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# Palladium-catalyzed epimerization of γ-alkenyl-γ-butyrolactone derivatives

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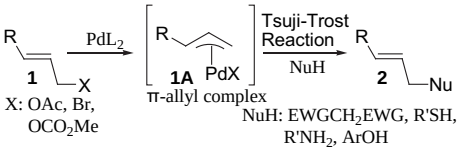
ABSTRACT

γ-Alkenyl-α,β,γ-trisubstituted-γ-butyrolactones (**12**–**16**) and γ-alkenyl-furofurandione derivatives (**21**-**Z**-**24**-**Z**; **21**-**E**-**24**-**E**; **25**-**Z**-**28**-**Z**; and **25**-**E**-**28**-**E**) were successfully epimerized in high yield by a palladium catalyst.

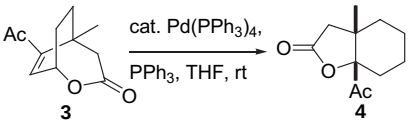


## 1. Introduction

The Tsuji–Trost reaction is the palladium-catalyzed allylation of nucleophiles, such as active methylenes, enolates, amines, and phenols with allylic compounds, such as allyl acetates, allyl carbonates, and allyl bromides. The reaction occurs via intermediate allylpalladium complexes, typically with overall retention of stereochemistry (Eq. 1).[1–5] In the absence of a nucleophile, Pd-catalyzed allylic isomerization is possible. For example, substituted bicyclo [2.2.2]oct-5-en-2-one (**3**) can be converted to *cis*-fused hydrobenzofuran derivative (**4**) when catalyzed by Pd(0) (Eq. 2).[6]




(1)

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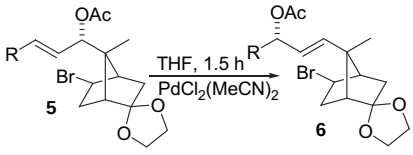


(3)

Complete transfer of chirality in the [3,3]-sigmatropic rearrangement of allylic acetates **5** can be catalyzed by $Pd^{2+}$ (Eq. 3). The reaction has been applied to stereocontrolled synthesis of prostaglandins that possess either the C-l5(*S*) or C-15(*R*) configuration.[7,8]

We have completed the total syntheses of furofurandione natural products by using 4-*endo*-hydroxy-2-oxabicyclo[3.3.0]oct-7-en-3-one (**7**)[9] as a building block. In this process, the key step is palladium-catalyzed epimerization of the γ-alkenyl substituted of bislactones.[10] To the best of our knowledge, studies of the recombination of the $\eta^3$ π-allyl complex to give epimerized allylic esters are rare in the literature. Herein, we describe palladium-catalyzed epimerization of γ-alkenyl-γ-butyrolactone derivatives.

## 2. Results and discussions

### 2.1. Synthesis of γ-alkenyl-α,β,γ-trisubstituted-γ-butyrolactones and their Pd-catalyzed epimerization

The *endo*-hydroxylactone **7** was treated with sodium hydride and benzyl bromide to give the corresponding benzyl ether **8** and *exo*-benzyloxylactone **9**. Due to the α-acidity of the benzyl ether **8**, it was epimerized in situ to give **9** as the major product. Ozonolysis

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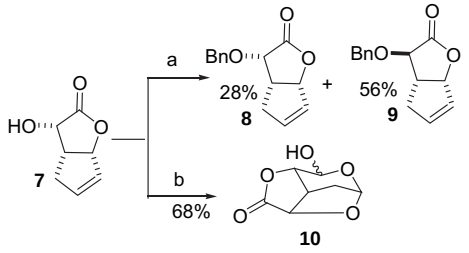
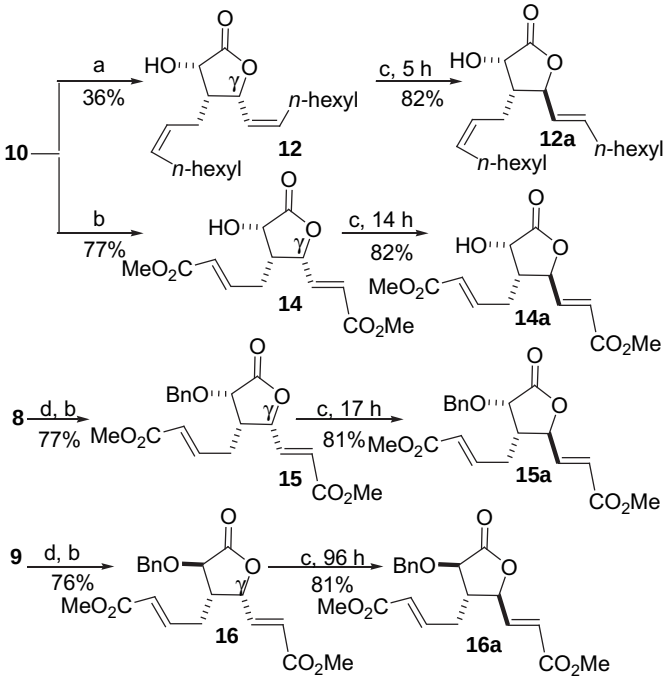
of lactone **7** in $CH_2Cl_2$ at −78 °C followed by reduction with $Me_2S$ gave tricyclic hemiacetal **10** as a 10:1 mixture of two diastereomers in 68% yield. The axial anomer was the major isomer, as confirmed by its 2D-NOESY spectrum (Scheme 1).




**Scheme 1.** Reagents and conditions: (a) NaH, BnBr, THF, 0 °C to rt; 8 h. (b) (1) $O_3$, $CH_2Cl_2$, −78 °C; (2) $Me_2S$, $CH_2Cl_2$, 0 °C, 6 h.

The tricyclic hemiacetal **10** reacted with 2 equiv of $Ph_3P{=}CHC_6H_{13}$-*n* (**11**) or 2 equiv of $Ph_3P{=}CHCO_2Me$ (**13**) to give the corresponding *Z,Z*-Wittig product **12** in 36% yield[11] and *E,E*-Wittig product **14** in 77% yield, respectively. Compound **8** was cleaved by ozone followed by reduction with $Me_2S$. The resulting product was reacted with 2 equiv of $Ph_3P{=}CHCO_2Me$ (**13**) to give the corresponding *E,E*-Wittig product **15** in 77% yield. Similarly, compound **9** was converted to the corresponding *E,E*-Wittig product **16** in 76% yield (Scheme 2).




**Scheme 2.** Reagents and conditions: (a) 2 equiv $Ph_3P{=}CHC_6H_{13}$ (**11**), THF; (b) 2 equiv $Ph_3P{=}CHCO_2Me$ (**13**), THF; (c) 0.1 equiv $Pd(OAc)_2$, 1 equiv $Ph_3P$, THF, rt; (d) (1) $O_3$, $CH_2Cl_2$, −78 °C; (2) $Me_2S$, $CH_2Cl_2$, 0 °C, 6 h.

All of the substituents of γ-alkenyl-γ-butyrolactones **12**, **14**, and **15** were *syn* to each other. When they were treated with palladium catalyst, their γ-chiral centers were epimerized to give the corresponding **12a**–**15a**. In the case of compound **12**, γ-chiral center epimerization was concomitant with γ-(*Z*)-octenyl group isomerization. Interestingly, the geometry of its β-(*Z*)-octenyl group was unchanged. The relative stereochemistries of compound **16** at the α, β, and γ positions were *anti-syn* to each other. Its γ-chiral center was also epimerized by the palladium catalyst to give the corresponding *anti–anti* diastereomer **16a** (Scheme 2).

A plausible mechanism for the palladium-catalyzed epimerization is illustrated using the example of conversion of compound **12** to **12a** in Figure 1. The coordination of the Pd(0)-catalyst to the double bond forms an $\eta^2$ π-allyl complex. An oxidative addition, during which the leaving group is expelled, gives the $\eta^3$ π-allyl complex **A**. The isomerization from **A** to **B** occurs to relieve $A^{1,3}$-strain.[11] The interconversion of intermediate **B** to **C** is ascribed to electrostatic attraction of the ion pair. Recombination of the C–O bond of **C** causes γ-stereogenic center epimerization and γ-octenyl group isomerization. The torsional strain from β and γ substituents is relieved. The double bond geometry of the β-substituent is retained (Fig. 1).

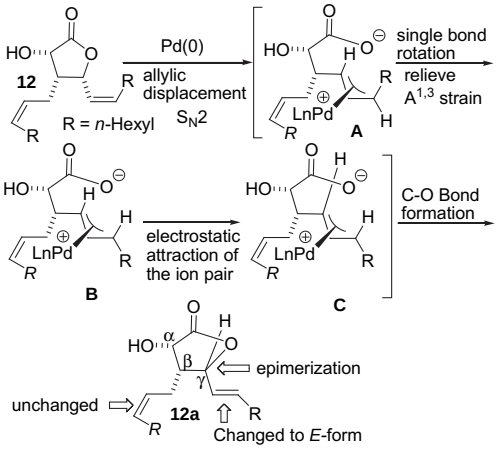



**Figure 1.** Plausible mechanism of the Pd-catalyzed epimerization of compound **12**.

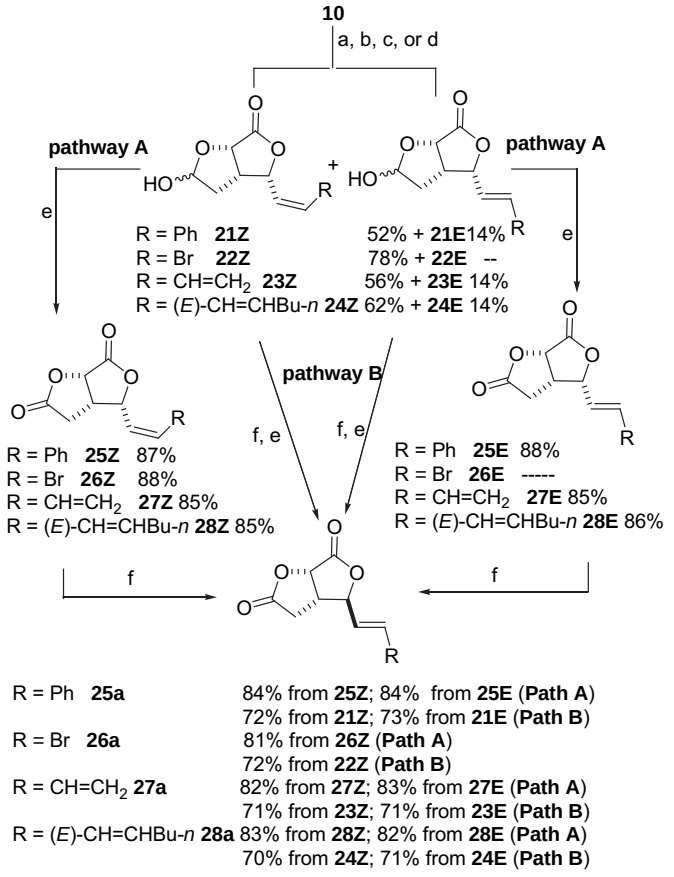
## 2.2. Synthesis of γ-alkenyl-furofurandione derivatives and their Pd-catalyzed epimerization

Tricyclic hemiacetal **10** reacted with semistable phosphonium ylide **17** to give separable lactols **21Z** (52%) and **21E** (14%). Compound **10** reacted with semistable phosphonium ylide **18** to give lactol **22Z** in 78% yield stereoselectively. The hemiacetal **10** reacted with semistable phosphonium ylides **19**–**20** to give Wittig products **23Z**–**24Z** and **23E**–**24E**, respectively. The cis-isomer is the major one in each case. In this study, there were two pathways for epimerization starting from lactols **22Z**–**24Z** and **22E**–**24E**. The oxidation of lactol to lactone followed by epimerization is pathway A in Scheme 3, and the epimerization of lactol followed by oxidation is pathway B in Scheme 3.

By way of pathway A, lactols **21Z**–**24Z** were oxidized by Jones reagent to give the corresponding bislactones **25Z**–**28Z**, respectively, in high yields. The *trans*-analogues **21E**–**24E** were oxidized by Jones reagent to give the corresponding bislactones **25E**–**28E**, respectively, in high yields. Both bislactones **25Z** and **25E** were treated with Pd catalyst to give the same epimerized product **25a**, in which the γ-stereogenic center was epimerized and the *Z*-olefinic side chain of **25Z** was converted to a more stable *E*-form. Similarly, both **26Z**–**28Z** and **26E**–**28E** were converted to **26a**–**28a**, respectively (Scheme 3).

By way of pathway B, the lactol **21Z** was epimerized with Pd catalyst first. The crude product was then oxidized by Jones reagent to give furofurandione **25a**, in which the γ-stereogenic center was epimerized and the *Z*-olefinic side chain was isomerized to a more stable *E*-form. Similarly, both **26Z**–**28Z** and **26E**–**28E** were converted to **26a**–**28a**, respectively (Scheme 3).

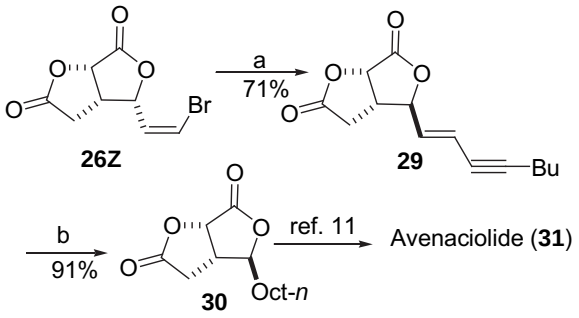
Interestingly, under Sonogashira coupling reaction conditions,[13] vinyl bromide **26Z** reacted with 1-hexyne to give the crossed coupling product **29** in 71% yield. The crossed coupling epimerization at the C-4 chiral center and the isomerization of the *Z*-double




| | |
|---|---|
| R = Ph **25a** | 84% from **25Z**; 84% from **25E** (**Path A**) |
| | 72% from **21Z**; 73% from **21E** (**Path B**) |
| R = Br **26a** | 81% from **26Z** (**Path A**) |
| | 72% from **22Z** (**Path B**) |
| R = $CH=CH_2$ **27a** | 82% from **27Z**; 83% from **27E** (**Path A**) |
| | 71% from **23Z**; 71% from **23E** (**Path B**) |
| R = (*E*)-CH=CHBu-*n* **28a** | 83% from **28Z**; 82% from **28E** (**Path A**) |
| | 70% from **24Z**; 71% from **24E** (**Path B**) |

**Scheme 3.** Reagents and conditions: (a) (1) 1.1 equiv $Ph_3P{=}CHPh$ (**17**), THF, −78 °C to rt, 13 h; (2) separation; (b) (1) 1.1 equiv $Ph_3P{=}CHBr$ (**18**), THF, −78 °C to rt, 13 h; (2) separation; (c) (1) 1.1 equiv (*E*)-$Ph_3P{=}CHCH{=}CH_2$ (**19**), THF, −78 °C to rt, 13 h; (2) separation; (d) (1) 1.1 equiv $Ph_3P{=}CHCH{=}CH_2Ph_3P{=}CHBu$-*n* (**20**), THF, −78 °C to rt, 13 h; (2) separation; (e) Jones reagent, acetone, 0 °C, 2 h; (f) 0.1 equiv $Pd(OAc)_2$, 1 equiv $Ph_3P$, THF, rt.

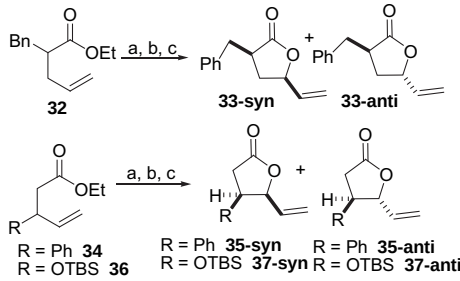
bond occurred in the same flask. The catalytic hydrogenation of compound **29** yielded the corresponding saturated product **30** in 91% yield (Scheme 4). Compound **30** is known to introduce an α-methylene moiety to give avenaciolide (**31**).[14]




**Scheme 4.** Reagents and conditions: (a) cat. $PdCl_2(PPh_3)_2$, cat. CuI, $Et_3N$, THF, 60 °C, 5 h; (b) (1) $H_2$, Pd/C, EtOAc, rt.

## 2.3. Synthesis of di-substituted-γ-vinyl-γ-butyrolactones and their Pd-catalyzed epimerization

The γ,δ-unsaturated esters **32**, **34**, and **36** were prepared according to Johnson–Claisen rearrangement.[15,16] The double bond was cleaved by ozone, followed by treatment with triethylamine[17] to give the corresponding aldehyde, which was treated with vinylmagnesium bromide to give the γ-butyrolactones (**33**-*syn* and **33**-*anti*; **35**-*syn* and **35**-*anti*; **37**-*syn* and **37**-*anti*). Two diastereomers were separated by silica gel column chromatography (Scheme 5).




**Scheme 5.** Reagents and conditions:(a) (1) $O_3$, $CH_2Cl_2$, −78 °C; (2) $Et_3N$; (b) $CH_2{=}CHMgBr$; (c) Separation.

When the α-benzyl-γ-vinyl-γ-butyrolactone **33**-*syn* was treated with Pd catalyst in tetrahydrofuran for 48 h, a mixture of **33**-*syn* and **33**-*anti* in a ratio of 65:35 with 74% mass recovery was obtained (Table 1, entry 1). The product ratio was determined by integration of the benzylic methylene resonance peaks of the crude products. Similarly, when compound **33**-*anti* was treated with Pd catalyst, it gave a 63:37 mixture of the epimerized **33**-*syn* and starting material **33**-*anti* (entry 2). Presumably, the relative energy difference between **33**-*syn* and **33**-*anti* is not big enough to allow the reactant and product existing in an equilibrium state. The epimerization of β-phenyl-γ-vinyl-γ-butyrolactone **35**-*syn* for 40 h gave a mixture of **35**-*syn* and **35**-*anti* in a ratio of 91:9 with 81% mass recovery (entry 3). The product ratio was determined by integration of the peaks of the benzylic proton. When **35**-*anti* was used as the reactant, a similar equilibrium ratio of **35**-*syn* and **35**-*anti* was obtained (entry 4). The epimerization of β-silyoxy-γ-vinyl-γ-butyrolactone **37**-*syn* for 32 h gave a mixture of **37**-*syn* and **37**-*anti* in a ratio of 54:46 with 81% mass recovery (entry 5). The product ratio was determined by integration of the vinylic proton. When **37**-*anti* was used as the reactant, a similar equilibrium ratio of **37**-*syn* and **37**-*anti* was obtained (entry 6).

**Table 1**
Pd-catalyzed epimerization of di-substituted-γ-vinyl-γ-butyrolactones **33**–**37**

| Entry | Reactant | Time (h) | Product ratio | Mass recovery yield (%) |
|---|---|---|---|---|
| 1 | **33**-*syn* | 48 | **33**-*syn*/**33**-*anti*=65:35[a] | 81 |
| 2 | **33**-*anti* | 48 | **33**-*syn*/**33**-*anti*=63:37[a] | 79 |
| 3 | **35**-*syn* | 40 | **35**-*syn*/**35**-*anti*=91:9[b] | 81 |
| 4 | **35**-*anti* | 40 | **35**-*syn*/**35**-*anti*=90:10[b] | 78 |
| 5 | **37**-*syn* | 32 | **37**-*syn*/**37**-*anti*=54:46[c] | 81 |
| 6 | **37**-*anti* | 36 | **37**-*syn*/**37**-*anti*=57:43[c] | 78 |

[a] Determined by integration of the peaks of the benzylic proton (δ 3.31 for **33**-*syn*; δ 3.21 for **33**-*anti*).
[b] Determined by integration of the peaks of the benzylic proton (δ 3.41–3.43 for **35**-*syn*; δ 3.86–3.91 for **35**-*anti*).
[c] Determined by integration the peaks of the vinylic proton (δ 5.82 for **37**-*syn*; δ 5.97 for **37**-*anti*).

## 3. Conclusions

The γ-alkenyl-α,β,γ-trisubstituted-γ-butyrolactones (**12**–**16**) and γ-alkenyl-furofurandione derivatives (**21**-**Z**–**24**-**Z**; **21**-**E**–**24**-**E**) were successfully epimerized in high yield by a palladium catalyst. Their γ-(*Z*)-alkenyl substituent was also isomerized to

a more stable *E*-form. For the di-substituted-γ-vinyl-γ-butyrolactones (**33**, **35**, **36**), Pd-catalyzed epimerization could only attain an equilibrium mixture. The Sonogashira coupling of vinyl bromide **26Z** with 1-hexyne gave crossed coupling product **29**. This reaction is highly efficient because three different reactions are involved in the same flask. Compound **29** is an important precursor of the avenaciolide (**31**).

## 4. Experimental

### 4.1. General

All reactions were carried out under nitrogen. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Melting points were determined by using a Thomas–Hoover melting point apparatus and were uncorrected. The $^1$H and $^{13}$C NMR spectra were recorded on a Bruker Avance DPX400 spectrometer, and chemical shifts were given in parts per million downfield from tetramethylsilane (TMS). IR spectra were taken with a Perkin–Elmer 682 spectrophotometer and only noteworthy absorptions were listed. Mass spectra were measured on a JEOL JMS-700/Shimazu QP2010 (National Cheng Kung University) by electronic impact at 70 eV (unless otherwise indicated). High Resolution Mass Spectroscopy (HRMS) was measured on a Finnigan/Thermo Quest MAT mass spectrometer (National Chung Hsing University). ESI was measured on a ESI trap tadem mass spectrometer (Thermo Finnigan LCQ-DUO, CA, USA) (National Sun Yat-sen University). Compound **7** was prepared by the reported procedure.[9]

### 4.2. (3*S**,3a*R**,6a*R**)-3-(Benzyloxy)-3,3a,4,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one (8) and (3*R**,3a*R**,6a*R**)-3-(benzyloxy)-3,3a,4,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one (9)

To a flask containing NaH (4.02 g, 100.2 mmol, 60% dispersion in mineral oil) in THF (110 mL) was added a solution of compound **7** (11.7 g, 83.5 mmol) in THF (50 mL) dropwise at 0 °C and stirred it for 10 min. To the resulted solution was added benzyl bromide (11.9 mL, 100.2 mmol) at 0 °C and then warmed slowly to rt. After 8 h, the reaction mixture was cooled at 0 °C and quenched with saturated $NaHCO_3$ solution. The aqueous solution was extracted with ethyl acetate and the organic layer was dried over $MgSO_4$, concentrated, and chromatographed on the silica gel column to give compound **8** (5.38 g, 23.4 mmol, 28% yield) and compound **9** (10.76 g, 46.76 mmol, 56% yield). Compound **8**: TLC $R_f$=0.34 (hexane/EtOAc=3:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.32–7.40 (m, 5H), 6.19 (dd, *J*=5.6 and 2.8 Hz, 1H), 5.88–5.91 (m, 1H), 5.25 (dd, *J*=6.6 and 2.2 Hz, 1H), 4.94 (d, *J*=12.0 Hz, 1H), 4.77 (d, *J*=12.0 Hz, 1H), 4.39 (d, *J*=9.2 Hz, 1H), 3.06–3.13 (m, 1H), 2.76–2.84 (m, 1H), 2.34–2.42 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 174.5, 140.3, 137.0, 128.4, 128.0, 127.9, 127.8, 85.7, 74.3, 72.7, 39.6, 31.3; IR ($CH_2Cl_2$): 3063, 2931, 2860, 1774, 1144, 1103, 995 cm$^{-1}$; EI Mass (*m*/*z*): 230 ($M^+$, 0.43), 124 (23), 91 (100), 79 (32), 67 (27); HRMS (*m*/*z*) calcd for $C_{14}H_{14}O_3$ 230.0943, found: 230.0938. *Compound* **9**: TLC $R_f$=0.41 (hexane/EtOAc=3:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.31–7.39 (m, 5H), 6.01–6.03 (m, 1H), 5.86–5.89 (m, 1H), 5.49–5.50 (m, 1H), 4.98 (d, *J*=11.8 Hz, 1H), 4.73 (d, *J*=11.8 Hz, 1H), 3.90 (d, *J*=5.8 Hz, 1H), 3.01–3.07 (m, 1H), 2.67–2.75 (m, 1H), 2.28–2.34 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 175.0, 137.1, 136.8, 129.5, 128.5, 128.2, 127.1, 87.0, 79.5, 72.3, 43.2, 36.6; IR ($CH_2Cl_2$): 3065, 2926, 2858, 1776, 1123, 1020, 919 cm$^{-1}$; EI Mass (*m*/*z*): 230 ($M^+$, 0.10), 124 (45), 91 (100), 79 (37), 67 (24); HRMS (*m*/*z*) calcd for $C_{14}H_{14}O_3$ 230.0943, found: 230.0945.

### 4.3. General procedure of the double bond cleavage by ozone 3-hydroxy-2,5,10-trioxa-tricyclo[5.2.1.0$^{4,8}$]decan-6-one (10)

A 100 mL of two-necked flask fitted with a glass tube to admit ozone, a $CaCl_2$ drying tube, and a magnetic stirring bar were charged with compound **7** (280 mg, 2.0 mmol) in $CH_2Cl_2$ (20 mL). The flask was cooled to −78 °C and ozone was bubbled through the solution. When the solution turned blue, ozone addition was stopped. Nitrogen was passed through the solution until the blue color was discharged. To the reaction mixture was added $Me_2S$ (525 mg, 0.28 mL). After the addition, the cooling bath was removed and the reaction mixture was stirred at rt. The reaction was complete in 6 h and the reaction mixture was concentrated, chromatographed on the silica gel column to give a mixture of two diastereomers (axial–equatorial=10:1) **10** (234 mg, 1.36 mmol) in 68% yield as a colorless oil. TLC $R_f$=0.28 (hexane/EtOAc=1:4). *Axial anomer*: $^1$H NMR (acetone-$d_6$, 400 MHz) $\delta$ 6.21 (s, 1H), 5.46 (d, *J*=3.6 Hz, 1H), 5.02 (s, 1H), 4.69 (d, *J*=8.3 Hz, 1H), 4.37 (d, *J*=4.8 Hz, 1H), 3.53 (ddd, *J*=3.6, 4.8, and 8.3 Hz, 1H), 2.97 (d, *J*=12.4 Hz, 1H), 1.79 (ddd, *J*=3.6, 3.6, and 12.4 Hz, 1H); $^{13}$C NMR (acetone-$d_6$, 100 MHz) $\delta$ 173.9, 98.9, 91.8, 81.1, 76.6, 37.4, 30.6. *Equatorial anomer*: $^1$H NMR (acetone-$d_6$, 400 MHz) $\delta$ 6.21 (s, 1H), 5.51 (d, *J*=10.4 Hz, 1H), 5.06 (d, *J*=8.7 Hz, 1H), 4.86 (dd, *J*=2.2 and 8.7 Hz, 1H), 4.28 (d, *J*=5.2 Hz, 1H), 3.53 (ddd, *J*=2.2, 3.8, and 5.2 Hz, 1H), 2.54 (d, *J*=12.9 Hz, 1H), 1.84 (ddd, *J*=3.8, 10.4, and 12.9 Hz, 1H); $^{13}$C NMR (acetone-$d_6$, 100 MHz) $\delta$ 174.2, 99.6, 90.1, 81.2, 76.3, 38.3, 30.4; IR ($CH_2Cl_2$): 3472, 3059, 2957, 1740, 1440, 1230, 1131, 1038 cm$^{-1}$; EI Mass (*m*/*z*): 172 ($M^+$, 24), 143 (27), 128 (63), 97 (100), 82 (53), 69 (94), 55 (32); HRMS (*m*/*z*) calcd for $C_7H_8O_5$ 172.0372, found: 172.0368.

### 4.4. (3a*R**,4*R**,6a*S**)-2-Hydroxy-4-[(*Z*)-1-octenyl]perhydrofuro[3,4-*b*]furan-6-one (12′) and (3*S**,4*R**,5*R**)-3-hydroxy-4-[(*Z*)-2-nonenyl]-5-[(*Z*)-1-octenyl]tetrahydro-2-furanone (12)

To a flask containing $Ph_3P^+$–$CH_2$–$C_6H_{13}$–*n* $Br^-$ (1042 mg, 2.36 mmol) in THF (12 mL) was added *n*-BuLi (1.48 mL, 2.36 mmol, 1.6 M in hexane) at −78 °C and stirred for 15 min. To the resulted ylide solution was added a solution of compound **10** (200 mg, 1.18 mmol) in THF (2 mL). After the addition, the cooling bath was removed and the reaction mixture was warmed slowly to rt. After 12 h, the reaction mixture was cooled at 0 °C and quenched with a saturated $NH_4Cl$ solution. The aqueous solution was extracted with ethyl acetate and the organic layer was dried over $MgSO_4$, concentrated, and chromatographed on the silica gel column to give compound **12′** (48 mg, 0.19 mmol, 16% yield)[13] and compound **12** (143 mg, 0.42 mmol, 36% yield).

*Compound* **12′**:[12] TLC $R_f$=0.45 (hexane/EtOAc=3:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.70–5.78 (m, 2H), 5.36–5.67 (m, 6H), 4.90 (d, *J*=8.0 Hz, 1H), 4.83 (d, *J*=8.8 Hz, 1H), 3.48–3.53 (m, 1H), 3.23–3.30 (m, 1H), 2.90 (s, 1H), 2.80 (s, 1H), 1.95–2.27 (m, 8H), 1.15–1.33 (m, 8H), 0.87–0.90 (m, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 164.7, 163.9, 137.1, 135.1, 125.8, 123.5, 100.4, 99.4, 78.5, 78.0, 75.8, 73.9, 42.6, 40.7, 34.4, 33.4, 31.6, 30.8, 29.23, 29.25, 28.8, 28.2, 28.0, 22.56, 22.55, 14.0; IR ($CH_2Cl_2$): 3458, 3198, 3025, 2967, 1776, 1432, 1253, 1125 cm$^{-1}$; EI Mass (*m*/*z*): 254 ($M^+$, 13), 131 (59), 104 (100), 77 (47); HRMS (*m*/*z*) calcd for $C_{14}H_{22}O_4$ 254.1518, found: 254.1515.

*Compound* **12**: TLC $R_f$=0.52 (hexane/EtOAc=4:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.71–5.78 (m, 1H), 5.52–5.57 (m, 1H), 5.32–5.46 (m, 2H), 5.23–5.28 (m, 1H), 4.49–4.54 (m, 1H), 2.65–2.71 (m, 1H), 2.55 (s, 1H), 1.95–2.34 (m, 6H), 1.27–1.39 (m, 16H), 0.86–0.88 (m, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 177.2, 136.5, 132.2, 126.0, 123.9, 76.6, 70.6, 44.9, 31.7, 31.6, 29.3, 29.2, 28.9, 28.8, 27.8, 27.3, 22.6, 22.5, 21.0, 14.05, 14.02; IR ($CH_2Cl_2$): 3458, 3125, 3048, 2913, 1783, 1452, 1235, 1199 cm$^{-1}$; EI Mass (*m*/*z*): 336 ($M^+$, 4),

261 (68), 55 (100), 53 (15); HRMS (*m*/*z*) calcd for $C_{21}H_{36}O_3$ 336.2664, found: 336.2659.

### 4.5. General procedure of the Pd-catalyzed epimerization

*4.5.1. (3S*,4R*,5S*)-3-Hydroxy-4-[(Z)-2-nonenyl]-5-[(E)-1-octenyl]-tetrahydro-2-furanone (**12a**).* Under nitrogen atmosphere, to a solution of compound **12** (100 mg, 0.30 mmol) in THF (6 mL) were added $Pd(OAc)_2$ (7.3 mg, 0.03 mmol) and $Ph_3P$ (86.6 mg, 0.30 mmol) at rt. After stirring for 5 h, the reaction mixture was filtered through Celite. The filtrate was concentrated and chromatographed on the silica gel column to give compound **12a** (83 mg, 0.25 mmol, 82% yield) as a pale yellow oil. TLC $R_f$=0.48 (hexane/EtOAc=4:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.80 (dt, *J*=6.8 and 15.6 Hz, 1H), 5.50–5.56 (m, 1H), 5.44 (ddt, *J*=1.2, 6.8, and 15.6 Hz, 1H), 5.30–5.38 (m, 1H), 4.71 (dd, *J*=4.4 and 6.8 Hz, 1H), 4.48 (d, *J*=6.8 Hz, 1H), 2.57 (s, 1H), 2.28–2.43 (m, 1H), 1.98–2.13 (m, 6H), 1.27–1.39 (m, 16H), 0.88 (t, *J*=7.2 Hz, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 176.9, 136.2, 133.3, 126.0, 125.2, 83.1, 68.9, 45.9, 32.1, 31.7, 31.6, 29.5, 28.9, 28.76, 28.71, 27.3, 23.1, 22.6, 22.5, 14.0; IR ($CH_2Cl_2$): 3466, 3148, 3092, 2956, 1766, 1477, 1245, 1123 cm$^{-1}$; EI Mass (*m*/*z*): 336 ($M^+$, 1.74), 261 (33), 55 (100), 53 (14); HRMS (*m*/*z*) calcd for $C_{21}H_{36}O_3$ 336.2664, found: 336.2668.

*4.5.2. Methyl (E)-4-(2R*,3R*,4R*)-4-(hydroxy)-2-[(E)-3-methoxy-3-oxo-1-propenyl]-5-oxotetrahydro-3-furanyl-2-butenoate (**14**).* To a flask containing compound **10** (150 mg, 0.87 mmol) in $CH_2Cl_2$ (12 mL) was added $Ph_3P{=}CHCO_2Me$ (610.9 mg, 1.83 mmol) at rt and stirred for 3 h. The reaction mixture was concentrated and chromatographed on the silica gel column to give compound **14** (193.3 mg, 0.67 mmol) as a colorless oil in 77% yield. The polarity of product **14** is very close to that of $Ph_3PO$. The purification of compound **14** from $Ph_3PO$ is tedious. The contamination of $Ph_3PO$ did not affect the following Pd-catalyzed epimerization reaction. TLC $R_f$=0.25 (hexane/EtOAc=1:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.92–6.85 (m, 2H), 6.15 (dd, *J*=1.6 and 15.6 Hz, 1H), 5.85 (dd, *J*=1.6 and 15.6 Hz, 1H), 5.11 (ddd *J*=2.0, 5.6 and 6.0 Hz, 1H, OC*H*CH=CH), 4.61 (d, *J*=7.2 Hz, 1H, C*H*OH), 3.75 (s, 3H), 3.71 (s, 3H), 2.97–2.90 (m, 1H), 2.52–2.47 (m, 1H), 2.26–2.19 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 175.6, 166.6, 165.6, 145.4, 140.7, 123.6, 123.6, 78.4, 69.7, 52.0, 51.6, 43.8, 26.1; IR ($CH_2Cl_2$): 3358, 2950, 2917, 2851, 1783, 1712, 1655, 1441, 1313, 1280, 1194, 1171, 1137, 1038, 981 cm$^{-1}$; EI Mass (*m*/*z*): 284 ($M^+$, 1.2), 169 (38), 98 (100), 65 (52); HRMS (*m*/*z*) calcd for $C_{13}H_{16}O_7$ 284.0896, found: 284.0899.

*4.5.3. Methyl (E)-4-(2S*,3R*,4S*)-4-hydroxy-2-[(E)-3-methoxy-3-oxo-1-propenyl]-5-oxotetrahydro-3-furanyl-2-butenoate (**14a**).* Compound **14a** was prepared by the general procedure of the Pd-catalyzed epimerization described in Section 4.5. Starting from compound **14** (100 mg, 0.35 mmol) gave compound **14a** (81.5 mg, 0.29 mmol) in 82% yield. TLC $R_f$=0.48 (hexane/EtOAc=1:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.86–6.96 (m, 2H), 6.11 (dd, *J*=1.6 and 15.6 Hz, 1H), 5.96 (d, *J*=15.6 Hz, 1H), 4.90 (ddd, *J*=1.6, 4.8 and 4.8 Hz, 1H), 4.50 (d, *J*=6.8 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 2.70–2.77 (m, 1H), 2.52–2.58 (m, 1H), 2.22–2.29 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 175.4, 166.3, 165.7, 144.2, 142.1, 124.2, 122.7, 79.6, 67.7, 52.0, 51.7, 44.2, 28.1; IR ($CH_2Cl_2$): 3457, 3149, 3023, 2944, 1789, 1782, 1778, 1325, 1237, 1082 cm$^{-1}$; EI Mass (*m*/*z*): 284 ($M^+$, 1.23), 169 (41), 98 (100), 65 (54); HRMS (*m*/*z*) calcd for $C_{13}H_{16}O_7$ 284.0896, found: 284.0898.

*4.5.4. Methyl (E)-4-(2R*,3R*,4R*)-4-(benzyloxy)-2-[(E)-3-methoxy-3-oxo-1-propenyl]-5-oxotetrahydro-3-furanyl-2-butenoate (**15**).* Compound **8** was cleaved by ozone according to the general procedure described in Section 4.3. Compound **8** (230.1 mg, 1.0 mmol) in $CH_2Cl_2$ (10 mL) reacted with ozone followed by reduction with $Ph_3P$ (262.3 mg, 1.0 mmol). After stirring for 3 h, the reaction mixture was concentrated. To a flask containing crude product in THF (12 mL) was added $Ph_3P{=}CHCO_2Me$ (735.6 mg, 2.2 mmol) at rt and stirred for 3 h. The reaction mixture was concentrated and chromatographed on the silica gel column to give compound **15** (291.7 mg, 0.78 mmol, 77% yield) as a pale yellow oil. TLC $R_f$=0.43 (hexane/EtOAc=3:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.32–7.37 (m, 5H), 6.82 (dt, *J*=7.2 and 15.6 Hz, 1H), 6.27 (dd, *J*=8.0 and 11.6 Hz, 1H), 6.10 (ddd, *J*=1.2, 6.8, and 8.0 Hz, 1H), 6.01 (dd, *J*=1.2 and 11.6 Hz, 1H), 5.81 (dd, *J*=1.2 and 15.6 Hz, 1H), 4.92 (d, *J*=12.0 Hz, 1H), 4.68 (d, *J*=12.0 Hz, 1H), 4.10 (d, *J*=6.4 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.96–3.03 (m, 1H), 2.39–2.47 (m, 1H), 2.26–2.33 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.5, 166.4, 165.8, 145.3, 144.2, 136.4, 128.6, 128.3, 128.2, 123.1, 122.8, 76.6, 73.4, 72.3, 51.7, 51.4, 43.0, 26.1; IR ($CH_2Cl_2$): 3143, 3126, 2976, 1789, 1784, 1775, 1456, 1326, 1248, 1158 cm$^{-1}$; EI Mass (*m*/*z*): 374 ($M^+$, 0.25), 169 (19), 98, 91 (100), 65 (5); HRMS (*m*/*z*) calcd for $C_{20}H_{22}O_7$ 374.1366, found: 374.1360.

*4.5.5. Methyl (E)-4-(2S*,3R*,4R*)-4-(benzyloxy)-2-[(E)-3-methoxy-3-oxo-1-propenyl]-5-oxotetrahydro-3-furanyl-2-butenoate (**15a**).* Compound **15a** was prepared by the general procedure of the Pd-catalyzed epimerization described in Section 4.5. Starting from compound **15** (100 mg, 0.35 mmol) gave compound **15a** (106.0 mg, 0.28 mmol) in 81% yield. Compound **15a**: TLC $R_f$=0.38 (hexane/EtOAc=3:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.32–7.40 (m, 5H), 6.76–6.87 (m, 2H), 6.12 (dd, *J*=1.2 and 15.6 Hz, 1H), 5.88 (d, *J*=13.2 Hz, 1H), 4.90 (d, *J*=11.6 Hz, 1H), 4.86 (dd, *J*=6.0 and 6.0 Hz, 1H), 4.62 (d, *J*=11.6 Hz, 1H), 4.06 (d, *J*=5.6 Hz, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 2.65–2.69 (m, 1H), 2.26–2.35 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 172.2, 166.1, 165.6, 144.0, 141.7, 136.1, 128.5, 128.3, 128.2, 123.7, 123.2, 80.3, 72.8, 72.2, 51.9, 51.5, 45.1, 27.2; IR ($CH_2Cl_2$): 3156, 3094, 2956, 1784, 1781, 1771, 1423, 1354, 1218, 1115 cm$^{-1}$; EI Mass (*m*/*z*): 374 ($M^+$, 0.33), 169 (21), 98 (45), 91 (100), 65 (7); HRMS (*m*/*z*) calcd for $C_{20}H_{22}O_7$ 374.1366, found: 374.1363.

*4.5.6. Methyl (E)-4-(2R*,3R*,4R*)-4-(benzyloxy)-2-[(E)-3-methoxy-3-oxo-1-propenyl]-5-oxotetrahydro-3-furanyl-2-butenoate (**16**).* Compound **9** was cleaved by ozone according to the general procedure described in Section 4.3. Compound **9** (193.3 mg, 0.52 mmol) in $CH_2Cl_2$ (6 mL) reacted with ozone followed by reduction with $Ph_3P$ (136.4 mg, 0.52 mmol). After stirring for 3 h, the reaction mixture was concentrated. To a flask containing crude product in THF (12 mL) was added $Ph_3P{=}CHCO_2Me$ (367.8 mg, 1.1 mmol) at rt and stirred for 3 h. The reaction mixture was concentrated and chromatographed on the silica gel column to give compound **16** (150.0 mg, 0.40 mmol, 76% yield) as a pale yellow oil. TLC $R_f$=0.49 (hexane/EtOAc=3:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.29–7.39 (m, 5H), 6.79–6.88 (m, 2H), 6.12 (dd, *J*=1.6 and 16.0 Hz, 1H), 5.87 (d, *J*=15.6 Hz, 1H), 5.22 (dd, *J*=1.6 and 6.4 Hz, 1H), 5.03 (d, *J*=11.2 Hz, 1H), 4.68 (d, *J*=11.2 Hz, 1H), 3.89 (d, *J*=8.4 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 2.81–2.89 (m, 1H), 2.30–2.36 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.2, 165.9, 165.3, 143.7, 140.2, 136.4, 128.4, 128.2, 128.1, 123.7, 123.5, 76.6, 75.7, 72.3, 51.8, 51.5, 44.2, 30.2; IR ($CH_2Cl_2$): 3156, 3095, 2908, 1792, 1786, 1781, 1425, 1377, 1214, 1196 cm$^{-1}$; EI Mass (*m*/*z*): 374 ($M^+$, 0.81), 169 (25), 98 (44), 91 (100), 65 (11); HRMS (*m*/*z*) calcd for $C_{20}H_{22}O_7$ 374.1366, found: 374.1364.

*4.5.7. Methyl (E)-4-(2S*,3R*,4R*)-4-(benzyloxy)-2-[(E)-3-methoxy-3-oxo-1-propenyl]-5-oxotetrahydro-3-furanyl-2-butenoate (**16a**).* Compound **16a** was prepared by the general procedure of the Pd-catalyzed epimerization described in Section 4.5. Starting from compound **16** (100 mg, 0.35 mmol) gave compound **16a** (106.0 mg, 0.28 mmol) in 81% yield. Compound **16a**: TLC $R_f$=0.42 (hexane/EtOAc=3:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.31–7.41 (m,

5H), 6.75–6.87 (m, 2H), 6.13 (dd, *J*=1.2 and 15.6 Hz, 1H), 5.80 (d, *J*=15.6 Hz, 1H), 5.06 (d, *J*=11.6 Hz, 1H), 4.75 (d, *J*=11.6 Hz, 1H), 4.57 (dd, *J*=6.0 and 6.0 Hz, 1H), 3.98 (d, *J*=9.6 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 2.38–2.48 (m, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.2, 165.9, 165.6, 142.7, 141.1, 136.3, 128.6, 128.5, 128.4, 124.4, 123.7, 77.9, 76.0, 72.4, 52.0, 51.6, 46.8, 31.3; IR ($CH_2Cl_2$): 3102, 3088, 2905, 1787, 1783, 1769, 1456, 1377, 1245, 1123 cm$^{-1}$; EI Mass (*m*/*z*): 374 ($M^+$, 0.83), 169 (25), 98 (51), 91 (100), 65 (13); HRMS (*m*/*z*) calcd for $C_{20}H_{22}O_7$ 374.1366, found: 374.1361.

*4.5.8. (3aR*,4R*,6aS*)-4-[(Z)-2-Phenyl-1-ethenyl]perhydro-furo[3,4-b]furan-2,6-dione (**25Z**) and (3aR*,4R*,6aS*)-4-[(E)-2-phenyl-1-ethenyl]perhydro-furo[3,4-b]furan-2,6-dione (**25E**).* To a flask containing $Ph_3P^+-CH_2-Ph\ Br^-$ (1018 mg, 2.35 mmol) in THF (8 mL) was added *n*-BuLi (1.47 mL, 2.35 mmol, 1.6 M in hexane) at −78 °C and stirred for 15 min. To the resulted ylide **17** solution was added a solution of compound **10** (367 mg, 2.13 mmol) in THF (2 mL). The reaction was stirred at −78 °C for 1 h and the reaction mixture was warmed slowly to rt. After 12 h, the reaction mixture was cooled at 0 °C and quenched with a saturated $NH_4Cl$ (10 mL) solution. The aqueous solution was extracted with ethyl acetate and the organic layer was dried over $MgSO_4$, concentrated, and chromatographed on the silica gel column to give compound **21Z** (270.2 mg, 1.11 mmol, 52% yield) and compound **21E** (72.3 mg, 0.29 mmol, 14% yield). To a solution of lactol **21Z** (123 mg, 0.50 mmol) in 5 mL of acetone was added Jones reagent at 0 °C dropwise until the persistence of the orange solution. After stirring at 0 °C for 30 min, the excess Jones reagent was quenched by 2-propanol. The reaction was diluted by water (2 mL) and extracted with $CH_2Cl_2$. The organic layer was dried over anhydrous $MgSO_4$. The filtrate was concentrated and chromatographed on the silica gel column to give compound **25Z** as a white solid (106 mg, 0.43 mmol) in 87% yield. Similarly, the lactol **21E** (50.0 mg, 0.20 mmol) was also oxidized by Jones reagent to give **25E** as a white solid (42.9 mg, 0.18 mmol) in 88% yield.

*Compound* **25Z**: TLC $R_f$=0.33 (hexane/EtOAc=1:1); mp 79.6–80.4 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.20–7.43 (m, 5H), 6.96 (d, *J*=11.6 Hz, 1H), 5.69 (dd, *J*=8.8, and 11.6 Hz, 1H), 5.53 (dd, *J*=8.8 and 8.8 Hz, 1H), 5.13 (d, *J*=8.0 Hz, 1H), 3.57 (dddd, *J*=8.0, 8.0, 8.8, and 9.6 Hz, 1H), 2.77 (dd, *J*=8.0 and 18.4 Hz, 1H), 2.70 (dd, *J*=9.6 and 18.4 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.3, 170.0, 137.3, 134.9, 128.7, 128.5, 128.3, 123.9, 77.2, 75.5, 39.8, 28.3; IR ($CH_2Cl_2$): 3187, 3052, 2963, 1789, 1787, 1415, 1398, 1184 cm$^{-1}$; EI Mass (*m*/*z*): 244 ($M^+$, 13), 131 (39), 104 (100), 77 (17); HRMS (*m*/*z*) calcd for $C_{14}H_{12}O_4$ 244.0736, found: 244.0729.

*Compound* **25E**: TLC $R_f$=0.25 (hexane/EtOAc=1:1) mp 81.8–82.6 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.29–7.41 (m, 5H), 6.82 (d, *J*=16.0 Hz, 1H), 6.07 (dd, *J*=6.4 and 16.0 Hz, 1H), 5.35 (dd, *J*=6.4 and 6.4 Hz, 1H), 5.20 (d, *J*=8.4 Hz, 1H), 3.64 (ddt, *J*=6.4, 8.4, and 8.8 Hz, 1H), 2.70 (d, *J*=8.8 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 171.2, 169.3, 138.1, 135.8, 128.3, 128.1, 127.9, 122.8, 77.8, 76.0, 38.7, 30.7; IR ($CH_2Cl_2$): 3165, 3024, 2954, 1778, 1772, 1424, 1305, 1174 cm$^{-1}$; EI Mass (*m*/*z*): 244 ($M^+$, 25), 131 (42), 104 (100), 77 (19); HRMS (*m*/*z*) calcd for $C_{14}H_{12}O_4$ 244.0736, found: 244.0726.

*4.5.9. (3aR*,4S*,6aS*)-4-[(E)-2-Phenyl-1-ethenyl]perhydro-furo[3,4-b]furan-2,6-dione (**25a**).* Compound **25a** was prepared by the general procedure of the Pd-catalyzed epimerization described in Section 4.5. Starting from compound **25Z** (216.7 mg, 0.89 mmol) gave compound **25a** (182.4 mg, 0.75 mmol) in 84% yield. Starting from compound **25E** (216.7 mg, 0.89 mmol) gave compound **25a** (182.4 mg, 0.75 mmol) in 84% yield. Compound **25a** can also be prepared from either **21E** or **21Z** sequentially by Pd-catalyzed epimerization and Jones oxidation (pathway B).

*Compound* **25a**: TLC $R_f$=0.21 (hexane/EtOAc=1:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.33–7.42(m, 5H), 6.75 (d, *J*=16.0 Hz, 1H), 6.16 (dd, *J*=7.2 and 16.0 Hz, 1H), 5.07 (d, *J*=7.6 Hz, 1H), 4.94 (dd, *J*=7.2 and 7.2 Hz, 1H), 3.25 (dddd, *J*=4.0, 7.2, 7.6, and 9.2 Hz, 1H), 2.98 (d, *J*=9.2 and 18.0 Hz, 1H), 2.67 (dd, *J*=4.0 and 18.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 171.4, 169.7, 138.3, 135.6, 128.5, 128.2, 127.7, 123.4, 78.4, 75.6, 38.8, 30.5; IR ($CH_2Cl_2$): 3198, 3124, 2926, 1766, 1760, 1438, 1356, 1155 cm$^{-1}$; EI Mass (*m*/*z*): 244 ($M^+$, 3), 131 (6), 104 (100), 77 (51); HRMS (*m*/*z*) calcd for $C_{14}H_{12}O_4$ 244.0736, found: 244.0738.

*4.5.10. (3aR*,4R*,6aS*)-4-[(Z)-2-Bromo-1-ethenyl]perhydro-furo-[3,4-b]furan-2,6-dione (**26Z**).* Compound **26Z** was prepared by the general procedure described in **4.11**. Compound **10** (367 mg, 2.13 mmol) reacted with ylide **18** to give compound **22Z** (413.8 mg, 1.66 mmol, 78% yield). The lactol **22Z** (123 mg, 0.49 mmol) was oxidized by Jones reagent to give compound **26Z** as a white solid (107.4 mg, 0.43 mmol) in 88% yield. TLC $R_f$=0.55 (hexane/EtOAc=2:1); mp: 84.9–85.7 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.61 (dd, *J*=2.0, and 7.6 Hz, 1H), 6.35 (dd, *J*=6.8 and 7.6 Hz, 1H), 5.52 (ddd, *J*=2.0, 6.8, and 7.0 Hz, 1H), 5.15 (d, *J*=6.8 Hz, 1H), 3.78–3.86 (m, 1H), 2.73 (dd, *J*=9.8 and 18.6 Hz, 1H), 2.59 (dd, *J*=7.4 and 18.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.0, 169.7, 129.6, 113.2, 77.5, 75.9, 38.5, 28.3; IR ($CH_2Cl_2$): 3054, 2987, 1801, 1265, 1190, 1160, 1078 cm$^{-1}$; ESI Mass (*m*/*z*): 269 ($M^+$+23); HRMS (*m*/*z*) calcd for $C_8H_7{}^{79}BrO_4Na$ 268.9425, found: 268.9427.

*4.5.11. (3aR*,4S*,6aS*)-4-[(E)-2-Bromo-1-ethenyl]perhydro-furo[3,4-b]furan-2,6-dione (**26a**).* Compound **26a** was prepared by the general procedure of the Pd-catalyzed epimerization described in Section 4.5. Starting from compound **26Z** (216.7 mg, 0.89 mmol) gave compound **26a** (177.3 mg, 0.72 mmol) in 81% yield. Compound **26a** can also be prepared from compound **22Z** sequentially by Pd-catalyzed epimerization and Jones oxidation (pathway B, 72% yield). TLC $R_f$=0.24 (hexane/EtOAc=2:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.63 (dd, *J*=0.8 and 13.6 Hz, 1H), 6.26 (dd, *J*=6.8 and 13.6 Hz, 1H), 5.03 (d, *J*=7.6 Hz, 1H), 4.75 (dd, *J*=5.6 and 6.8 Hz, 1H), 3.19 (dddd, *J*=4.4, 5.6, 7.6, and 9.2 Hz, 1H), 2.97 (dd, *J*=9.2 and 18.6 Hz, 1H), 2.60 (dd, *J*=4.4 and 18.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.2, 169.5, 133.3, 119.6, 83.8, 76.3, 40.7, 32.1; IR ($CH_2Cl_2$): 3055, 2989, 1798, 1421, 1266, 1199, 1148, 1075 cm$^{-1}$; EI Mass (*m*/*z*): 246 ($M^+$, 0.6), 183 (4) 139 (14), 123 (45), 95 (52), 81 (100), 55 (27); HRMS (*m*/*z*) calcd for $C_8H_7{}^{79}BrO_4$ 245.9528, found: 245.9522.

*4.5.12. (3aR*,4R**,6aS*)-4-[(1Z)-1,3-Butadienyl]perhydro-furo[3,4-b]-furan-2,6-dione (**27Z**) and (3aR*,4R*,6aS*)-4-[(1E)-1,3-butadienyl] perhydro-furo[3,4-b]furan-2,6-dione (**27E**).* Compounds **27Z** and **27E** were prepared by the general procedure described in Section 4.5.7. Compound **10** (300 mg, 1.74 mmol) reacted with ylide **19** to give compound **23Z** (191.2 mg, 0.97 mmol, 56% yield) and compound **23E** (47.8 mg, 0.24 mmol, 14% yield). The lactol **23Z** (100 mg, 0.51 mmol) was oxidized by Jones reagent to give compound **27Z** as a white solid (84.1 mg, 0.43 mmol) in 85% yield. The lactol **23E** (32 mg, 0.16 mmol) was oxidized by Jones reagent to give compound **27E** as a white solid (26.4 mg, 0.14 mmol) in 85% yield.

*Compound* **27Z**: TLC $R_f$=0.48 (hexane/EtOAc=1:1); mp 87.2–88.1 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.51 (ddd, *J*=10.8, 11.2, and 18.8 Hz, 1H), 6.35 (dd, *J*=11.2 and 11.2 Hz, 1H), 5.59 (dd, *J*=7.2 and 7.2 Hz, 1H), 5.39–5.47 (m, 3H), 5.15 (d, *J*=8.0 Hz, 1H), 3.60 (ddt, *J*=7.2, 8, and 8.8 Hz, 1H), 2.66 (d, *J*=8.8 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.3, 170.1, 135.4, 130.1, 123.3, 123.0, 76.5, 75.3, 39.8, 28.1; IR ($CH_2Cl_2$): 3156, 3048, 2933, 1781, 1777, 1325, 1298, 1184 cm$^{-1}$; EI Mass (*m*/*z*): 194 ($M^+$, 2.34), 169 (21), 98 (100), 65 (31); HRMS (*m*/*z*) calcd for $C_{10}H_{10}O_4$ 194.0579, found: 194.0577.

*Compound* **27E**: TLC $R_f$=0.42 (hexane/EtOAc=1:1) mp 89.6–90.3 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.34–6.48 (m, 2H), 5.58 (dd, *J*=6.4 and 14.8 Hz, 1H), 5.38 (d, *J*=16.0 Hz, 1H), 5.30 (d, *J*=9.2 Hz, 1H), 5.21 (dd, *J*=6.4 and 6.4 Hz, 1H), 5.15 (d, *J*=8.4 Hz, 1H), 3.57

(dddd, $J$=4.4, 6.4, 8.4, and 8.4 Hz, 1H), 2.65 (dd, $J$=4.4 and 8.4 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.3, 169.9, 136.0, 134.6, 124.4, 121.3, 78.4, 76.6, 39.7, 28.1; IR ($CH_2Cl_2$): 3184, 3092, 2988, 1784, 1776, 1324, 1287, 1176 cm$^{-1}$; EI Mass ($m/z$): 194 ($M^+$, 3), 169 (41), 98 (100), 65 (33); HRMS ($m/z$) calcd for $C_{10}H_{10}O_4$ 194.0579, found: 194.0574.

*4.5.13. (3aR*,4S*,6aS*)-4-[(1E)-1,3-Butadienyl]perhydro-furo[3,4-b]-furan-2,6-dione (**27a**).* Compound **27a** was prepared by the general procedure of the Pd-catalyzed epimerization described in Section 4.5. Starting from compound **27Z** (100 mg, 0.52 mmol) gave compound **27a** (82.7 mg, 0.43 mmol) in 82% yield. Starting from compound **27E** (60 mg, 0.31 mmol) gave compound **27a** (49.9 mg, 0.26 mmol) in 83% yield. Compound **27a** can also be prepared from either **22Z** or **22E** sequentially by Pd(0)-epimerization and Jones oxidation (pathway B). TLC $R_f$=0.38 (hexane/EtOAc=1:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.29–6.41 (m, 2H), 5.67 (dd, $J$=6.0 and 14.0 Hz, 1H), 5.37 (d, $J$=13.2 Hz, 1H), 5.30 (d, $J$=10.4 Hz, 1H), 5.02 (d, $J$=7.6 Hz, 1H), 4.81 (dd, $J$=6.0 and 6.0 Hz, 1H), 3.15 (dddd, $J$=4.0, 6.0, 7.6, and 9.2 Hz, 1H), 2.94 (dd, $J$=9.2 and 18.0 Hz, 1H), 2.61 (dd, $J$=4.0 and 18.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 172.3, 169.6, 137.1, 134.0, 123.9, 121.1, 79.1, 76.1, 39.8, 27.9; IR ($CH_2Cl_2$): 3175, 3065, 2915, 1765, 1763, 1316, 1298, 1125 cm$^{-1}$; EI Mass ($m/z$): 194 ($M^+$, 6), 169 (45), 98 (100), 65 (31); HRMS ($m/z$) calcd for $C_{10}H_{10}O_4$ 194.0579, found: 194.0578.

*4.5.14. (3aR*,4R*,6aS*)-4-[(1Z,3E)-1,3-Octadienyl]perhydro-furo[3,4-b]furan-2,6-dione (**28Z**) and (3aR*,4R*,6aS*)-4-[(1E,3E)-1,3-octadienyl]perhydro-furo[3,4-b]furan-2,6-dione (**28E**).* Compounds **28Z** and **28E** were prepared by the general procedure described in Section 4.5.7. Compound **10** (300 mg, 1.74 mmol) reacted with ylide **20** to give compound **24Z** (272.2 mg, 1.08 mmol, 62% yield) and compound **18E** (60.5 mg, 0.24 mmol, 14% yield). The lactol **24Z** (100 mg, 0.40 mmol) was oxidized by pyridinium chlorochromate to give compound **28Z** as a white solid (85.0 mg, 0.34 mmol) in 85% yield. The lactol **24E** (30.1 mg, 0.14 mmol) was oxidized by pyridinium chlorochromate to give compound **228Z** as a white solid (27.8 mg, 0.12 mmol) in 86% yield.

*Compound* **28Z**: TLC $R_f$=0.47 (hexane/EtOAc=2:1); mp: 61.5–62.3 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.31 (dd, $J$=11.0 and 12.9 Hz, 1H), 6.16 (dd, $J$=7.5 and 12.9 Hz, 1H), 5.93 (dt, $J$=7.2 and 14.8 Hz, 1H), 5.58 (dd, $J$=7.5 and 14.8 Hz, 1H), 5.23 (dd, $J$=8.0 and 11.0 Hz, 1H), 5.13 (d, $J$=8.4 Hz, 1H), 3.58 (ddt, $J$=8.0, 8.4, and 8.8 Hz, 1H), 2.66 (d, $J$=8.8 Hz, 2H), 2.15 (td, $J$=7.2 and 7.2 Hz, 1H), 1.30–1.43 (m, 4H), 0.91 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.4, 170.1, 141.8, 135.5, 123.6, 119.7, 76.6, 75.4, 39.9, 32.6, 30.9, 28.2, 22.2, 13.8 ($CH_3$); IR ($CH_2Cl_2$): 3055, 2964, 1799, 1266, 1197, 1147, 1077 cm$^{-1}$; EI Mass ($m/z$): 250 ($M^+$, 72), 129, 110 (38), 91 (90), 81 (100), 67 (63), 54 (53); HRMS ($m/z$) calcd for $C_{14}H_{18}O_4$ 250.1205, found: 250.1206.

*Compound* **28E**: TLC $R_f$=0.35 (hexane/EtOAc=2:1); mp: 63.6–64.2 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.39 (dd, $J$=10.4 and 15.2 Hz, 1H), 6.05 (dd, $J$=10.4 and 15.2 Hz, 1H), 5.86 (dt, $J$=6.8 and 15.2 Hz, 1H), 5.42 (dd, $J$=10.4 and 15.2 Hz), 5.18 (dd, $J$=6.8 and 10.4 Hz, 1H), 5.14 (d, $J$=8.0 Hz, 1H), 3.54 (ddd, $J$=8.0, 8.8, and 10.4 Hz, 1H), 2.65 (d, $J$=8.8 Hz, 2H), 2.12 (td, $J$=6.8 and 9.9 Hz, 1H), 1.29–1.41 (m, 4H), 0.90 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.4, 170.1, 139.7, 136.4, 127.8, 121.0, 79.0, 76.6, 39.7, 32.2, 30.9, 28.1, 22.1, 13.8; IR ($CH_2Cl_2$): 3056, 2928, 1793, 1286, 1150, 1073, 1005 cm$^{-1}$; ESI Mass ($m/z$): 273 ($M^+$+23); HRMS ($m/z$) calcd for $C_{14}H_{18}O_4Na$ 273.1103, found: 273.1105.

*4.5.15. (3aR*,4S*,6aS*)-4-[(1E,3E)-1,3-Octadienyl]perhydro-furo[3,4-b]furan-2,6-dione (**28a**).* Compound **28a** was prepared by the general procedure of the Pd-catalyzed epimerization described in Section 4.5. Starting from compound **28Z** (210.0 mg, 0.84 mmol) gave compound **28a** (173.4 mg, 0.76 mmol) in 83% yield. Starting from compound **28E** (200 mg, 0.68 mmol) gave compound **28a** (164 mg, 0.65 mmol) in 82% yield. Compound **28a** can also be prepared from either **24Z** or **24E** sequentially by Pd-catalyzed epimerization and Jones oxidation (pathway B). TLC $R_f$=0.5 (hexane/EtOAc=2:1); mp: 60.8–61.5 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 6.33 (dd, $J$=10.4 and 15.2 Hz, 1H), 6.04 (dd, $J$=7.2 and 15.2 Hz, 1H), 5.87 (dt, $J$=7.2 and 15.2 Hz, 1H), 5.51 (dd, $J$=7.2 and 15.2 Hz, 1H), 5.01 (d, $J$=7.2 Hz, 1H), 4.77 (dd, $J$=6.8 and 10.4 Hz, 1H), 3.11–3.17 (m, 1H), 2.93 (dd, $J$=9.2 and 18.4 Hz, 1H), 2.59 (dd, $J$=4.0 and 18.4 Hz, 1H), 2.12 (td, $J$=7.2 and 13.6 Hz, 2H), 1.25–1.42 (m, 4H), 0.90 (t, $J$=6.8 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 172.8, 170.5, 140.0, 135.9, 127.8, 124.0, 84.4, 77.1, 41.3, 32.3, 32.2, 31.0, 22.1, 13.8; IR ($CH_2Cl_2$): 2925, 2854, 1790, 1212, 1145, 1074 cm$^{-1}$; EI Mass ($m/z$): 250 ($M^+$, 58), 138 (23) 113 (29), 81 (100), 68 (44), 55 (69); HRMS ($m/z$) calcd for $C_{14}H_{18}O_4$ 250.1205, found: 250.1211.

*4.5.16. (3aR*,4S*,6aS*)-4-[(E)-1-Octen-3-ynyl]perhydro-furo[3,4-b]-furan-2,6-dione (**29**).* To a mixture of vinyl bromide **26Z** (100 mg, 0.40 mmol), $PdCl_2(PPh_3)_2$ (5.6 mg, 0.008 mmol), and CuI (3.1 mg, 0.0016 mmol) in THF (10 mL) was added $Et_3N$ (0.05 mL, 0.4 mmol) and 1-hexyne (0.13 mL, 1.2 mmol) in THF (1 mL). The reaction was heated to 60 °C for 5 h. The reaction mixture was filtered through Celite. The filtrate was concentrated and chromatographed on silica gel column to give product **29** (71.3 mg, 0.29 mmol, 71% yield) as a pale yellow oil. TLC $R_f$=0.63 (hexane/EtOAc=2:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.96 (dd, $J$=6.0 and 15.6 Hz, 1H), 5.85 (d, $J$=15.6 Hz, 1H), 5.02 (d, $J$=7.6 Hz, 1H), 4.78 (dd, $J$=6.0 and 6.0 Hz, 1H), 3.12–3.19 (m, 1H), 2.95 (dd, $J$=9.2 and 18.4 Hz, 1H), 2.60 (dd, $J$=4.0 and 18.4 Hz, 1H), 2.32 (td, $J$=2.0 and 7.2 Hz, 1H), 1.25–1.57 (m, 4H), 0.92 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.0, 169.2, 134.7, 116.0, 83.3, 77.2, 76.3, 40.9, 32.1, 30.4, 21.9, 19.0, 13.5; IR ($CH_2Cl_2$): 2960, 2934, 2217, 1797, 1266, 1205, 1145, 1076 cm$^{-1}$; EI Mass ($m/z$): 248 ($M^+$, 20), 178 (18), 108 (55), 93 (100), 79 (88), 65 (56); HRMS ($m/z$) calcd for $C_{14}H_{16}O_4$ 248.1049, found: 248.1048.

*4.5.17. (3aR*,4S*,6aS*)-4-Octylperhydro-furo[3,4-b]furan-2,6-dione (**30**).* A mixture of enyne **29** (50 mg, 0.20 mmol) and 10%Pd/C (2.0 mg, 0.02 mmol) in ethyl acetate (2 mL) was stirred under hydrogen balloon for 9 h. The reaction mixture was filtered through Celite. The filtrate was concentrated and chromatographed on silica gel column to give product **30** (46.6 mg, 0.18 mmol, 91% yield) as a colorless oil. TLC $R_f$=0.72 (hexane/EtOAc=1.5:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.01 (d, $J$=7.6 Hz, 1H), 4.34 (td, $J$=5.2 and 7.6 Hz, 1H), 3.01–3.07 (m, 1H), 2.94 (dd, $J$=9.2 and 18.0 Hz, 1H), 2.55 (dd, $J$=4.0 and 18.0 Hz, 1H), 1.83–1.87 (m, 2H), 1.27–1.48 (m, 12H), 0.88 (t, $J$=6.8 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.4, 169.7, 84.7, 77.2, 40.2, 35.4, 32.8, 31.7, 29.2, 29.1, 29.1, 24.9, 22.6, 14.0; IR ($CH_2Cl_2$): 3054, 2928, 1797, 1265, 1145, 1076 cm$^{-1}$; EI Mass ($m/z$): 254 ($M^+$, 3.9), 179 (14), 150 (22), 113 (46), 97 (100), 55 (86); HRMS ($m/z$) calcd for $C_{14}H_{22}O_4$ 254.1518, found: 254.1510.

*4.5.18. (3S*,5S*)-3-Benzyl-5-vinyltetrahydro-2-furanone (**33**-syn) and (3R*,5S*)-3-benzyl-5-vinyltetrahydro-2-furanone (**33**-anti).* Under nitrogen atmosphere, to a solution of compound **33**-*syn* (100 mg, 0.49 mmol) in THF (4 mL) were added $Pd(OAc)_2$ (11.0 mg, 0.049 mmol) and $Ph_3P$ (141.4 mg, 0.30 mmol) at rt. After stirring for 40 h, the reaction mixture was filtered through Celite. The filtrate was concentrated and chromatographed on the silica gel column to give a mixture of compound **33**-*syn* and **33**-*anti* in 81% mass recovery yield. Their ratio was determined by the integration of the benzylic proton ($\delta$ 3.31 for **33**-*syn*; $\delta$ 3.21 for **33**-*anti*). If the reactant of the Pd-catalyzed epimerization was **33**-*anti*, a mixture of compound **33**-*syn* and **33**-*anti* in 79% mass recovery yield.

*Compound* **33**-*syn*: TLC $R_f$=0.56 (hexane/EtOAc=4:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.18–7.32 (m, 5H), 5.80 (ddd, $J$=6.0, 10.4, and

17.2 Hz, 1H), 5.34 (d, $J$=17.2 Hz, 1H), 5.23 (d, $J$=10.4 Hz, 1H), 4.75 (dt, $J$=6.0 and 10.4 Hz, 1H), 3.31 (dd, $J$=4.0 and 13.6 Hz, 1H), 2.90–2.94 (m, 1H), 2.71 (dd, $J$=2.0 and 13.6 Hz, 1H), 2.33–2.40 (m, 1H), 1.67–1.75 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 177.8, 138.9, 136.5, 128.7, 128.4, 127.9, 120.8, 116.6, 79.7, 38.2, 37.1, 34.3; IR ($CH_2Cl_2$): 3133, 2944, 1787, 1423, 1346, 1105, 1015 cm$^{-1}$; ESI Mass ($m/z$): 225 ($M^+$+23); HRMS ($m/z$) calcd for $C_{13}H_{14}O_2Na$ 225.0891, found: 225.0890.

*Compound* **33**-*anti*: TLC $R_f$=0.53 (hexane/EtOAc=4:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.19–7.33 (m, 5H), 5.81 (ddd, $J$=5.2, 10.8, and 17.2 Hz, 1H), 5.30 (d, $J$=17.2 Hz, 1H), 5.20 (d, $J$=10.8 Hz, 1H), 4.78–4.82 (m, 1H), 3.21 (dd, $J$=4.4 and 14.0 Hz, 1H), 2.87–2.93 (m, 1H), 2.77 (dd, $J$=9.6 and 14.0 Hz, 1H), 2.13–2.21 (m, 1H), 2.02–2.09 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 178.3, 138.2, 135.5, 128.8, 128.7, 126.9, 116.8, 77.9, 40.2, 36.1, 33.0; IR ($CH_2Cl_2$): 3145, 2925, 1785, 1415, 1222, 1145, 1035 cm$^{-1}$; ESI Mass ($m/z$): 225 ($M^+$+23); HRMS ($m/z$) calcd for $C_{13}H_{14}O_2Na$ 225.0891, found: 225.0892.

*4.5.19. (4S*,5R*)-4-Phenyl-5-vinyltetrahydro-2-furanone (**35**-syn) and (4R*,5R*)-4-phenyl-5-vinyltetrahydro-2-furanone (**35**-anti).* Under nitrogen atmosphere, to a solution of compound **35**-*syn* (100 mg, 0.53 mmol) in THF (5 mL) were added $Pd(OAc)_2$ (11.9 mg, 0.053 mmol) and $Ph_3P$ (139.0 mg, 0.53 mmol) at rt. After stirring for 40 h, the reaction mixture was filtered through Celite. The filtrate was concentrated and chromatographed on the silica gel column to give a mixture of compound **35**-*syn* and **35**-*anti* in 81% mass recovery yield. Their ratio was determined by the integration of the benzylic proton ($\delta$ 3.41–3.43 for **35**-*syn*; $\delta$ 3.86–3.91 for **35**-*anti*). If the reactant of the Pd-catalyzed epimerization was **35**-*anti*, a mixture of compound **35**-*syn* and **35**-*anti* in 78% mass recovery yield.

*Compound* **35**-*anti*: TLC $R_f$=0.78 (hexane/EtOAc=4:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.24–7.39 (m, 5H), 5.90 (ddd, $J$=6.0, 7.2, and 12.8 Hz, 1H), 5.29 (dt, $J$=1.2 and 12.8 Hz, 1H), 5.25 (dt, $J$=1.2 and 6.0 Hz, 1H), 4.86 (dd, $J$=7.2 and 7.2 Hz, 1H), 3.41 (ddd, $J$=7.2, 8.8, and 10.4 Hz, 1H), 2.97 (dd, $J$=8.8 and 17.2 Hz, 1H), 2.79 (dd, $J$=10.4 and 17.2 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 175.2, 138.0, 133.8, 129.0, 127.8, 127.2, 118.6, 86.6, 47.8, 36.5; IR ($CH_2Cl_2$): 3157, 2988, 1776, 1466, 1306, 1128, 1073 cm$^{-1}$; ESI Mass ($m/z$): 211 ($M^+$+23); HRMS ($m/z$) calcd for $C_{12}H_{12}O_2Na$ 211.0735, found: 211.0733.

*Compound* **35**-*anti*: TLC $R_f$=0.75 (hexane/EtOAc=4:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.12–7.36 (m, 5H), 5.33–5.36 (m, 2H), 5.19–5.23 (m, 1H), 5.13–5.16 (m, 1H), 3.86–3.91 (m, 1H), 2.90 (dd, $J$=8.0 and 17.2 Hz, 1H), 2.83 (dd, $J$=7.6 and 17.2 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 176.2, 132.0, 128.7, 127.8, 127.6, 118.5, 83.3, 45.1, 33.9; IR ($CH_2Cl_2$): 3122, 2954, 1756, 1452, 1322, 1156, 1071 cm$^{-1}$; ESI Mass ($m/z$): 211 ($M^+$+23); HRMS ($m/z$) calcd for $C_{12}H_{12}O_2Na$ 211.0735, found: 211.0732.

*4.5.20. (4R*,5R*)-4-1-(tert-Butyl)-1,1-dimethylsilyl]oxy-5-vinyltetrahydro-2-furanone (**37**-syn) and (4S*,5R*)-4-1-(tert-butyl)-1,1-dimethylsilyl]oxy-5-vinyltetrahydro-2-furanone (**37**-anti).* Under nitrogen atmosphere, to a solution of compound **37**-*syn* (100 mg, 0.41 mmol) in THF (7 mL) were added $Pd(OAc)_2$ (9.3 mg, 0.041 mmol) and $Ph_3P$ (107.5 mg, 0.41 mmol) at rt. After stirring for 32 h, the reaction mixture was filtered through Celite. The filtrate was concentrated and chromatographed on the silica gel column to give a mixture of compound **37**-*syn* and **37**-*anti* in 81% mass recovery yield. Their ratio was determined by the integration of the vinylic proton ($\delta$ 5.86 for **37**-*syn*; $\delta$ 6.00 for **37**-*anti*). If the reactant of the Pd-catalyzed epimerization was **37**-*anti*, a mixture of compound **37**-*syn* and **37**-*anti* in 78% mass recovery yield.

*Compound* **37**-*syn*: TLC $R_f$=0.50 (hexane/EtOAc=6:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.82 (ddd, $J$=5.6, 10.8, and 17.2 Hz, 1H), 5.41 (d, $J$=17.2 Hz, 1H), 5.30 (d, $J$=10.8 Hz, 1H), 4.70–4.72 (m, 1H), 4.24 (dt, $J$=4.0 and 6.4 Hz, 1H), 2.74 (dd, $J$=6.4 and 17.6 Hz, 1H), 2.44 (dd, $J$=4.0 and 17.6 Hz, 1H), 0.88 (s, 9H), 0.03 (s, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 174.5, 132.8, 118.1, 87.4, 72.5, 37.3, 25.4, 17.8, −4.90, −4.93; IR ($CH_2Cl_2$): 3123, 2978, 1745, 1423, 1315, 1105, 1025 cm$^{-1}$; ESI Mass ($m/z$): 265 ($M^+$+23); HRMS ($m/z$) calcd for $C_{12}H_{22}O_3SiNa$ 265.1236, found: 265.1235.

*Compound* **37**-*anti*: TLC $R_f$=0.56 (hexane/EtOAc=6:1); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 5.97 (ddd, $J$=6.0, 10.4 and 16.8 Hz, 1H), 5.43 (d, $J$=16.8 Hz, 1H), 5.35 (d, $J$=10.4 Hz, 1H), 4.75–4.81 (m, 1H), 4.46–4.52 (m, 1H), 2.73 (dd, $J$=6.8 and 17.6 Hz, 1H), 2.48 (dd, $J$=4.4 and 17.6 Hz, 1H), 0.86 (s, 9H), 0.01 (s, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 173.6, 132.8, 120.8, 79.7, 73.4, 36.5, 27.5, 19.4, −4.3, −4.5; IR ($CH_2Cl_2$): 3138, 2945, 1758, 1333, 1325, 1145, 1075 cm$^{-1}$; ESI Mass ($m/z$): 265 ($M^+$+23); HRMS ($m/z$) calcd for $C_{12}H_{22}O_3SiNa$ 265.1236, found: 265.1235.

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