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An Enantioselective Approach to 4-*O*-Protected-2-cyclopentene-l,4-diol Derivatives via a Rhodium-Catalyzed Redox-Isomerization Reaction

Kai Ren,[†] Mengmeng Zhao,[†] Bei Hu,[†] Bin Lu,[†] Xiaomin Xie,[†] Virginie Ratovelomanana-Vidal,*[,§] and Zhaoguo Zhang*[,†,‡]

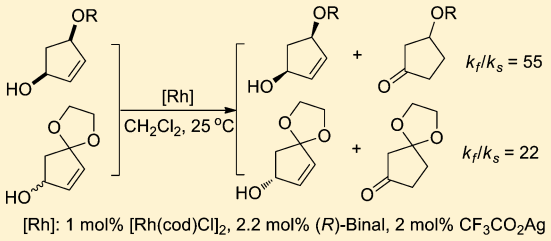
[†]School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P. R. China

[‡]State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, 345 Lingling Road, Shanghai 200032, P. R. China

[§]PSL Research University, Chimie ParisTech-CNRS, Institut de Recherche de Chimie Paris, 75005 Paris, France

Supporting Information

ABSTRACT: Kinetic resolution of a series of cyclopentene-1,4-diol derivatives has been successfully achieved with enantiomeric excess up to 99.4% and a k_f/k_s ratio of 55 by a rhodium-catalyzed redox-isomerization reaction in a noncoordinating solvent.



INTRODUCTION

Optically active cyclopentene-1,4-diol derivatives represent compounds of fundamental biological importance found at the core of many natural products and pharmaceutically active molecules,[4] such as Noraristeromvcin,[1] Prostacyclins,[2] and the HIV protease inhibitor GRL-06579[3] (Figure 1).

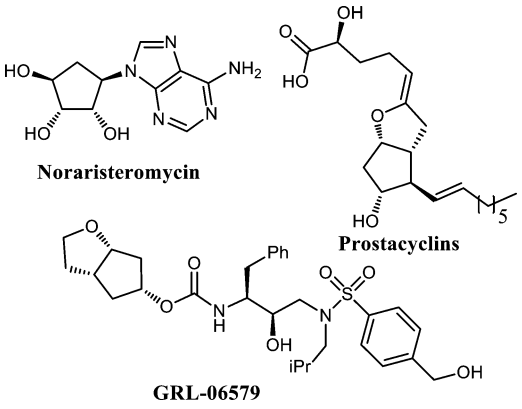


Figure 1. Examples of chiral 2-cyclopentene-1,4-diols in drugs.

Therefore, it is of considerable interest to develop efficient routes to such relevant building blocks, minimizing the number of synthetic steps while maximizing the overall chemical and optical yields. Among a number of asymmetric approaches to cyclopentene-1,4-diols, utilization of the chiral pool and chiral reagents or catalysts has been reported.[8] To date, the most commonly employed synthetic routes for the preparation of enantiomerically pure *cis*-cyclopentene-1,4-diol derivatives rely on desymmetrization of *meso*-2-cyclopentene-l,4-diol[5] or *meso*-cyclopentene-l,4-diacetates[6] and enzymatic resolution of 4-acetoxy-cyclopentenone.[7] Although these protocols have been proven straightforward, there are some drawbacks, including the need for expensive reagents, the use of complicated reaction apparatus, and/or the challenge of scaling up.

The transition metal-catalyzed isomerization of allylic alcohols is an efficient way of generating saturated carbonyl compounds and therefore represents an atom-economical and elegant shortcut to valuable carbonyl compounds.[9] Various transition metals, such as Rh,[10] Ru,[11] Ir,[12] Ni,[13] and Fe,[14] have been employed for this transformation. Among them, the asymmetric isomerization of allylic alcohols has attracted much attention in recent years. Such transformations can be divided into two categories: (1) a primary allylic alcohol possessing two different substituents at the 3-position that can be converted into an enantioenriched aldehyde with a newly created stereogenic center at the β-position,[15] and (2) one enantiomer of the racemic allylic alcohol that is selectively converted to a saturated ketone, leaving the other isomer enantiomerically enriched by way of a kinetic resolution,[16] which is an alternative synthetic method of enantiomerically allylic alcohol. Herein, we describe an efficient procedure for the kinetic resolution of cyclic secondary allylic alcohols through an isomerization reaction.

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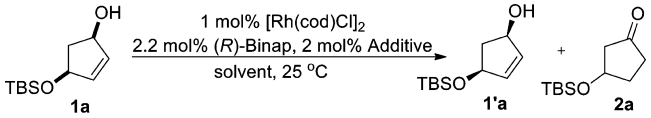
RESULTS AND DISCUSSION

Recently, we studied the kinetic resolution of allylic alcohols catalyzed by the Rh/BINAP system in a noncoordinating solvent.[16a] A series of enantiomerically pure aromatic and aliphatic allylic alcohols were effectively resolved with k_f/k_s ratios up to 24 at 20 °C. The tremendous importance of chiral cyclopentene-1,4-diol derivatives prompted us to explore the kinetic resolution method to obtain the enantiomerically pure compounds. However, when *cis*-cyclopentene-1,4-diol was treated under our standard reaction conditions, no conversion was observed even after 24 h. We hypothesized that intramolecular hydrogen bonding in the *cis*-cyclopentene-1,4-diol led to the inactivation of the substrate. In this context, we envisioned that if the kinetic resolution of *cis*-cyclopentene-1,4-diol through redox-isomerization could be successfully performed using a protected OH group it would provide complementary access to the chiral *cis*-cyclopentene-1,4-diol derivatives. *cis*-4-*t*-Butyldimethylsilyloxy-2-cyclopentenol **1a** was chosen as a model substrate to determine the optimal reaction conditions. To our delight, when the noncoordinating solvent CH_2Cl_2 was used, 55% conversion and 98.7% ee of the remaining enantiomer were obtained with a k_f/k_s {k_f/k_s = ln[(1 − C)(1 − ee)]/ln[(1 − C)(1 + ee)]}[17] ratio of 46 after 4 h at room temperature (Table 1, entry 1). On the basis of this result, additional noncoordinating solvents, such as $CHCl_3$, DCE, and toluene, were investigated with k_f/k_s ratios of 21−44 (Table 1, entries 2−4). Moreover, when the coordinating solvent THF was used instead of noncoordinating solvents, the reactivity and enantioselectivity decreased significantly (50% conversion in 33 h, 49.4% ee of the remaining isomer; Table 1, entry 5). No conversion of the starting material was detected when the reaction was carried out in EtOH, *i*-PrOH, or in CF_3CH_2OH (Table 1, entries 6−8).

Table 1. Optimization of the Solvents and Counterions for the Resolution of *cis*-4-*t*-Butyldimethylsilyloxy-2-cyclopentenol[a]



1a 1'a 2a

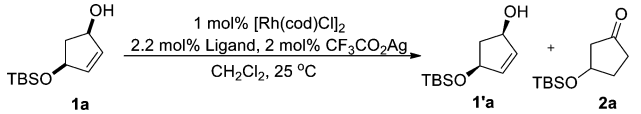
entry	solvent	additive	*T* [h]	conv. [%][b]	ee (**1'a**) [%][c]	k_f/k_s[d]
1	CH_2Cl_2	CF_3CO_2Ag	4	55	98.7 (43)	46
2	toluene	CF_3CO_2Ag	6	50	79.1 (49)	21
3	CH_2ClCH_2Cl	CF_3CO_2Ag	4	51	88.8 (46)	38
4	$CHCl_3$	CF_3CO_2Ag	4	54	97.0 (45)	44
5	THF	CF_3CO_2Ag	33	50	49.4 (47)	5
6	EtOH	CF_3CO_2Ag	12	0	0	0
7	CF_3CH_2OH	CF_3CO_2Ag	12	0	0	0
8	*i*-PrOH	CF_3CO_2Ag	12	0	0	0
9	CH_2Cl_2	$AgClO_4$	3	51	87.4 (47)	33
10	CH_2Cl_2	$AgBF_4$	3	50	84.2 (48)	31
11	CH_2Cl_2	Na[BArF]	2	52	89.2 (45)	31
12	CH_2Cl_2	CH_3CO_2Ag	24	53	93.8 (45)	38

[a]All reactions were carried out with *cis*-4-*t*-butyldimethylsilyloxy-2-cyclopentenol (**1a**) (134 mg, 1.0 mmol) in 4 mL of solvent at 25 °C with 100:1:2.2:2 of **1a**/[Rh(cod)Cl]$_2$/(*R*)-Binap/additive. [b]Measured by GC with durene as the internal standard. [c]Values of ee were determined by GC on a Gamma Dex 120 column. In parentheses is the isolated yield of the corresponding alcohol (**1a'**). [d]k_f/k_s = ln[(1 − C)(1 − ee)]/ln[(1 − C)(1 + ee)].

Next, several counterions were investigated for the isomerization reaction. Counterions such as BF_4^-, ClO_4^-, and [BArF]$^-$ [tetrakis(3,5-bis(trifluoromethyl)phenyl borate] were examined, leading to a slight improvement of the reaction rate with an obvious decrease in the k_f/k_s ratios (Table 1, entries 9−11). Changing the counterion to the weakly coordinating OAc^- ion, the reaction rate decreased remarkably (Table 1, entry 12). When no additive was added, no conversion was observed.

Subsequently, a series of atropisomeric biaryl diphosphine ligands was screened for the kinetic resolution. The results are summarized in Table 2. When (*S*)-SunPhos, (*S*)-SegPhos, and (*R*)-SynPhos (**L2**−**L4**) were used for the transformation, the selectivity factors (k_f/k_s) decreased remarkably to as low as 3−5 (Table 2, entries 1−3). However, no reaction occurred after 12 h, when ligand **L5**, possessing an electron-withdrawing substituent on the aryl moiety of the phosphorus atom, was used (Table 2, entry 4). The enantioselectivity was not remarkably affected, but the reaction time could be shortened from 4 to 2 h when the reaction was conducted at 45 °C (Table 2, entry 7). No reaction occurred when the reaction was carried out at 0 °C (Table 2, entry 8). Furthermore, the effects of substrate concentration and reaction temperature were also investigated. A higher concentration (0.5 M) led to a significant decrease of the k_f/k_s ratio to 28 (Table 2, entry 9). Nevertheless, no conspicuous improvement of the k_f/k_s value

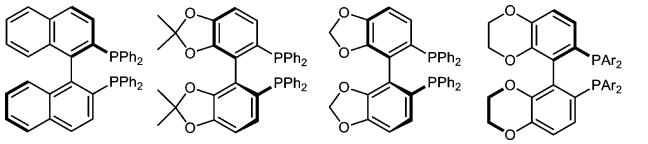
Table 2. Optimization of the Ligands and Temperature for the Resolution of *cis*-4-*t*-Butyldimethylsilyloxy-2-cyclopentenol[a]



1a 1'a 2a

entry	ligand	*T* [h]	conv. [%][b]	ee (**1'a**) [%][c]	k_f/k_s[d]
1	**L2**	3	62	−59.8 (35)	4
2	**L3**	3	65	−52.6 (32)	3
3	**L4**	2	50	49.5 (47)	5
4	**L5**	12	0	0	0
7[e]	**L1**	2	53	93.2 (45)	45
8[f]	**L1**	12	0	0	0
9[g]	**L1**	2	50	83.0 (48)	28
10[h]	**L1**	5	54	97.5 (44)	47

[a]All reactions were carried out with *cis*-4-*t*-butyldimethylsilyloxy-2-cyclopentenol (**1a**) (134 mg, 1.0 mmol) in 4 mL of solvent at 25 °C with 100:1:2.2:2 of **1a**/[Rh(cod)Cl]$_2$/Ligand/CF_3CO_2Ag. [b]Measured by GC with durene as the internal standard. [c]Values of ee were determined by GC on a Gamma Dex 120 column. In parentheses is the isolated yield of the corresponding alcohol (**1a'**). [d]k_f/k_s = ln[(1 − C)(1 − ee)]/ln[(1 − C)(1 + ee)]. [e]Reaction temperature of 45 °C. [f]Reaction temperature of 0 °C. [g]Substrate concentration = 0.5 M. [h]Substrate concentration = 0.125 M.



(*R*)-Binap **L1** (*S*)-SunPhos **L2** (*S*)-SegPhos **L3** (*R*)-SynPhos **L4**

(*R*)-*p*-CF_3-SynPhos **L5**

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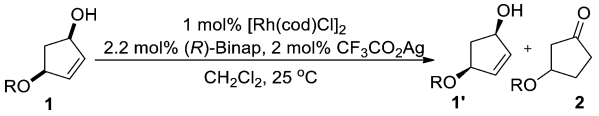
was observed when the substrate concentration was decreased from 0.25 to 0.125 M (Table 2, entry 10).

On the basis of these results, the optimized reaction conditions were therefore set as the following: 1 mol % of $[Rh(cod)Cl]_2$/(*R*)-Binap/CF_3CO_2Ag as the catalyst, CH_2Cl_2 as the solvent with a substrate concentration of 0.25 M, and room temperature (25 °C).

For the flexibility of the method to be demonstrated, the kinetic resolution of a series of 4-substituted-2-cyclopentenol derivatives was studied under the optimized reaction conditions. A wide range of silyl-substituted derivatives was tested for the kinetic resolution, providing excellent enantioselectivities of 97.0−99.4% ee (k_f/k_s = 44−55) with 54−55% of conversion in a short reaction time (Table 3, entries 1−3). For

Table 3. Kinetic Resolution of 4-*O*-Protected-2-cyclopentene-l,4-diols[a]



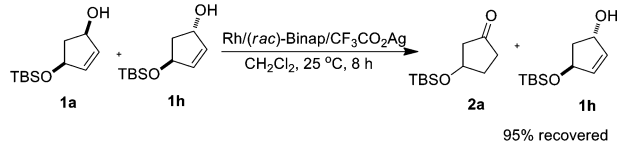
entry	R	*T* [h]	conv. [%][b]	ee (**1′**) [%][c]	k_f/k_s[d]
1	TBS (**1a**)	4	55	98.7 (43)	46
2	TIPS (**1b**)	4	54	97.0 (43)	44
3	TBDPS (**1c**)	4	55	99.4 (43)	55
4	Bn (**1d**)	3	55	94.6 (43)	28
5	CPh_3 (**1e**)	6	52	93.0 (47)	44
6	Ac (**1f**)	12	0	0	0
7	Bz (**1g**)	12	53	85.6 (46)	20
8[e]	TBS (**1a**)	4	55	99.2 (44)	52
9[f]	TBS (**1h**)	24	51	81.1 (47)	20

[a]All reactions were carried out with a substrate (2.0 mmol) concentration of 0.25 M in CH_2Cl_2 at 25 °C, $[Rh(cod)Cl]_2$ (9.9 mg, 0.02 mmol), (*R*)-Binap (27.4 mg, 0.044 mmol), and CF_3CO_2Ag (8.8 mg, 0.04 mmol). [b]Conversions were measured by GC using durene as an internal standard. [c]Values of ee were determined by chiral HPLC or GC. Isolated yield of the corresponding alcohol (**1′**). [d]k_f/k_s = ln[(1 − C)(1 − ee)]/ln[(1 − C)(1 + ee)]. [e]Run at 50 mmol scale. [f]*trans*-4-*t*-Butyldimethylsilyloxy-2-cyclopentenol was used.

the alkyl-substituted derivatives, the steric hindrance showed an obvious influence on both the reactivity and enantioselectivity. For instance, the chiral alcohol **1′d** was recovered in 45% yield and 94.6% ee with a k_f/k_s ratio of 28 after 3 h, whereas substrate **1e** (R = CPh_3) reacted very slowly to give a k_f/k_s ratio of 44 (Table 3, entries 4 and 5). Meanwhile, *O*-acyl-substituted derivatives were also investigated (Table 3, entries 6 and 7). When the *O*-benzoyl-substituted derivative (**1g**) was employed, the desired product (**1′g**) was recovered in 47% yield with 85.6% ee after 12 h (Table 3, entry 7). However, no trace of the corresponding ketone **1f** was isolated, and the starting material was recovered quantitatively (Table 3, entry 6). When **1a** and **1f** (1:1) were mixed under the same conditions, a rapid isomerization of **1a** was detected, whereas **1f** was inert toward isomerization. The result showed that the purity of **1f** had no effect and was inert toward isomerization. Pleasingly, the reaction could be successfully scaled up to 50 mmol scale with slightly improved results (Table 3, entry 8). However, the catalytic system was sensitive toward steric hindrance of the double bond; 2-bromo-4-[(*t*-butyldimethylsilyl)oxy]cyclopent-2-enol was essentially inert under the reaction conditions. Furthermore, when the kinetic resolution of **1a** was reacted for 3 h at the optimized conditions, the corresponding ketone (**2a**) was obtained in 45% yield and 98.0% ee.

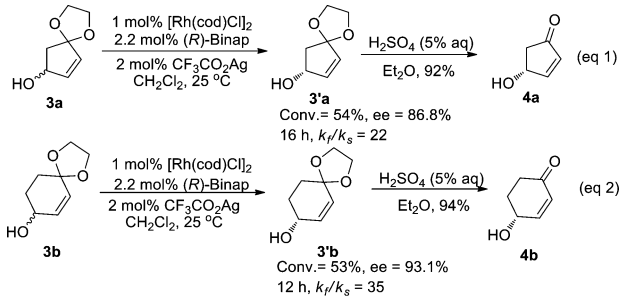
Additionally, for *trans*-*O*-protected-cyclopentene-1,4-diol (**1h**), the reactivity and enantioselectivity significantly decreased in the redox-isomerization. As a result, enantiomerically enriched **1′h** with a ee of 81.1% was recovered in 49% yield after 24 h, and the k_f/k_s value dropped to 20 (Table 3, entry 9). When a mixture of *cis*-(**1a**) and *trans*-(**1h**) were used with (*rac*)-Binap as ligand, **1a** was rapidly isomerized, and **1h** was recovered (95%) after 8 h (Scheme 1).

Scheme 1. Redox Isomerization of 1a in the Presence of 1h



Optically active 4-hydroxy-2-cyclopentenone (**4a**) is the key framework for the synthesis of biorelevant targets, such as prostaglandins, pentenomycin antibiotics, and ophiobolins.[18] However, when 4-hydroxy-2-cyclopentenone was treated under the optimized reaction conditions, the starting material remained essentially intact even after 24 h, and only traces of cyclopent-4-ene-1,3-dione, resulting from β-hydride elimination of the allylic alcohol, were detected. We have demonstrated in our previous report that the isomerization intermediate of cyclopent-4-ene-1,3-dione strongly coordinated Rh^I, forming a stable complex that inhibited the activity of the Rh catalyst.[16a] For this issue to be circumvented, the generation of cyclopent-4-ene-1,3-dione must be avoided. Consequently, we tried to perform the kinetic resolution of 4-hydroxy-2-cyclopentenone through redox-isomerization by protecting the carbonyl group with ethylene glycol. Gratifyingly, using the ketal derivative **3a** as the starting material, the desired product (*R*)-**3′a** was recovered in 46% yield and 86.8% ee with a k_f/k_s ratio of 22 after 16 h and (*R*)-**3′a** in 39% yield and 99.2% ee after prolonging the reaction time to 24 h (Scheme 2, eq 1). A

Scheme 2. Kinetic Resolution of 3a and 3b



further investigation of the kinetic resolution of 1,4-dioxaspiro[4.5]dec-6-en-8-ol (**3b**) was also pursued. Although the reaction proceeded at a slightly lower rate, (*R*)-**3′b** was recovered after 12 h with 53% yield and 93.1% ee and a k_f/k_s value of 35, providing straightforward access to the optically active 4-hydroxycyclohex-2-en-1-one (**4b**) (Scheme 2, eq 2), which is a useful structural unit in many pharmaceutically active compounds and important building blocks for the asymmetric synthesis of natural products.[19]

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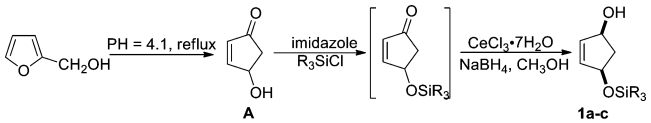
CONCLUSIONS

In summary, we have demonstrated a successful kinetic resolution of *mono*-*O*-protected-cyclopentene-1,4-diol derivatives via rhodium-catalyzed redox-isomerization in a non-coordinating solvent. A series of 4-substituted-cyclopentene-1,4-diol derivatives, which are employed as key intermediates for the synthesis of prostaglandins and natural products, were efficiently recovered with up to 99.4% ee in short reaction times and mild conditions, allowing the efficient multigram scale production of 4-substituted-cyclopentene-1,4-diol derivatives.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques or in a nitrogen-filled glovebox unless otherwise noted. Commercially available reagents were used throughout without further purification other than those detailed below. Anhydrous EtOH and CF_3CH_2OH were freshly distilled from Mg. Anhydrous CH_2ClCH_2Cl, $CHCl_3$, and CH_2Cl_2 were freshly distilled from CaH_2. Anhydrous toluene and THF were freshly distilled from Na/benzophenone. Anhydrous acetone was freshly distilled from $CaSO_4$. ^{1}H NMR spectra were recorded at 400 MHz with TMS as the internal standard. ^{13}C {^{1}H} NMR spectra were recorded at 100 MHz and referenced to the central peak of 77.00 ppm for $CDCl_3$. Coupling constants (J) are reported in Hz and refer to apparent peak multiplications. Analytical GC was performed on an FID detector. HRMS were obtained on an ESI-TOF mass spectrometer. Flash column chromatography was performed on silica gel (300−400 mesh). The $[\alpha]_D$ values are given in deg cm^2 g^{-1} and were recorded at the $_D$ line of sodium (589 nm) in a 0.5 dm cell.

General Procedure for the Synthesis of Compounds 1a, 1b, 1c, and 1h.[20]



Furfuryl alcohol (30.0 g, 306.0 mmol) was dissolved in water (1000 mL), and the solution was degassed prior to the addition of hydroquinone (0.4 g, 3.7 mmol) and sodium dihydrogen orthophosphate (1.6 g, 10.5 mmol). The pH of the solution was adjusted to 4.1 using orthophosphoric acid before the reaction mixture was heated under reflux under N_2 for 48 h. The formed brown oil was dispersed with 1,4-dioxane (200 mL). After a further 24 h, the reaction mixture was allowed to cool to room temperature and extracted with toluene (3 × 100 mL). The remaining aqueous phase was concentrated to 150 mL and extracted with ethyl acetate (6 × 100 mL), dried ($NaSO_4$), and concentrated to give crude brown oil **A** (10.5 g, 35% yield), which is also commercially available. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, J = 5.6, 2.4 Hz, 1H), 6.10 (dd, J = 5.6, 0.8 Hz, 1H), 4.94−4.88 (m, 1H), 4.13 (br, 1H), 2.64 (dd, J = 18.4, 6.0 Hz, 1H), 2.15 (dd, J = 18.4, 6.4 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 207.4, 164.0, 134.7, 70.1, 44.1.

To a solution of **A** (980.0 mg, 10.0 mmol) in CH_2Cl_2 (20 mL) were added imidazole (817.0 mg, 12.0 mmol) and TBSCl, TIPSCl, or TBDPSCl (10.0 mmol), and the reaction mixture was stirred at room temperature overnight. Saturated $NaHCO_3$ was added to the solution, and the resulting mixture was extracted with EtOAc three times. The combined extracts were dried over Na_2SO_4 and concentrated to afford the corresponding ether. $CeCl_3{\cdot}7H_2O$ (3.0 g, 8.0 mmol) was dissolved in 20 mL of methanol. Then, the corresponding ether (8.0 mmol) was introduced. After 5 min of vigorous stirring, 0.31 g (8.0 mmol) of sodium borohydride was carefully added portionwise at −15 °C, and the resulting heterogeneous mixture was stirred for 15 min at room temperature. Saturated aqueous NH_4Cl was added dropwise until a clear solution was obtained, and then the mixture was extracted with diethyl ether (3 × 20 mL). The organic layers were combined and dried over Na_2SO_4, and the solvents were removed under vacuum. The residue (*cis*-**1a**:*trans*-**1h** = 85:15 detected by GC) was purified by flash chromatography on silica gel to afford the corresponding alcohols **1a** (1.1 g, 61%), **1h** (0.2 g, 10%), **1b** (1.3 g, 65%), and **1c** (1.9 g, 70%).

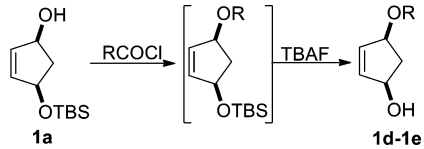
*cis-4-(t-Butyldimethylsilanyloxy)-cyclopent-2-en-1-ol (**1a**).*[20] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95−5.93 (m, 1H), 5.90−5.86 (m, 1H), 4.67−4.64 (m, 1H), 4.60−4.53 (m, 1H), 2.72−2.65 (m, 1H), 1.51 (dd, J = 13.6, 4.4 Hz, 1H), 0.89 (s, 9H), 0.08 (s, 6H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.4, 135.7, 75.2, 74.8, 44.4, 25.8, 18.1, −4.7, −4.8.

*cis-4-Triisopropylsilyloxy-1-hydroxycyclopent-2-ene (**1b**).*[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95−5.93 (m, 2H), 4.75−4.72 (m, 1H), 4.59−4.57 (m, 1H), 2.71 (dt, J = 14.0, 7.2 Hz, 1H), 1.77 (br, 1H), 1.57 (dt, J = 13.6, 4.4 Hz, 1H), 1.09−1.05 (m, 21H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.7, 135.6, 75.1, 74.8, 44.8, 17.9, 12.0.

*cis-4-((t-Butyldiphenylsilanyloxy)cyclopent-2-enol (**1c**).*[24] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.65 (m, 4H), 7.45−7.37 (m, 6H), 5.91−5.87 (m, 1H), 5.84−5.81 (m, 1H), 4.66−4.61 (m, 1H), 4.54−4.51 (m, 1H), 2.54 (dt, J = 13.8, 6.8, 1H), 1.66 (dt, J = 14.0, 4.8 Hz, 1H), 1.55 (br, 1H), 1.06 (s, 9H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.7, 135.7, 135.6, 134.0, 129.7, 127.6, 76.0, 74.9, 44.4, 26.9, 19.0.

*trans-4-(t-Butyldimethylsilanyloxy)cyclopent-2-en-1-ol (**1h**).*[29] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97−5.91 (m, 2H), 5.10−4.98 (m, 2H), 2.09−1.98 (m, 2H), 1.65 (br, 1H), 0.88 (s, 9H), 0.07 (s, 6H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.0, 135.5, 76.6, 75.9, 44.2, 25.8, 18.2, −4.7.

General Procedure for the Synthesis of Compounds 1d and 1e.

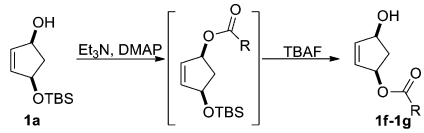


In a 25-ml flask was dissolved *cis*-4-(*t*-butyldimethylsilanyloxy)-cyclopent-2-en-1-ol (2.1 g, 10.0 mmol) in 15 mL of THF, and then sodium hydride (0.4 g, 10 mmol, 1.0 equiv) (60% dispersion in mineral oil) was added under N_2 at 0 °C. The reaction mixture was allowed to warm to rt and stirred for 30 min. Next, benzyl bromide or triphenylmethyl chloride (11.0 mmol) was added and stirring was continued for 90 min. The reaction mixture was cooled back to −10 °C and quenched with saturated aqueous NH_4Cl (40.0 mL) followed by the addition of ether (60.0 mL). The organic phase was washed with saline, dried over anhydrous sodium sulfate, and removed the solvent under reduced pressure. The crude product was dissolved in THF, and then triethylamine was added at rt followed by dropwise addition of TBAF solution. The reaction mixture was stirred until the reaction had been completed. The solvent was removed in vacuo to give a brown oil, which was purified by silica-gel column chromatography, giving **1d** (1.5 g, 80%) and **1f** (2.9 g, 85%).

*cis-4-(Benzyloxy)cyclopent-2-enol (**1d**).*[26] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.26 (m, 5H), 6.04 (s, 2H), 4.63 (br, 1H), 4.56 (q, J = 11.6 Hz, 2H), 4.44 (dd, J = 6.8, 4.0 Hz, 1H), 2.66 (dt, J = 10.4, 3.6 Hz, 1H), 1.67 (dt, J = 14.0, 4.0 Hz, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.0, 137.2, 133.4, 128.2, 127.7, 127.5, 81.4, 74.4, 70.8, 40.5.

*cis-4-(Trityloxy)cyclopent-2-enol (**1e**).*[22] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.53 (m, 6H), 7.34−7.22 (m, 9H), 5.79 (d, J = 5.6 Hz, 1H), 5.15 (d, J = 5.6 Hz, 1H), 4.49−4.46 (m, 1H), 4.39−4.36 (m, 1H), 2.27−2.20 (m, 1H), 1.68 (br, 1H), 1.46−1.40 (m, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.7, 136.0, 135.2, 128.7, 127.8, 127.0, 87.4, 77.1, 74.4, 42.7.

General Procedure for the Synthesis of Compounds 1f and 1g.



In a 25-ml flask was dissolved *cis*-4-(*t*-butyldimethylsilanyloxy)-cyclopent-2-en-1-ol (2.1 g, 10.0 mmol) in 15 mL of CH_2Cl_2, and

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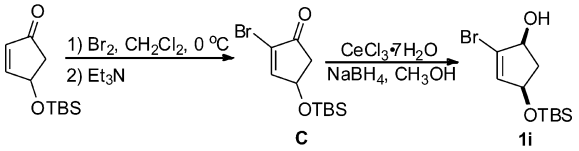
then triethylamine (1.2 g, 12.0 mol, 1.2 equiv) and DMAP (0.06 g, 0.5 mmol, 0.05 equiv) were added under N_2 at rt. Then, acyl chloride (11.0 mmol) was added and stirred overnight. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (40.0 mL) followed by the addition of ether (60.0 mL). The organic phase was washed with brine and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The crude product was dissolved in THF, and triethylamine was added at rt followed by dropwise addition of TBAF solution. The reaction mixture was stirred until the reaction had been completed. The solvent was removed in vacuo to give a brown oil, which was purified by silica-gel column chromatography, giving **1f** (1.0 g, 70%) and **1g** (1.5 g, 75%).

*cis-4-Hydroxycyclopent-2-en-1-yl Acetate (**1f**).*[22] ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13−6.09 (m, 1H), 5.99−5.97 (m, 1H), 5.52−5.47 (m, 1H), 4.76−4.71 (m, 1H), 2.80 (dt, J = 14.6, 7.4 Hz, 1H), 2.05 (s, 3H), 1.80 (br, 1H), 1.71−1.59 (m, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.2, 138.8, 132.3, 74.5, 40.5, 21.3.

*cis-4-Hydroxycyclopent-2-en-1-yl Benzoate (**1g**).*[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−8.00 (m, 2H), 7.56−7.51 (m, 1H), 7.44−7.38 (m, 2H), 6.14−6.13 (m, 1H), 6.09−6.07 (m, 1H), 5.75−5.70 (m, 1H), 4.77 (s, 1H), 2.92 (dt, J = 14.8, 7.6 Hz, 1H), 2.40 (br, 1H), 1.80 (dt, J = 14.8, 4.0 Hz, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.3, 138.6, 133.0, 132.4, 130.0, 129.5, 128.3, 77.6, 74.8, 40.6.

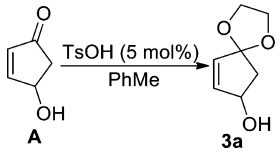
Preparation of *cis*-2-Bromo-4-((*t*-butyldimethylsilyl)oxy)-cyclopent-2-enol (1i).[36]



Bromine (1.4 mL, 27.1 mmol) was added dropwise at 0 °C to a solution of 4-((*t*-butyldimethylsilyl)oxy)cyclopent-2-enone (5.3 g, 25.0 mmol) in CH_2Cl_2 (250.0 mL). After 30 min, triethylamine (5.2 mL, 37.4 mmol) was added, and the reaction was stirred for 1 h at 0 °C. The reaction mixture was washed with water (100.0 mL) and brine (100.0 mL), dried, and concentrated. **C** was obtained as a colorless oil (4.8 g, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 2.4 Hz, 1H), 4.94−4.92 (m, 1H), 2.87 (dd, J = 18.4, 6.0 Hz, 1H), 2.42−2.33 (m, 1H), 0.93(s, 9H), 0.12 (s, 6H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 198.0, 161.1, 127.6, 69.5, 43.6, 25.6, 18.0, −4.8.

$CeCl_3$·7H_2O (6.0 g, 16.5 mmol) was dissolved in 20 mL of methanol. Then, the above product (4.4 g, 15.0 mmol) was introduced. After 5 min of vigorous stirring, sodium borohydride (0.76 g, 20.0 mmol) was carefully added portionwise at −15 °C, and the resulting heterogeneous mixture was stirred for 15 min at room temperature. Saturated aqueous NH_4Cl was added dropwise until a clear solution was obtained, and then the mixture was extracted with diethyl ether (3 × 20 mL). The organic layers were collected and dried over Na_2SO_4, and the solvents were removed under vacuum. Purification of the residue by flash chromatography on silica gel provided **1i** as a yellow oil (2.9 g, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (d, J = 1.2 Hz, 1H), 4.61 (m, 1H), 4.46 (m, 1H), 2.82−2.74 (m, 1H), 2.22 (d, J = 7.2 Hz, 1H), 1.75−1.67 (m, 1H), 0.88 (s, 9H), 0.08 (s, 6H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.1, 130.3, 76.7, 73.3, 42.6, 25.6, 18.0, −3.6.

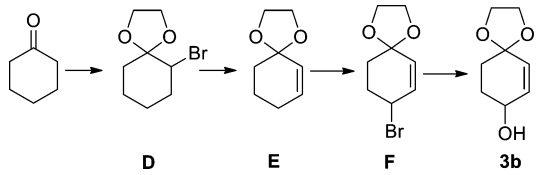
Preparation of Substrate (3a).



A mixture of 4-hydroxyl-cyclopentenone (**A**) (2.0 g, 20.0 mmol), ethylene glycol (2.5 g, 40.0 mmol), and *p*-toluenesolfonic acid (182.0 mg, 1.0 mmol) in toluene (50.0 mL) was heated under reflux with a Dean−Stark apparatus for 5 h. After **A** was completely consumed, toluene was evaporated under vacum followed by the addition of saturated aqueous $NaHCO_3$ solution (20.0 mL), and then the reaction mixture was extracted with ethyl acetate (50.0 mL × 2). The ethyl acetate layer was washed with brine (30.0 mL), dried over anhydrous Na_2SO_4, and concentrated in a vacuum to give crude **3a**. Purification of the residue by flash chromatography on silica gel provided **3a** as a yellow oil (2.1 g, 75% yield).

*1,4-Dioxaspiro[4.4]non-8-en-7-ol (**3a**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (dd, J = 5.6, 2.0 Hz, 1H), 5.83 (dd, J = 5.6, 0.8 Hz, 1H), 4.78 (br, 1H), 3.97−3.92 (m, 4H), 2.49 (dd, J = 14.4, 5.6 Hz, 1H), 1.89 (dd, J = 14.4, 3.6 Hz, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 139.4, 132.2, 117.3, 72.7, 64.6, 64.3, 44.8. HRMS-ESI (m/z): calcd for $[C_7H_{10}O_3Na]^+$, 165.0528; found, 165.0547.

Preparation of Substrate (3b).[30]



Bromine (64.0 g, 400.5 mmol) was added dropwise at 15−20 °C to a solution of cyclohexanone (39.2 g, 400.0 mmol) in ethylene glycol (500.0 mL). Then, the reaction mixture was poured into a stirred mixture of Na_2CO_3 (100.0 g) and 400.0 mL of petroleum ether. After stirring for several minutes, approximately 500 mL of water was added; the organic phase was separated and dried, and the solvent was removed under reduce pressure to give **D**.

Crude product **D** was dissolved in DMSO (200.0 mL), and sodium methoxide (64.8 g, 1.2 mol) was added. Then, the reaction mixture was stirred at 50 °C for 5 h. The reaction mixture was poured into 400.0 mL brine, and the residue was extracted with petroleum ether (3 × 400.0 mL). The extracts were combined and dried, and the solvent was evaporated under atmospheric pressure to give crude product **E**.

Crude product **E** (10.0 g, 80.0 mmol) was dissolved in CCl_4 (100.0 mL), and *N*-bromosuccinimide (14.2 g, 80.0 mmol), azobis-(isobutyronitri1e) (0.4 g, 3.2 mmol), and 2,6-lutidine (0.8 g, 8.0 mmol) were added. Next, the mixture was stirred at reflux for 30 min under the irradiation of a high pressure mercury lamp. After the solution was cooled, the solid was filtered with suction, and the filtrate was concentrated under a vacuum. Purification of the residue by flash chromatography on silica gel provided **F** (15.3 g, 94%) as a yellow oil.

F was dissolved in the mixture of dioxane and water (200.0 mL, V/V (1:1), and then K_2CO_3 (19.3 g, 140.0 mmol) was added. The reaction mixture was stirred at 90 °C for 12 h. The reaction mixture was poured into 100 mL of saline, and the product was extracted with EtOAc (3 × 400.0 mL). The organic layers were combined and dried over anhydrous Na_2SO_4, and the solvents were removed under vacuum. Purification of the residue by flash chromatography on silica gel provided yellow oil **3b** (11.4 g, 97% yield).

*1,4-Dioxaspiro[4.5]dec-6-en-8-ol (**3b**).*[30] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94−5.92 (m, 1H), 5.62 (dt, J = 12.0, 4.0 Hz, 1H), 4.20 (br, 1H), 4.01−3.90 (m, 4H), 2.14−2.06 (m, 1H), 1.97−1.93 (m, 1H), 1.79−1.64 (m, 4H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 135.3, 128.6, 105.0, 65.6, 64.5, 64.4, 30.9, 30.4.

A Typical Procedure for Redox Isomerization Kinetic Resolution of Allylic Alcohols. In a dried Schlenk tube, $[Rh(cod)Cl]_2$ (9.9 mg, 20.0 μmol), (*R*)-Binap (27.4 mg, 44.0 μmol), and durene (20.0 mg, an internal standard) were dissolved in CH_2Cl_2 (8.0 mL); then, 2 mmol of substrate was added to the solution at room temperature under nitrogen. After stirring for 1 min, CF_3CO_2Ag (8.8 mg, 40.0 μmol) was added to the mixture. The solution was stirred at 25 °C under nitrogen and monitored by gas chromatography or HPLC to determine the conversion and ee values. After the solvent was evaporated, the residue was purified by chromatography, using EtOAc/hexane (20/80) as the eluent to afford the product.

*(1R,4S)-4-(t-Butyldimethylsilanyloxy)cyclopent-2-en-1-ol (**1′a**).* Colorless oil, 43% yield (184 mg), 98.7% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those of **1a**. The enantiomeric excess (**1′a**) was determined by GC analysis: Gamma Dex 120 capillary column, 0.25 mm × 30 m. Column temperature = 105 °C (isothermal); inject temperature = 220 °C; detector temperature = 220 °C. Flow = 1.5

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mL/min; t_R = 32.1 min (major), 34.0 min (minor). $[\alpha]_D^{20}$ −24.4 (*c* 1.53, $CHCl_3$); lit.[21] $[\alpha]_D^{20}$ −24.5 (*c* 1.52, $CHCl_3$) for the (1*R*,4*S*) isomer.

*3-((t-Butyldimethylsilyl)oxy)cyclopentanone (**2a**).*[22] Colorless oil, 53% yield (226 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52−4.49 (m, 1H), 2.45−2.28 (m, 2H), 2.20−1.83 (m,5H), 0.84 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 217.4, 70.0, 48.1, 35.4, 32.6, 25.5, 17.8, −5.0, −5.1.

*(1R,4S)-4-Triisopropylsilyloxy-1-hydroxycyclopent-2-ene (**1′b**).* Colorless oil, 43% yield (220 mg), 97.0% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those of **1b**. The enantiomeric excess (**1′b**) was determined by GC analysis: Alpha Dex 120 capillary column, 0.25 mm × 30 m; column temperature = 135 °C (isothermal); inject temperature = 220 °C; detector temperature = 220 °C. Flow = 1.0 mL/min; t_R = 48.3 min (minor), 50.0 min (major). $[\alpha]_D^{20}$ −18.0 (*c* 0.71, MeOH); lit.[23] $[\alpha]_D^{20}$ −19.4 (*c* 0.50, MeOH) for the (1*R*,4*S*) isomer.

*3-((Triisopropylsilyl)oxy)cyclopentanone (**2b**).* Colorless oil, 52% yield (267 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62 (dt, *J* = 8.0, 3.6 Hz, 1H), 2.48−2.34 (m, 2H), 2.27−2.02 (m, 4H), 1.10−0.95 (m, 21H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 217.8, 70.3, 48.5, 35.5, 32.9, 17.8, 17.8, 12.2, 11.9. HRMS-ESI (*m*/*z*): calcd for $[C_{14}H_{28}O_2SiNa]^+$, 279.1756; found, 279.1762.

*(1R,4S)-4-((t-Butyldiphenylsilanyloxy)cyclopent-2-enol (**1′c**).* Colorless oil, 43% yield (290 mg), 99.4% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those **1c**. The enantiomeric excess (**1′c**) was determined by HPLC on Chiralcel OJ-H column, hexane/*i*-PrOH = 99:1. Flow rate = 0.5 mL/min; UV detection = 220 nm; t_R = 25.0 min (minor), 35.3 min (major). $[\alpha]_D^{20}$ −2.4 (*c* 1.70, $CHCl_3$).

*3-((t-Butyldiphenylsilyl)oxy)cyclopentanone (**2c**).*[25] Colorless oil, 53% yield (358 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.61 (m, 4H), 7.48−7.36 (m, 6H), 4.55−4.51 (m, 1H), 2.54−2.45 (m, 1H), 2.26−2.23 (m, 2H), 2.16−1.96 (m, 3H), 1.06 (s, 9H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 217.3, 135.4, 133.5, 133.4, 129.7, 127.6, 71.1, 47.9, 35.6, 32.3, 26.7, 26.5, 19.0.

*(1R,4S)-4-(Benzyloxy)cyclopent-2-enol (**1′d**).* Colorless oil, 43% yield (163 mg), 94.6% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those of **1d**. The enantiomeric excess (**1′d**) was determined by HPLC on Chiralcel OJ-H column, hexane/*i*-PrOH = 95:5. Flow rate = 0.8 mL/min; UV detection = 220 nm; t_R = 29.4 min (major), 31.5 min (minor). $[\alpha]_D^{20}$ −15.8 (*c* 1.20, $CHCl_3$); lit.[22] $[\alpha]_D^{20}$ −16.2 (*c* 0.72 g, $CHCl_3$) for the (1*R*,4 *S*) isomer.

*3-(Benzyloxy)cyclopentanone (**2d**).*[27] Colorless oil, 53% yield (201 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.26 (m, 5H), 4.53 (s, 2H), 4.30−4.24 (m, 1H), 2.46−2.42 (m, 3H), 2.22−2.10 (m, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 216.8, 137.8, 128.1, 127.4, 127.3, 76.0, 70.3, 44.7, 35.5, 28.7.

*(1R,4S)-4-(Trityloxy)cyclopent-2-enol (**1′e**).* Colorless oil, 47% yield (321 mg), 93.0% ee; ^{11}H and ^{13}C {^{1}H} NMR are identical to those of **1e**. The enantiomeric excess (**1′e**) was determined by HPLC on Chiralcel OJ-H column, hexane/*i*-PrOH = 95:5. Flow rate = 0.8 mL/min; UV detection = 220 nm; t_R = 22.7 min (minor), 39.0 min (major). $[\alpha]_D^{20}$ −11.0 (*c* 1.10, $CHCl_3$).

*3-(Trityloxy)cyclopentanone (**2e**).* Colorless oil, 51% yield (349 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57−7.45 (m, 6H), 7.34−7.24 (m, 9H), 4.35−4.29 (m, 1H), 2.41−2.33 (m, 1H), 2.06−1.83 (m, 4H), 1.77−1.67 (m, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 217.0, 144.4, 128.5, 127.8, 127.1, 87.2, 71.9, 46.0, 36.6, 30.6. HRMS-ESI (*m*/*z*): calcd for $[C_{24}H_{22}O_2Na]^+$, 365.1517; found, 365.1532.

*(1R,4S)-4-Hydroxycyclopent-2-en-1-yl Benzoate (**1′g**).* Colorless oil, 46% yield (187 mg), 85.6% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those of **1g**. The enantiomeric excess (**1′g**) was determined by HPLC on Chiralcel OJ-H column, hexane/*i*-PrOH = 95:5. Flow rate = 0.8 mL/min; UV detection at 220 nm; t_R = 17.7 min (minor), 19.9 min (major). $[\alpha]_D^{23}$ −100.1 (*c* 1.81, $CHCl_3$); lit.[28] $[\alpha]_D^{23}$ −105.7 (*c* 1.00, $CHCl_3$) for the (1*R*,4 *S*) isomer.

*3-Oxocyclopentyl Benzoate (**2g**).* Colorless oil, 50% yield (204 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−7.94 (m, 2H), 7.58−7.52 (m, 1H), 7.45−7.39 (m, 2H), 5.70−5.64 (m, 1H), 2.67−2.60 (m, 1H), 2.52−2.43 (m, 2H), 2.38−2.31 (m, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 215.8, 165.8, 133.2, 129.8, 128.4, 72.9, 44.6, 35.7, 29.2. HRMS-ESI (*m*/*z*): calcd for $[C_{12}H_{12}O_3Na]^+$, 227.0687; found, 227.0699.

*(1R,4R)-4-(t-Butyldimethylsilanyloxy)cyclopent-2-en-1-ol (**1′h**).* Colorless oil, 47% yield (200 mg), 81.1% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those of **1h**. The enantiomeric excess (**1′h**) was determined by GC analysis: Beta Dex 120 capillary column, 0.25 mm × 30 m; column temperature = 105 °C (isothermal); inject temperature = 220 °C; detector temperature = 220 °C. Flow = 1.5 mL/min; t_R = 39.2 min (minor), 40.4 min (major). $[\alpha]_D^{20}$ 88.4 (*c* 2.15, $CHCl_3$); lit.[31] $[\alpha]_D^{20}$ −65.0 (*c* 1.00, $CHCl_3$) for the (1*S*,4 *S*) isomer.

*3-((t-Butyldimethylsilyl)oxy)cyclopentanone (**2h**).*[22] Colorless oil, 51% yield (220 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52−4.49 (m, 1H), 2.45−2.28 (m, 2H), 2.20−1.83 (m, 5H), 0.84 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 217.4, 70.0, 48.1, 35.4, 32.6, 25.5, 17.8, −5.0, −5.1.

*(R)-1,4-Dioxaspiro[4.4]non-8-en-7-ol (**3′a**).* Colorless oil, 45% yield (133 mg), 86.8% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those of **3a**. The enantiomeric excess (**3′a**) was determined by GC analysis: Beta Dex 110 capillary column, 0.25 mm × 30 m; column temperature = 110 °C (isothermal); inject temperature = 220 °C; detector temperature = 220 °C. Flow = 0.5 mL/min; t_R = 43.2 min(minor), 45.2 min(major). $[\alpha]_D^{20}$ −17.1 (*c* 1.91, $CHCl_3$). $[\alpha]_D^{20}$ +55.2 (*c* 1.11, $CHCl_3$) for 4-hydroxycyclopent-2-enone was obtained by deprotection of **3′a**; lit.[33] $[\alpha]_D^{20}$ +56.0 (*c* 1.0, $CHCl_3$) for the (*R*) isomer.

*(R)-4-Hydroxycyclopent-2-enone (**4a**).*[35] A mixture of **3′a** (133 mg, 0.94 mmol) and 5% H_2SO_4 (1.0 mL) in Et_2O (2.0 mL) was stirred at room temperature (25 °C). After **3′a** was completely consumed, saturated aqueous $NaHCO_3$ solution (5.0 mL) was added, and then the reaction mixture was extracted with Et_2O (5.0 mL × 2). The Et_2O layer was washed with saturated aqueous brine (30.0 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuum to give colorless oil **4a** (84.7 mg, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.61 (m, 1H), 6.23−6.20 (m, 1H), 5.11(s, 1H), 3.01−2.93 (m, 1H) 2.70−2.62 (m, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 207.4, 164.0 134.7, 70.8, 44.1. The enantiomeric excess (**4a**) was determined by GC analysis: Alpha Dex 120 capillary column, 0.25 mm × 30 m; column temperature = 90 °C (isothermal); inject temperature = 220 °C; detector temperature = 220 °C. Flow = 1.19 mL/min; t_R = 26.8 min (major), 27.8 min (minor).

*(R)-1,4-Dioxaspiro[4.5]dec-6-en-8-ol (**3′b**).* Colorless oil, 48% yield (136 mg), 93.1% ee; ^{1}H and ^{13}C {^{1}H} NMR are identical to those of **3b**. The enantiomeric excess (**3′b**) was determined by GC analysis: Alpha Dex 120 capillary column, 0.25 mm × 30 m; column temperature = 130 °C (isothermal); inject temperature = 220 °C; detector temperature = 220 °C. Flow = 0.8 mL/min; t_R = 30.4 min (minor), 31.5 min (major). $[\alpha]_D^{20}$ 39.8 (*c* 1.21, $CHCl_3$); lit.[32] $[\alpha]_D^{20}$ −40.5 (*c* 1.24, $CHCl_3$) for the (*S*) isomer.

*(R)-4-Hydroxycyclohex-2-enone (**4b**).*[34] A mixture of **3′b** (136 mg, 0.87 mmol) and 5% H_2SO_4 (1.0 mL) in Et_2O (2.0 mL) was stirred at room temperature (25 °C). After **3′b** was completely consumed, saturated aqueous $NaHCO_3$ solution (5.0 mL) was added, and then the reaction mixture was extracted with Et_2O (5.0 mL × 2). The Et_2O layer was washed with saturated aqueous brine (30.0 mL), dried over anhydrous Na_2SO_4, and concentrated in a vacuum to give colorless oil **4b** (98.5 mg, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (d, *J* = 10.0 Hz, 1H), 5.98 (d, *J* = 10.0 Hz, 1H), 4.59−4.54 (m, 1H), 3.01(br, 1H), 2.58−2.52 (m, 1H), 2.40−2.33 (m, 2H), 2.02−1.96 (m, 1H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 199.3, 153.4, 128.8, 66.0, 35.3, 32.2. The enantiomeric excess (**4b**) was determined by GC analysis: Alpha Dex 110 capillary column, 0.25 mm × 30 m; column temperature = 125 °C (isothermal); inject temperature = 220 °C; detector temperature = 220 °C. Flow = 1.5 mL/min; t_R = 32.1 min (minor), 34.1 min (major).

1,4-Dioxaspiro[4.5]decan-8-one.[31] Colorless oil, 50% yield (156 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (s, 4H), 2.54 (t, *J* = 6.8 Hz, 4H), 2.04 (t, *J* = 7.2 Hz, 4H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 199.3, 153.4, 128.8, 66.0, 35.3, 32.2.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02519.

Copies of ^{1}H and ^{13}C {^{1}H} NMR spectra for all compounds and HPLC/GC chromatograms of chiral products (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*Fax: (+86) 21-5474-8925; E-mail: zhaoguo@sjtu.edu.cn (Z.Z.).

*Fax: (+33) 144-071-062; E-mail: virginie.vidal@chimie-paristech.fr (V.R.).

Notes

The authors declare no competing financial interest.

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