_2I$ calcd.: C, 49.19; H, 7.43%.

General Procedure for the Deiodination of Iodolactones. A mixture of iodolactone (3.1 mmol), tributyltin hydride (2.5 mL, 9.3 mmol), AIBN (100 mg), and THF (65 mL) was refluxed for 40 min. The reaction mixture was diluted with reagent grade (undried) ether (100 mL). DBU (1.7 g, 11 mmol) was added to the reaction mixture and then titrated with 0.1 *M* iodine solution in ether. During this time, DBU-hydroiodide precipitated as a white solid. After the iodine color just persisted, the solution was transferred to a short column (SiO_2); after solution with ether (50 mL), the solvent was removed. The residue was almost tin-free. [This DBU workup procedure was suggested by D. P. Curran et al.[28]] The residue was purified by column chromatography on silica gel (eluent : first with hexane, then hexane-EtOAc) to give a colorless oil of the corresponding lactone

(7*R*,9*R*)-7,9-Dimethylnonanolide (19): TLC, R_f=0.33 (hexane-EtOAc, 4 : 1); IR (film) 2950, 2890, 2370, 2350, 1735, 1455, 1252, 1095, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80-1.69 (m, 10H), 0.93 (d, *J*=6.0 Hz, 3H, C*H*$_3$), 1.26 (d, *J*=6.0 Hz, 3H, C*H*$_3$), 1.85-2.33 (m, 2H), 2.43-2.59 (m, 1H), 4.88-5.02 (m, 1H, OC*H*Me); Anal. Found: C, 71.65; H, 10.96. $C_{11}H_{20}O_2$ calcd.: C, 71.68; H, 10.96%.

(3*S*,5*S*,7*R*,9*R*)-3,5,7,9-Tetramethylnonanolide (11): TLC, R_f=0.43 (hexane-EtOAc, 10 : 1); IR (film) 2980, 2950, 2900, 2380, 2360, 1740, 1465, 1315, 1245, 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77-2.25 (m, 10H), 0.87 (d, *J*=5.4 Hz, 3H, C*H*$_3$), 0.90 (d, *J*=6.6 Hz, 3H, C*H*$_3$), 0.95 (d, *J*=6.4 Hz, 3H, C*H*$_3$), 1.25 (d, *J*=6.4 Hz, 3H, C*H*$_3$), 2.31 (dd, *J*=1.1, 8.7 Hz, 2H, C*H*$_2$CO$_2$), 4.89-5.03 (m, 1H, OC*H*); Anal. Found: C, 73.42; H, 11.42. $C_{13}H_{24}O_2$ calcd.: C, 73.52; H, 11.41%.

15-pentadecanolide (Exaltolide, 8):[17] TLC, R_f=0.59 (hexane-EtOAc, 5 : 2);mp: 30.5-31.0 °C; IR (film) 2950, 2890, 1750, 1470, 1360, 1245, 1180, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20-1.50 (m, 20H, (C*H*$_2$)$_{10}$), 1.55-1.75 (m, 4H, 2C*H*$_2$), 2.34 (t, *J*=6.7 Hz, 2H, C*H*$_2$C=O), 4.15 (t, *J*=5.4 Hz, 2H, C*H*$_2$O); Anal. Found: C, 75.06; H, 11.88. $C_{15}H_{28}O_2$ calcd.: C, 74.95; H, 11.74%.

Transformation of (11*R*)-8-Iodo-11-methyl-11-undecanolide into (+)-Recifeiolide (7).

Procedure for Dehydroiodination. The hindered amidine DBU (5 mL) and (11*R*)-8-iodo-11-methyl-11-undecanolide (2.14 g, 6.59 mmol) were mixed together and heated in an oil bath at 85±5 °C. Heating and stirring were continued for 40 min after the appearance (about 3 min) of a white precipitate or syrup. The reaction mixture was worked up with hexane, dried over magnesium sulfate, concentrated *in vacuo*, and purified by column chromatography on silica gel (eluent: hexane-EtOAc, 20 : 1) to give a 59 : 31 : 2 : 7 mixture of the four diastereoisomeric olefinic lactones ((8*E*)-11-methyl-8-undecen-11-olide (**7**), (7*E*)-11-methyl-7-undecen-11-olide, and two other minor cis isomers) as a colorless oil (1.26 g, 98% yield). Although we had no independent proof for the assigned stereochemistry of two minor cis isomers, (8*E*)-isomer **7**[16,28,29] and (7*E*)-isomer[29] were chromatographically and spectrally identical with the one reported in the literature. Chromatographic separation of the isomeric olefinic lactones, using silica gel impregnated with silver nitrate by immersing silica gel (E. Merck) into a 12.5% (w/v) solution of silver nitrate in acetonitrile and then dried for 1 day under reduced pressure (vacuum pump) and hexane-ethyl acetate (500 : 1) as the eluent, gave pure **7**. Silica gel TLC plates were immersed briefly in a 12.5% (w/v) solution of silver nitrate in acetonitrile and allowed to air-dry in the dark overnight. GLC (instrument, Shimadzu Model 8A; column, PEG-HT Bonded, 25 m × 0.25 mm at 130 °C+0.5 °C/min; carrier gas, N_2, 0.75 kg/cm^2) t_R 11.6 min ((8*E*)-isomer **7**), 12.9 min ((7*E*)-isomer), 13.6 min ((*Z*)-isomer), 13.9 min ((*Z*)-isomer).

(8*E*)-isomer 7: TLC, R_f=0.17 (hexane-EtOAc, 20 : 1); IR (film) 3000, 2950, 2890, 1740, 1240, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.252 (d, *J*=6.2 Hz, 3H, CH_3), 1.04-2.48 (m, 14H, $(CH_2)_6$ and CH_2), 5.08-5.27 (m, 1H, *CH*Me), 5.24-5.36 (m, 2H, *CH*=*CH*); $[\alpha]^{24}_D$=+71.18° (*c* 1.03, $CHCl_3$); lit.[16a] $[\alpha]_D$=+70° (*c* 1, $CHCl_3$).

(7*E*)-Isomer: TLC, R_f=0.14 (hexane-EtOAc, 20 : 1); ^1H NMR ($CDCl_3$) δ 1.247 (d, *J*=6.2 Hz, 3H, CH_3), 4.78-4.94 (m, 1H, *CH*O), 5.08-5.36 (m, 1H, *CH*=CH), 5.47 (ddd, *J*=4.8, 9.2, 14.3 Hz, 1H, CH=*CH*).

Transformation of 11 into (-)-Lardolure (14).

(3*R*,5*R*,7*R*,9*R*)-3,5,7-Trimethyl-1,9-decanediol (12): To a solution of **11** (0.903g, 4.25 mmol) in toluene (30 mL) was added dropwise diisobutylaluminum hydride (1 *M* in hexane, 12.8 mL, 12.8 mmol) at -78 °C. Stirring was continued for 3 h at that temperature. The reaction mixture was poured into cooled 1 *N* hydrochloric acid, extracted with ether repeatedly, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluent: hexane-EtOAc, 4 : 3) to give a colorless oil (846 mg, 92% yield). TLC, R_f=0.3 (hexane-EtOAc, 1 : 1); IR (film) 3570-3070 (br), 2975, 2940, 2375, 2350, 1460, 1185, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75-1.82 (m, 13H), 0.88 (d, *J*=6.6 Hz, 3H, CH_3), 0.907 (d, *J*=5.6 Hz, 3H, CH_3), 0.91 (d, *J*=6.8 Hz, 3H, CH_3), 1.21 (d, *J*=6.0 Hz, 3H, CH_3), 3.58-3.78 (m, 2H, CH_2OH), 3.84-3.98 (m, 1H, *CH*OH); Anal. Found: C, 71.85; H, 13.25. $C_{13}H_{24}O_2$ calcd.: C, 72.15; H, 13.07%.

(3*R*,5*R*,7*R*,9*R*)-1-*p*-Toluenesulfonyl-3,5,7-trimethyl-9-decanol: To a solution of **12** (0.60 g, 2.8 mmol), DMAP (50 mg), and pyridine (0.97 mL, 12 mmol) in dichloromethane (3 mL) was added TsCl (0.63 g, 3.3 mmol) at -20 ℃ under argon. Stirring was continued for 5.5 h at the same temperature. It was worked up with water, and extracted with ether. The organic layer was washed with hydrochloric acid (1*N*), dried over magnesium sulfate, concentrated *in vacuo* and purified by column chromatography on silica gel (eluent: hexane-EtOAc, 3 : 1) to give a colorless oil (0.66 g, 1.8 mmol, 64% yield). TLC, R_f=0.55 (hexane-EtOAc, 1 : 1); IR (film) 3700-3150 (br), 2960, 2935, 2365, 2340, 1455, 1355, 1185, 1165, 1095, 945, 815, 665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.69-1.81 (m, 12H), 0.82 (d, *J*=6.6 Hz, 3H, CH_3), 0.83 (d, *J*=6.4 Hz, 3H, CH_3), 0.89 (d, *J*=6.6 Hz, 3H, CH_3), 1.21 (d, *J*=6.0 Hz, 3H, CH_3), 2.47 (s, 3H, ArCH_3), 3.84-4.00 (m, 1H, *CH*OH), 4.03-4.15 (m, 2H, CH_2OTs), 7.37 (d, *J*=8.2 Hz, 2H, Ar), 7.81 (d, *J*=8.2 Hz, 2H, Ar); Anal. Found: C, 64.77; H, 9.31. $C_{20}H_{34}O_4S$ calcd.: C, 64.82; H, 9.27%.

(2*R*,4*R*,6*R*,8*R*)-Trimethyl-2-undecanol (13): To a solution of cuprous iodide (2.73 g, 14.3 mmol) in ether (18 mL) was added methyllithium (1.5 *M* solution, 19.1 mL, 28.6 mmol) at -78 ℃ under argon. It was stirred at -20 °C for 4 h. A solution of tosylate (0.656 g, 1.79 mmol) in ether (10 mL) was added to it at -78 °C. Stirring was continued for 2 h at -20 °C. The reaction mixture was worked up with aqueous ammonium chloride, extracted with ether, dried over magnesium sulfonate, concentrated *in vacuo*, and purified by column chromatography on silica gel (eluent: hexane-EtOAc, 6 : 1) to give a colorless oil (354 mg, 1.65 mmol, 92% yield). TLC, R_f=0.38 (hexane-EtOAc, 4:1); IR (film) 3600-3150, 2985, 2940, 2885, 2860, 2380, 2340, 1455, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.73-1.80 (m, 20H), 0.85 (d, *J*=6.2 Hz, 3H, CH_3); 0.91 (d, *J*=6.8 Hz, 3H, CH_3), 1.21 (d, *J*=6.2 Hz, 3H, CH_3), 3.88-3.98 (m, 1H, *CH*O); Anal. Found. C, 78.37; H, 14.25. $C_{14}H_{30}O$ calcd.: C, 78.41; H, 14.13%.

(1*R*,3*R*,5*R*,7*R*)-1,3,5,7-Tetramethyldecyl formate (14): A mixture of **13** (313 mg, 1.46 mmol) and formic acid (8.2 mL) was stirred for 1.5 h at 65 °C. It was then poured into cooled saturated aqueous

sodium hydrogen carbonate and extracted with hexane, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluent: hexane-EtOAc, 50 : 1) to give a colorless oil (336 mg, 1.39 mmol, 95% yield). TLC, R_f=0.25 (hexane-EtOAc, 50 : 1); IR (film) 2975, 2950, 2900, 2380, 2350, 1740, 1465, 1390, 1190, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83-1.80 (m, 6H), 0.84 (d, *J*=1.2 Hz, 3H, C*H*$_3$), 0.87 (d, *J*=1.8 Hz, 3H, C*H*$_3$), 0.90 (d, *J*=2.2 Hz, 3H, C*H*$_3$), 1.28 (d, *J*=6.2 Hz, 3H, C*H*$_3$), 5.13-5.22 (m, 1H, MeC*H*O), 8.08 (s, 1H, OC*H*O); ^{13}C NMR ($CDCl_3$) δ 14.55, 20.10, 20.34, 20.51, 20.71, 21.04, 26.60, 27.36, 29.83, 39.10, 43.15, 45.50, 45.67, 69.26, 161.42; $[\alpha]^{25}_D$=-3.64° (*c* 7.88, hexane); lit.[19] $[\alpha]^{23}_D$=-3.4° (c 7.86, hexane); GLC (instrument, Gasukuro Kogyo Model 370; column, OV-101, 25 m × 0.25 mm at 100 °C + 0.5 °C/min; carrier gas, N_2, 5 kg/cm^2) t_R 66.35 min.; authentic sample[19] t_R=66.35 min; Anal. Found: C, 74.24; H, 12.59. $C_{15}H_{30}O_2$ calcd.: C, 74.30; H, 12.50%. The ^1H NMR and ^{13}C NMR spectra and capillary GC retention time were identical with those of the natural pheromone.[19]

General Procedure for Ozonolysis of 2-Oxabicyclo[n.4.0]alk-1(6+n)-enes 4 or 2-Oxabicyclo[n.4.0]alk-1(6)-enes 5. A crude product of 2-oxabicyclo[n.4.0]alk-1(6+n)-ene **4** or 2-oxabicyclo[n.4.0]alk-1(6)-ene **5**, which was derived from the corresponding spiroacetal **1** (1 mmol) in two steps included *Method B* or *Method C*, was diluted in methanol (30 mL). After cooling to -78 °C, ozone was bubbled through the solution for about 20 min. After the colorless solution was turned purple, dimethyl sulfide (0.4 mL) was added at the same temperature and then warmed to ambient temperature. The resultant solution was concentrated *in vacuo* and purified by column chromatography on silica gel (eluent: hexane-EtOAc) to give (2+n)-Oxolactone **15** or 2-substituted-5-pentanolide **16**.

6-Oxo-9-nonanolide (15a):[21(c),31] TLC, R_f=0.49 (EtOAc); IR (film) 3021, 1728, 1215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20-2.50 (m, 12H), 4.27 (t, *J*=5.4 Hz, 2H, C*H*$_2$O).

2-(3-Formylpropyl)-5-pentanolide (16a): TLC, R_f=0.40 (EtOAc); IR (film) 2950, 1724, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47-2.20 (m 8H, (C*H*$_2$)$_2$CH(C*H*$_2$)$_2$), 2.40-2.54 (m, 3H, C*H*$_2$CHO and C*H*CO), 4.31 (dt, *J*=1.6, 8.6 Hz, 2H, C*H*$_2$O), 9.79 (t, *J*=2.9 Hz, 1H, C*H*O); Anal. Found. C, 63.38; H, 8.54. $C_9H_{14}O_3$ calcd.: C, 63.51; H, 8.29%.

(7*S*,9*R*)-7,9-Dimethyl-6-oxo-9-nonanolide (15b): TLC, R_f=0.22 (hexane-EtOAc, 5 : 2); IR (film) 2934, 1728, 1248, 1167, 1068 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (d, *J*=6.9 Hz, 3H, C*H*$_3$CH), 1.13 (d, *J*=6.2 Hz, 3H, C*H*$_3$CHO), 1.20-2.24 (m, 11H, (C*H*$_2$)$_4$ and MeC*H*C*H*$_2$), 4.15 (ddq, *J*=2.8, 6.2, 12.1 Hz, 1H, MeC*H*O); Anal. Found. C, 66.61; H, 9.23. $C_{11}H_{18}O_3$ calcd.: C, 66.64; H, 9.15%.

(3*S*,5*R*)-2-(3-Formylpropyl)-3,5-dimethyl-5-pentanolide (16b): TLC, R_f=0.09 (hexane-EtOAc, 5 : 2); IR (film) 2941, 1723, 1251, 1135, 1005 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (d, *J*=6.9 Hz 3H, C*H*$_3$CH), 1.00-1.95 (m, 6H, (C*H*$_2$)$_3$), 1.35 (d, *J*=6.2 Hz, 3H, C*H*$_3$CHO), 2.17-2.60 (m, 4H, C*H*$_2$CHO and COC*H*C*H*Me), 4.44 (ddq, *J*=4.2, 6.2, 11.7 Hz, 1H, MeC*H*O), 9.79 (t, *J*=3.0 Hz, 1H, C*H*O); Anal. Found. C, 66.75; H, 9.13. $C_{11}H_{18}O_3$ calcd.: C, 66.64; H, 9.15%.

12-Oxo-15-pentadecanolide (15c):[31,32] TLC, R_f=0.13 (hexane-EtOAc, 5 : 2); IR (KBr) 2936, 1770, 1370, 1250, 1130, 1024, 785 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15-2.70 (m, 24H), 3.62 (t, *J*=5.4 Hz, 2H, C*H*$_2$O).

2-(9-Formylnonyl)-5-pentanolide (16c): TLC, R_f=0.06 (hexane-EtOAc, 5 : 2); IR (KBr) 2900, 2847, 1770, 1718, 1470, 1395, 1167 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10-1.95 (m, 20H, OCH$_2$(C*H*$_2$)$_2$CH(C*H*$_2$)$_8$CH$_2$CHO), 2.03-2.17 (m, 1H, C*H*COO), 2.42 (t, *J*=2.9 Hz, 2H, C*H*$_2$OCO), 4.21-4.38

(m, 2H, CH_2CHO), 9.76 (s, 1H, C*H*O); Anal. Found. C, 70.92; H, 10.28. $C_{15}H_{26}O_3$ calcd.: C, 70.83; H, 10.30%.

General Procedure for Stereoselective Hydroboration of 2-Oxobicyclo[n.4.0]alk-1(6+n)-ene 5. 2-Oxobicyclo[n.4.0]alk-1(6+n)-ene **5**, which was derived from the corresponding spiroacetal **1** (1 mmol) in two steps included *Method C*, was diluted in THF (10 mL). After cooling to 0 °C, BH_3·THF (1.0 *M* solution in THF, 3.0 mL, 3.0 mmol) or 9-BBN (0.5 *M* solution in hexane, 6.0 mL, 3.0 mmol) was added dropwise, and the solution was stirred at that temperature for 2 h. Further, after warming to ambient temperature and stirring at that temperature for 2 h, the resulting solution was quenched with water (0.4 mL) and the mixture was treated with 2 *N* aqueous sodium hydroxide (0.8 mL) and 30% hydrogen peroxide (0.8 mL). The resulting mixture was poured into brine (10 mL), and extracted with ether for three times (10 mL × 3). The organic layers were dried over magnesium sulfate, concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluent: hexane-EtOAc) to give (6+n)-hydroxy-2-oxabicyclo[4.n.0]alkanes **17** and **18**.

10-Hydroxy-2-oxabicyclo[4.4.0]decane (the mixture of 17a and 18a): TLC, R_f=0.19 (hexane-EtOAc, 5 : 2); IR (film) 3700-3000, 2980, 1454, 1062, 921 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80-2.08 (m, 11H, $OCH_2(CH_2)_2CH(CH_2)_3$), 2.50-2.70 (br, 1H, O*H*), 2.76 (t, *J*=9.0 Hz, 1H, C*H*O), 3.43 (dt, *J*=2.5 and 11.5 Hz, 1H, OC*H*H), 3.42-3.58 (m, 1H, C*H*OH), 4.02 (m, 1H, OCH*H*); Anal. Found. C, 69.21; H, 10.15. $C_9H_{16}O_2$ calcd.: C, 69.19; H, 10.32%.

The relative configuration of the compounds were determined using the acetate form. The physical properties and analytical data are listed below.

(1*RS*,6*RS*,10*RS*)-10-Acetoxy-2-oxabicyclo[4.4.0]decane (the acetate of 17a): TLC, R_f=0.26 (hexane-EtOAc, 5 : 2); ^{1}H NMR ($CDCl_3$) δ 0.90-1.80 (m, 11H, $OCH_2(CH_2)_2CH(CH_2)_3$), 2.09 (s, 3H, CH_3CO), 2.97 (t, *J*=9.5 Hz, 1H, C*H*O), 3.39 (dt, *J*=2.0 and 12.0 Hz, 1H, OC*H*H), 3.86-4.16 (m, 1H, OCH*H*), 4.73-4.80 (m, 1H, C*H*OAc); ^{13}C NMR ($CDCl_3$) δ 21.5, 23.3, 26.3, 30.3, 30.7, 31.1, 40.1 (C(6)), 68.4 (C(3)), 74.6 (C(10)), 83.5 (C(1)), 170.8 (Me*C*O).

(1*SR*,6*RS*,10*SR*)-10-Acetoxy-2-oxabicyclo[4.4.0]decane (the acetate of 18a): TLC, R_f=0.56 (hexane-EtOAc, 5 : 2); ^{1}H NMR ($CDCl_3$) δ 0.85-1.85 (m, 11H, $OCH_2(CH_2)_2CH(CH_2)_3$), 2.06 (s, 3H, CH_3CO), 3.43-3.52 (complex of dt and m, *J*=2.5 and 11.5 Hz, 2H, OC*H*H and C*H*O), 3.92 (dt, *J*=4.0 and 11.5 Hz, 1H, OCH*H*), 4.98-5.20 (m, 1H, C*H*OAc); ^{13}C NMR ($CDCl_3$) δ 20.0, 21.3, 22.5, 25.7, 26.5, 27.6, 32.1 (C(6)), 67.5 (C(3)), 70.4, 76.2 (C(1)), 170.2 (Me*C*O).

(1*R*,3*R*,5*S*,6*S*,10*R*)-3,5-Dimethyl-10-hydroxy-2-oxabicyclo[4.4.0]decane (18b): TLC, R_f=0.27 (hexane-EtOAc, 5 : 2); IR (KBr) 3600-3050, 2861, 1391, 1183, 1090, 1013, 978, 918 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (d, *J*=6.9 Hz, 3H, CH_3), 1.10-1.80 (m, 11H, $OCHMeCH_2CHMeCH(CH_2)_3CHOH$), 1.17 (d, *J*=6.1 Hz, 3H, CH_3), 3.41 (t, *J*=2.6 Hz, 1H, C*H*O), 3.48 (ddq, *J*=2.6, 6.1 and 11.0 Hz, 1H, C*H*Me), 3.91 (m, 1H, C*H*OH); Anal. Found. C, 71.69; H, 11.21. $C_{11}H_{20}O_2$ calcd.: C, 71.70; H, 10.94%.

The physical properties and analytical data of the acetate form are listed below.

(1*R*,3*R*,5*S*,6*S*,10*R*)-3,5-Dimethyl-10-acetoxy-2-oxabicyclo[4.4.0]decane: TLC, R_f=0.31 (hexane-EtOAc, 5 : 2); ^{1}H NMR ($CDCl_3$) δ 0.90 (d, *J*=6.9 Hz, 3H, CH_3), 1.05-1.80 (m, 10H, $OCHMeCH_2CHMeCH(CH_2)_3$), 1.16 (d, *J*=6.3 Hz, 3H, CH_3), 2.06 (s, 3H, CH_3CO), 3.42 (t, *J*=2.7 Hz, 1H, C*H*O), 4.47 (ddq, *J*=2.5, 6.1 and 11.0 Hz, 1H, OC*H*Me), 4.94 (q, *J*=2.8 Hz, 1H, C*H*OAc); ^{13}C NMR

($CDCl_3$) δ 18.7, 20.0, 21.3, 21.9, 25.6, 30.3, 33.1, 35.9, 37.2, 70.4 (C(1)), 74.3 (C(3)), 75.2 (C(10)), 170.0 (Me*C*O).

16-Hydroxy-2-oxabicyclo[10.4.0]hexadecane (the mixture of 17c and 18c): TLC, R_f=0.40 (hexane-EtOAc, 5 : 2); GC (at 70 °C for 5 min and then + 10 °C/min), t_R=17.6 (minor isomer, M^+=240) and 18.0 (major isomer, M^+=240) min; IR ($CHCl_3$) 3700-3000, 2995, 1466, 1060, 904 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10-1.95 (m, 23H, $OCH_2(CH_2)_2CH(CH_2)_9$), 2.68-2.83 (br, 1H, O*H*), 3.07 (dd, *J*=1.1 and 9.4 Hz, 2H of minor isomer, C*H*O and OC*H*H), 3.38-3.52 (m, 1H of minor isomer, OCH*H* and 2H of major isomer, OC*H*H and C*H*O), 3.58-3.65 (m, 1H of minor isomer, C*H*OH), 3.75 (t, *J*=9.2 Hz, 1H of major isomer, OCH*H*), 3.98-4.09 (m, 1H of major isomer, C*H*OH); Anal. Found. C, 74.93; H, 12.03. $C_{15}H_{28}O_2$ calcd.: C, 74.95; H, 11.74%.

Determination of the Absolute Configuration of 18b. A solution of **18b** (0.11 g, 0.6 mmol; prepared from above procedure), 4-nitrobenzoyl chloride (0.13 g, 0.6 mmol) and 4-dimethylaminopyridine (0.75 g, 6 mmol) in dichloromethane (5 mL) was stirred at room temperature for 5.5 h. The resulting mixture was poured into 1 *N* aqueous hydrogen chloride (50 mL), washed with 2 *N* aqueous sodium hydroxide (10 mL), extracted with hexane (20 mL). The organic layer was dried over magnesium sulfate and concentrated *in vacuo*. The residue was chromatography on silica gel (eluent: hexane-EtOAc, 30 : 1 ~ 20 : 1) to give the *p*-nitrobenzoate as a white solid. Suitable crystals for single-crystal X-ray diffraction were grown from pentane and cyclohexane. The absolute configuration of this compound was established by single-crystal X-ray diffraction.

(1*R*,3*R*,5*S*,6*S*,10*R*)-3,5-Dimethyl-10-(4-nitrobenzoyloxy)-2-oxabicyclo[4.4.0]decane: TLC, R_f=0.60 (hexane-EtOAc, 5 : 2); mp. 115.3-117.0 °C; IR (KBr) 2975, 1730, 1528, 1339, 1266, 1117, 1013, 718 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (d *J*=6.9 Hz, 3H, CH_3), 1.20 (d, *J*=6.2 Hz, 3H, CH_3), 1.10-1.95 (m, 9H), 3.45-3.60 (complex of d and m, *J*=2.5 Hz, 2H, CH_3CHO and C*H*O), 5.25 (d, *J*=2.9 Hz, 1H, C*H*OAr), 8.20-8.32 (m, 4H, $C_6H_4NO_2$); Anal. Found. C, 64.74; H, 6.99; N, 4.15. $C_{18}H_{23}O_5N$ calcd.: C, 64.85; H, 6.95; N, 4.20%; $[\alpha]^{23.5}_D$=-38.71° (*c* 0.49, $CHCl_3$).

Conversion of 6 to a Diastereoisomeric Mixture of (7*S*,9*R*)-7,9-Dimethylnonanolide and 19. A mixture of **6** (1.10 mmol, 0.362 g) and DBU (1.10 mmol, 0.175 mL) was heated to 90 °C. Stirring was continued for 30 min. The reaction mixture was worked up with aqueous ammonium chloride and extracted with ether, dried over magnesium sulfate, concentrated *in vacuo* and purified by column chromatography on silica gel (eluent: hexane-EtOAc, 20 : 1) to give the isomeric mixture of 5-olefin and 6-olefin as a colorless oil (70.7 mg, 35% yield). (5-olefin): TLC, R_f=0.50 (hexane-EtOAc, 4 : 1); ^1H NMR ($CDCl_3$) δ 0.83-2.53 (m, 9H), 0.94 (d, *J*=5.0 Hz, 3H, CH_3), 1.18 (d, *J*=5.0 Hz, 3H, CH_3), 5.05-5.38 (m, 3H, OC*H*Me and C*H*=C*H*). (6-olefin): TLC, R_f=0.50 (hexane-EtOAc, 4 : 1); ^1H NMR ($CDCl_3$) δ 0.83-2.53 (m, 10H), 1.34 (d, *J*=6.0 Hz, 3H, CH_3), 1.75 (s, 3H, $CH=CCH_3$), 5.05-5.38 (m, 2H, C*H*=C and OC*H*).

To a solution of the olefins (70.7 mg, 0.39 mmol) in methanol (1.1 mL) was added 10% Pd-C (4 mg) and then the reaction atomosphere was substituted for hydrogen gas. Stirring was continued for 5 h at room temperature. The solution was filtrated. The filtrate was concentrated *in vacuo* and purified by column chromatography on silica gel (eluent: hexane-EtOAc, 50 : 1) to give a mixture of (7*S*,9*R*)-7,9-dimethylnonanolide and **19** as a colorless oil (47.6 mg, 66% yield). GLC analysis showed a mixture of (7*S*,9*R*)-7,9-dimethylnonanolide and **19**

present in a 56 : 44 ratio, respectively. TLC, R_f=0.33 (hexane-EtOAc, 4 : 1); IR (film) 2960, 2885, 2375, 2345, 1730, 1460, 1245, 1145, 1100, 965 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86-1.67 (m, 8H), 0.88 (d, *J*=6.8 Hz, 3H, CH_3 (7*S*)), 0.93 (d, *J*=5.8 Hz, 3H, CH_3 (7*R*)), 1.26 (d, *J*=6.2 Hz, 3H, CH_3 (7*R*)), 1.30 (d, *J*=6.6 Hz, 3H, CH_3 (7*S*)), 1.74-2.28 (m, 4H), 2.37-2.56 (m, 1H), 4.88-4.97 (m, 1H, MeC*H*O (7*S*)), 5.03-5.14 (m, 1H, MeC*H*O (7*R*)). GLC (instrument, Gasukuro Kogyo Model 370; column, PEG-20M Bonded, 25 m × 0.25 mm at 100 ℃ + 0.5 ℃/min; carrier gas, N_2, 5 kg/cm^2) t_R 32.8 min (44%, (7*R*)), 39.9 min (56%, (7*S*)). Anal. Found: C, 71.67; H, 10.86. $C_{11}H_{20}O_2$ calcd.: C, 71.68; H, 10.96%.

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References and Notes

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