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Asymmetric Desymmetrization of the Diallyl Acetals of Alkynals by the Enantioselective Pauson–Khand-Type Reaction Catalysts

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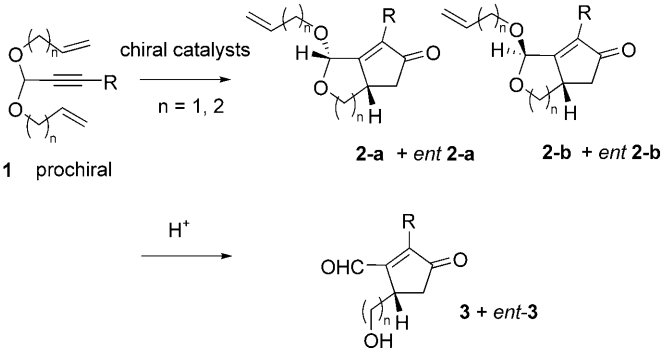
Abstract: Asymmetric desymmetrization of the diallyl acetals of alkynal (**1**) by an enantioselective Pauson–Khand-type reaction catalyst was studied. The corresponding 5-oxabicyclo[3.3.0]octenones (**2**) were obtained as a mixture of diastereomers (**2a** and **2b**), which were hydrolyzed to afford a single enantiomer (**3**), in high yields (up to 88%) as well as excellent enantioselectivities (up to 97%).

Keywords: asymmetrric desymmetrization; atropisomeric ligands; enantioselective; Pauson–Khand reaction; rhodium(I)

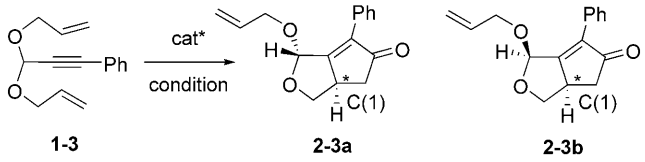
The asymmetric desymmetrization of *meso* compounds or prochiral compounds by chiral catalysts is among the most efficient strategies to generate optically pure compounds.[1] We reported previously an efficient catalytic asymmetric Pauson–Khand reaction based on chiral cationic Rh(I)-BINAP complexes (named APKR hereafter).[2] In an effort for determining the scope of this reaction and exploring its application to the synthesis of natural or unnatural biologically interesting compounds, we reported the efficient asymmetric desymmetrization of the prochiral dienynes such as propargyl 1-vinylallyl *N*-tosylamides and ethers.[3] We describe herein the synthesis of a wide range of highly functionalized cyclopentenones (**3**) in optically pure or enriched form based on the same concept. As seen in the previous study with dienynes,[3] asymmetric desymmetrization of acetals (**1**) by the chiral PKR catalyst also generates two stereogenic centers at the same time, raising issues of diastereoselectivity as well as enantioselectivity (Scheme 1).

Compound (**1**) had been previously subjected to PKR utilizing a stoichiometric amount of $Co_2(CO)_8$ and gave a diastereomeric and racemic mixture of **2-a** and **2-b**.[4a] The resulting products (**2**) were useful for the preparation of iridoids and carbocyclic nucleotide mimics.[4b,c] Having established an achiral $Co_2(CO)_8$ catalyst for the formation of racemic **2**, we next focused on the stereoselective version of the reaction by using APKR catalysts. The resultant products can serve as key intermediates in the synthesis of relevant natual products such as brefeldin A (**6**). We first checked the compatibility of the acetal substrates (**1**) with the currently available APKR catalysts. Several conditions previously reported based on either Rh(I) or Ir(I) to date together with the newly optimized conditions at ambient temperature by us[5] were tested to examine the characteristics of the reaction and find an optimized condition. The results are summarized in Table 1.



Scheme 1. Asymmetric desymmetrization of bisallyl propargyl acetals

Table 1. Optimization of desymmetrization of **1-3** by various asymmetric Pauson-Khand reaction catalysts.



1-3 2-3a 2-3b

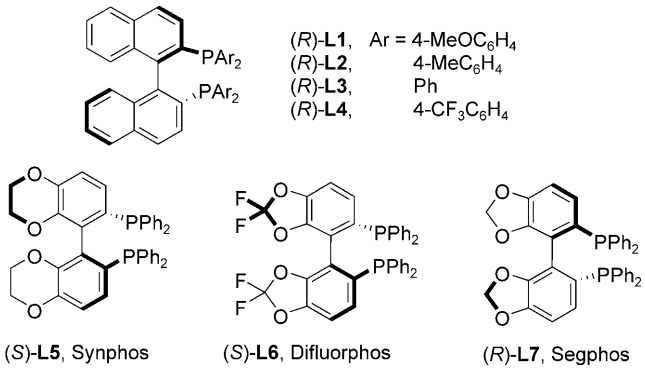
Entry	Conditions[a]	**2-3a** Yield/*ee* [%]	**2-3b** Yield/*ee* [%]
1	*a*	NR (decomposition of **1-3**)	
2	*b*	36/68	5/46
3	*c*	Only 20% of **1-3** was consumed.	
4	*d*	41/86	25/70

[a] *a* $[Rh(CO)_2Cl]_2$ (3 mol%), (*R*)-BINAP (9 mol%), AgOTf (12 mol%) in THF at 90 °C under CO (1 atm). *b* $[Rh(CO)_2Cl]_2$ (3 mol%), (*R*)-BINAP (9 mol%), AgOTf (12 mol%) in THF at 18-20 °C under Ar:CO (10:1, 1 atm). *c* $[Ir(COD)_2Cl]_2$ (15 mol%), (*R*)-BINAP (30 mol%) in toluene at 110 °C under CO (1 atm). *d*. [Rh-(COD)Cl]$_2$ (5 mol%), (*R*)-BINAP (12 mol%) in cinnamaldehyde (20 eq) at 120 °C under Ar (1 atm).

Compound **1-3**, a reference substrate, was too sensitive to the original cationic Rh(I) catalyst protocol pioneered by our laboratory.[2c] Consequently, the application of the original thermal reaction gave rise to substantial amounts of decomposed compounds (entry 1 in Table 1). At ambient temperature (entry 2 in Table 1), the cationic Rh(I) catalyst prepared by mixing $[Rh(CO)_2Cl]_2$ (3 mol%), (*R*)-BINAP (9 mol%) and AgOTf (12 mol%) did provide compounds **2-3a** (36% yield, 68% *ee*) and **2-3b** (5% yield, 46% *ee*) with moderate yields and enantioselectivities[5] On the other hand, a relatively insensitive neutral Ir(I) catalyst, generated from $[Ir(COD)_2Cl]_2$ (15 mol%) and (*R*)-BINAP (30 mol%) in toluene, which was our choice in the previous desymmetrization of dieneynes,[3,6a] was reluctant to react with substrate **1-3** even at high temperature (110 °C) and for a prolonged reaction time (24 h) (entry 3 in Table 1). Finally, by combining $[Rh(CO)_2Cl]_2$ (5 mol%) and (*R*)-BINAP (12 mol%) and cinnamaldehyde developed by Shibata and co-workers, which served not only as solvent but also as a source of carbon monoxide by rhodium(I)-catalyzed decarbonylation, the reaction proceeded at 120 °C to afford compounds **2-3a** (41% yield, 86% *ee*) and **2-3b** (25% yield, 70% *ee*).[6d]

The following characteristics of the reaction are worth mentioning: (1) Carefully dry conditions were required to obtain a good combined yield of 66%. (2) The reaction provided the PKR product **2-3** as a mixture of diastereomers, **2-3a** and **2-3b**, in 25% and 41%, respectively.[7] The ratio of diastereomers was variable depending on the exact conditions, but optimization for the exclusive formation of one diastereomer seemed improbable. The enantiomeric excesses of diasteromers were determined as 70% for minor product **2-3a** and 86% for major product **2-3b**. The assignment of relative stereochemistry was later unambiguously confirmed by the elucidation of the single crystal structure of **2-5a** obtained from entry 10 in Table 3 (Figure 1). (3) The absolute configuration at C*(1) of both diastereomers **2-3a** and **2-3b** was deter-

Table 2. Ligand effects on the desymmetrization of **1-3**.



Entry	Ligand	**2-3a** Yield/*ee* [%] config. C*(1)	**2-3b** Yield/*ee* [%] config. C*(1)
1	(*R*)-**L1** *p*-OMe-BINAP	21/67 (*R*)	49/81 (*R*)
2	(*R*)-**L2** *p*-Me-BINAP	36/65 (*R*)	46/87 (*R*)
3	(*R*)-**L3** BINAP	25/70 (*R*)	41/83 (*R*)
4	(*R*)-**L4** *p*-CF_3-BINAP	36/32 (*R*)	37/44 (*R*)
5	(*S*)-**L5** Synphos	30/67 (*S*)	55/90 (*S*)
6	(*S*)-**L6** Difluorphos	28/63 (*S*)	22/70 (*S*)
7	(*R*)-**L7** Segphos	27/74 (*R*)	48/83 (*R*)

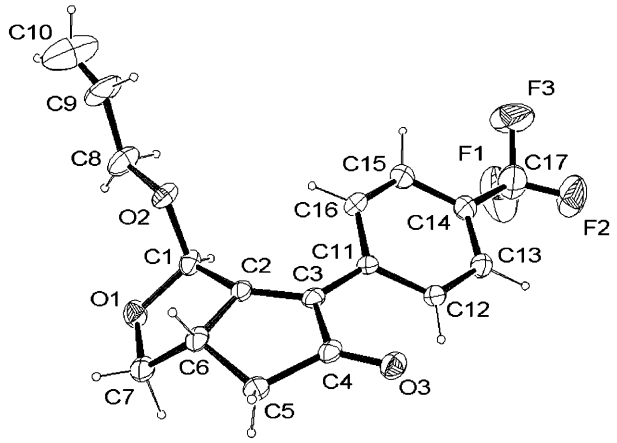


Figure 1. ORTEP drawing of **2-5a**.

mined after acidic hydrolysis. In each case, the same absolute configuration was obtained for compound **3** demonstrating a good stereocontrol at the C*(1) position. The absolute configuration at C*(1) was *R* as shown in Scheme 1, when (*R*)-BINAP was employed as a chiral ligand.[8] (4) Comparable results were obtained in a one-pot operation consisting of both APKR reaction and acidic hydrolysis.

As we have already noted that the efficiency and stereoselectivity of the reaction was sensitive not only to the electronic and steric characteristics of the ligands, but also to the electron density of the alkyne substrate,[9] further optimizations were attempted with various ligands (**L1** to **L7**).

The ligand effects were first examined with substrate **1-3** as summarized in Table 2, revealing that (*R*)-*p*-Me-BINAP (**L2**) and (*S*)-Synphos (**L5**) are the best ligands with regard to yields and enantioselectivities.

This result is contrary to those observed in the study under the thermal conditions using a cationic Rh(I) catalyst at atmospheric CO pressure, in which the electron-deficient phosphorus ligands such as (*R*)-*p*-CF_3-BINAP (**L4**) and (*S*)-Difluorphos (**L6**) provided better chemical yields and enantioselectivities.[9]

Although precedents indicated that the PKR reaction can be accelerated by catalysts bearing the more electron-rich phosphine ligands and/or having a narrower dihedral angle in a transition intermediate,[9a] the PKR was tainted by the formation of side products resulting from simultaneously facilitated β-hydride elimination of the metallacyclopentene intermediate. However, in this case, the formation of the presumed catalyst, [(CO)RhClL*], resulted from the decarbonylation of cinnamaldehyde, may be significantly expedited by the ligand bearing the more electron-rich phosphorus.

By carefully balancing electronic and steric factors, (*R*)-*p*-Me-BINAP (**L2**) and (*S*)-Synphos (**L5**) turned out to be the best ligands for this reaction (entries 2 and 5 in Table 2).

The experimental protocol was established as follows: a mixture of substrate **1** and the neutral Rh(I)-(*R*)-*p*-Me-BINAP (**L2**) or (*S*)-Synphos (**L5**) catalyst (prepared *in situ* by mixing 3 mol% $[RhCl(COD)]_2$ and 9 mol% of the corresponding ligand) in cinnamaldehyde was refluxed under argon until the starting material disappeared completely, usually within 2 h.

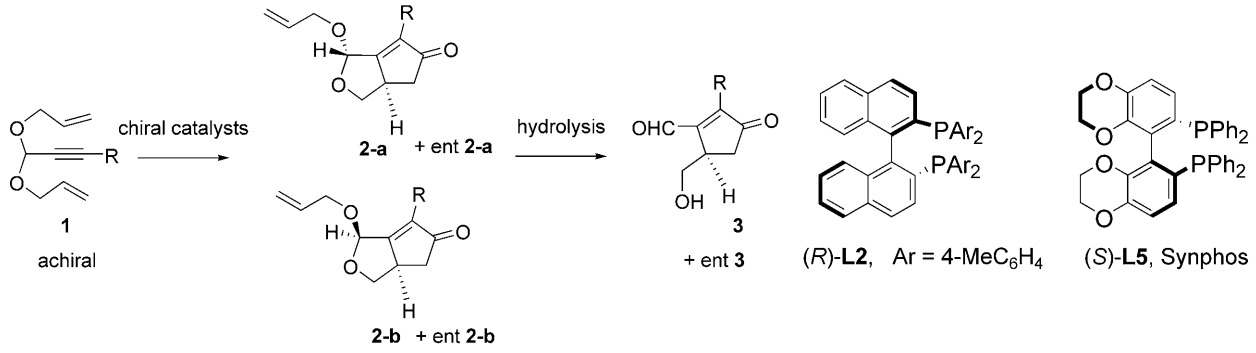
After extensive experimentations, we learned that (*R*)-*p*-Me-BINAP (**L2**) and (*S*)-Synphos (**L5**) have a different behavior depending on the considered substrates **1**. For example, (*S*)-Synphos (**L5**) was the better ligand for the relatively slow reacting substrates (**1-1** to **1-5**), bearing aryl substituents on the alkyne. The phosphorus on (*S*)-Synphos (**L5**) had comparable electron density with that of BINAP (**L3**) (respectively, ^{31}P NMR: −14.3 ppm and −14.4 ppm). As a result, the decarbonylation was affected efficiently as well. The overall reaction efficiency is also dependent on the electron density of the alkynes. As the electron density increased, the overall chemical yield of the PKR slightly decreased while the enantioselectivity increased. This might be attributed to the parallel kinetic resolution mentioned previously.

The poor diastereoselectivity in this Rh(I)-catalyzed reaction could be a potential drawback of this strategy,[4] However, when we carefully studied the enantioselectivity, this concern was minimized as the major diastereomer was obtained with excellent enantioselectivities (> 90% except one example, **1-5**) and in decent yields (range of 44 to 59%). In addition, since each diastereomer had the same stereogenic center at C*(1), a single product (**3**) substantially enriched by one enantiomer was obtained upon trace acidic hydrolysis in wet THF, either from the separated diastereomer **2a** and **2b** or from the mixture of diastereomers **2a** and **2b**. The combined yields of the two steps were in the range 61–75% with enantiomeric excesses of the combined mixture generally greater than 80% ($er \geq 9{:}1$).

Compound **1-1** having an electron-donating 4′-methoxyphenyl substituent (entry 2 in Table 3) provided a mixture of **2-1a** and **2-1b**, respectively, in 32% and 44% yield, with enantiomeric excesses of 68% and 90% by using (*S*)-Synphos (**L5**). On the other hand, the substrate **1-4** having an electron-withdrawing substituents such as 4-ClC_6H_4 (entry 10 in Table 3) afforded an improved diastereoselectivity (2:1) with (*S*)-Synphos (**L5**) but with slightly lower enantiomeric excess together with higher combined chemical yield (62% *ee* and 27% yield for **2-4a**, 90% *ee* and 59% yield for **2-4b**, respectively).

Meanwhile, for the substrates (**1-6** to **1-8**, entries 11 to 16 in Table 3) having alkyl group substituents at the alkynes, (*R*)-*p*-Me-BINAP (**L2**) turned out to be the best ligand. The reactions employing (*S*)-Synphos (**L5**) afforded a substantially reduced chemical yield of the PKR product (entries 12, 14 and 16 in Table 3),

Table 3. Asymmetric desymmetrization of the bisallenyl propargyl acetals **1** by an enantioselective PKR with (*R*)-*p*-Me-BINAP (**L2**) and (*S*)-Synphos (**L5**).



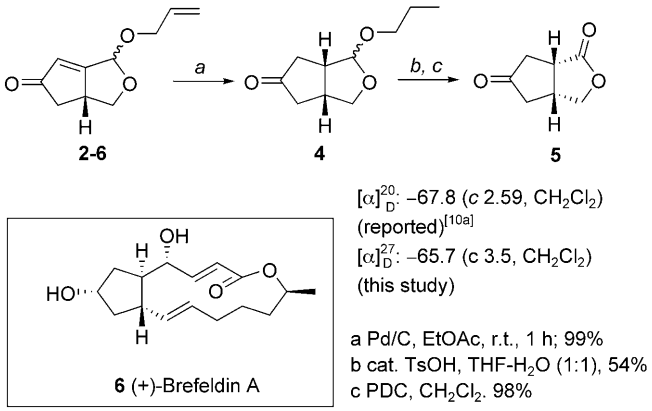
Entry	Substrate	Ligand	Time [h]	**2-a** Yield/*ee*[f] [%] (config. C1)	**2-b** Yield/*ee*[f] [%] (config. C1)	**3**[a] Yield/*ee*[f] [%] (config. C1)	**3**[b] Yield/*ee*[f] [%] (config. C1)	Overall[c] Yield/*ee*[f] [%] (config. C1)	Overall[d] Yield/*ee*[f] [%] (config. C1)
1	4′-	(*R*)-**L2**	1.5	30/75 (*R*)	46/80 (*R*)	82/74 (*R*)	84/80 (*R*)	63/78 (*R*)	64/76 (*R*)
2	$CH_3OC_6H_4$ (**1-1**)	(*S*)-**L5**	**1**	**32/68** (*S*)	**44/90** (*S*)	**78/70** (*S*)	**82/90** (*S*)	**61/83** (*S*)	**68/85** (*S*)
3	4′-	(*R*)-**L2**	3	32/65 (*R*)	44/87 (*R*)	82/65 (*R*)	82/85(*R*)	62/77 (*R*)	64/79 (*R*)
4	$CH_3C_6H_4$ (**1-2**)	(*S*)-**L5**	**1.5**	**30/64** (*S*)	**48/92** (*S*)	**84/64** (*S*)	**80/90** (*S*)	**63/80** (*S*)	**66/85** (*S*)
5	C_6H_5 (**1-3**)	(*R*)-**L2**	3	36/65 (*R*)	46/87 (*R*)	83/68 (*R*)	72/88 (*R*)	66/75 (*R*)	70/76 (*R*)
6		(*S*)-**L5**	**2.5**	**30/67** (*S*)	**55/90** (*S*)	**77/68** (*S*)	**80/90** (*S*)	**67/82** (*S*)	**74/86**(*S*)
7	4′-ClC_6H_4	(*R*)-**L2**	3	40/64 (*R*)	47/86(*R*)	78/65 (*R*)	84/86 (*R*)	70/77 (*R*)	74/81 (*R*)
8	(**1-4**)	(*S*)-**L5**	**2.5**	**27/62** (*S*)	**59/90** (*S*)	**80/62** (*S*)	**82/89** (*S*)	**70/81** (*S*)	**76/83** (*S*)
9	4′-$CF_3C_6H_4$	(*R*)-**L2**	3	36/58 (*R*)	50/77(*R*)	80/58 (*R*)	86/76 (*R*)	72/69 (*R*)	80/69 (*R*)
10	(**1-5**)	(*S*)-**L5**	**2.5**	**40/63** (*S*)	**53/84** (*S*)	**78/63** (*S*)	**84/83** (*S*)	**75/72** (*S*)	**80/77** (*S*)
11	H (**1-6**)	(*R*)-**L2**	**1**	**65**[e]		**20–80**[g]**/97** (*R*)		**60/97** (*R*)	[g]
12		(*S*)-**L5**	1	35[e]		20–90[g]/93 (*S*)		30/94 (*S*)	[g]
13	Me (**1-7**)	(*R*)-**L2**	**1**	**77**[e]		**84/94** (*R*)		**65/94** (*R*)	**66/94** (*R*)
14		(*S*)-**L5**	1	54[e]		88/90 (*S*)		48/90 (*S*)	50/92 (*S*)
15	allyl (**1–8**)	(*R*)-**L2**	**1.5**	**78**[e]		**82/93** (*R*)		**64/** $\geq$ **95**[f] (*R*)	**70/** $\geq$ **95**[f] (*R*)
16		(*S*)-**L5**	1	74[e]		86/95 (*S*)		64/95[f] (*S*)	64/95[f] (*S*)
17	TMS (**1–9**)	(*R*)-**L2**	NR	–		–		–	–
18		(*S*)-**L5**	NR	–		–		–	–

[a] Data for **3** obtained from **2-a**.
[b] Data for **3** obtained from **2-b**.
[c] Overall yield and enantioselectivity by weighted summation of the previous two data.
[d] Data were obtained after one-pot operation of two reaction steps.
[e] An inseparable mixture was obtained.
[f] The *ee* were determined by NMR using a chiral shifting agent, $Eu(hfc)_3$.
[g] Due to the inherent instability of **3-6**, yields of the isolated hydrolysis products were variable batch to batch. The reliable chemical yield and full characterization were made after direct hydrogenation of **2-6** to **4** instead of hydrolysis (Scheme 2).

consistent with side products arising from significant competition of β-hydride elimination of the metallacyclopentene intermediate.

Fortunately, the catalyst bearing (*R*)-*p*-Me- BINAP (**L2**) provided well-optimized results for these substrates with complementary effects. The catalyst had an electron-rich phosphorus ligand for facilitating the decarbonylation of the aldehyde, a wider dihedral angle of the ligand in the transition intermediate slowed the overall reaction rate,[9b] especially β-hydride elimination rate, more significantly. And thus, the formation of the side products was suppressed to a negligible level.

Most importantly, the alkyl-substituted substrates **1-7** and **1-8** provided excellent enantioselectivities with (*R*)-*p*-Me-BINAP (**L2**) without sacrificing the chemical yields. The only practical difficulty encountered with these cases was that the PKR products were obtained as an inseparable mixture of diastereomers. Thus, we determined the chemical yield and measured



Scheme 2. Further functionalization of **2-6**.

the optical purity of products **3** after hydrolysis of a mixture of diasteromers **2**. The overall chemical yields over two steps and the enantioselectivities obtained for **1-7**, and **1-8** were excellent: 65% together with 94% *ee* and 64% with 95% *ee*, respectively.

Even **1-6** having a terminal alkyne, previously considered to be too sensitive to the acidic cationic Rh(I) catalyst, gave a high chemical yield as well as an excellent enantioselectivity (97% *ee* in 60% yield over two steps). The compound **2-6** obtained by utilizing (*R*)-**L2** was readily transformed into **5**, which may potentially be a pivotal intermediate for the synthesis of (+)-brefeldin A (**6**; Scheme 2).[10]

However, TMS-substituted subtrate **1-9** remained inert to the Rh-catalyzed PKR conditions. Although this behavior was contrary to the cobalt-promoted reaction, it was consistent with previously reported observation with Rh(I)-catalyzed PKRs. The extension of this method to bis(3-butenyl) acetals of alkynal (**1**, $n=2$) was not successful as expected with the Rh(I) catalyst.

In conclusion, we have demonstrated that the asymmetric desymmetrization of the diallyl acetals of alkynal (**1**) by enantioselective Pauson–Khand reaction catalysts based on a neutral Rh(I) catalyst provided a useful enantioselective synthesis of bicyclic or monocyclic compounds (**2** or **3**) in excellent chemical yields as well as enantioselectivities. These products will serve as pivotal intermediates for the enantioselective synthesis of biologically interesting compounds, such as iridoids and brefeldine. The results will be reported in due course.

Experimental Section

The Asymmetric Desymmetrization

A mixture of $[Rh(COD)Cl]_2$ (4.8 mg, 0.010 mmol), (*R*)-*tol*-BINAP (**L2**, 15.8 mg, 0.023 mmol) or (*S*)-Synphos (**L5**), 1-[3,3-bis(allyloxy)prop-1-ynyl]-4-methoxybenzene (**1-1**) (50 mg, 0.194 mmol) in cinnamaldehyde (0.5 mL, 3.872 mmol, 20 equiv.) was placed in a flask under an atmosphere pressure of argon. The reaction mixture was stirred at 120 °C for 1.5 h. After the completion of the reaction, the crude mixture was purified by column chromatography on silica gel with *n*-hexane/ethyl acetate (8/1, v/v) as an eluent to give the corresponding products **2-1a** (yield; 16 mg, 0.056 mmol, 30%) and **2-1b** (yield: 24.0 mg, 0.084 mmol, 46%), respectively.

1-(Allyloxy)-6-(4-methoxyphenyl)-3a,4-dihydro-1*H*-cyclopenta[*c*]furan-5(3H)-one (2-1a): IR (KBr): $\nu=1712\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta=2.35$ (dd, $J=18.2$, 3.0 Hz, 1H), 2.90 (dd, $J=18.2$, 6.4 Hz, 1H), 3.44 (dd, $J=8.7$, 8.4 Hz, 1H), 3.50–3.56 (m, 1H), 3.83 (s, 3H), 4.23 (dd, $J=12.4$, 6.3 Hz, 1H), 4.39 (dd, $J=12.4$, 5.5 Hz, 1H), 4.46 (dd, $J=8.0$, 8.0 Hz, 1H), 5.28 (d, $J=10.2$ Hz, 1H), 5.39 (dd, $J=17.1$, 0.6 Hz, 1H), 5.62 (s, 1H), 6.05 (dddd, $J=17.1$, 10.2, 6.3, 5.2 Hz, 1H), 6.94 (d, $J=8.8$ Hz, 2H), 7.59 (d, $J=8.8$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=39.7$, 42.0, 55.5, 69.0, 71.3, 97.8, 114.3, 118.4, 123.1, 130.4, 134.1, 135.3, 160.5, 170.0, 208.2; HR-MS (EI^+): $m/z=286.1205$ [M^+], calcd. for $C_{17}H_{18}O_4$: 286.1205; $[\alpha]_D^{23}$: +100.9 (*c* 5.3, CH_2Cl_2); HPLC: The *ee* value was determined as 75% by HPLC analysis using a chiral column (DAICEL CHIRALPAK AS-H, *n*-hexane/2-PrOH = 9/1, flow 1.0 mL min^{-1}, detection at 254 nm); retention time: 12.04 min (minor) and 20.39 min (major).

1-(Allyloxy)-6-(4-methoxyphenyl)-3a,4-dihydro-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (2-1b): IR (KBr): $\nu=1712\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta=2.39$ (dd, $J=17.6$, 3.9 Hz, 1H), 2.76 (dd, $J=17.6$, 6.3 Hz, 1H), 3.26–3.35 (m, 1H), 3.60 (dd, $J=10.8$, 7.9 Hz, 1H), 3.82 (s, 3H), 4.09 (dd, $J=12.7$, 6.3 Hz, 1H), 4.17 (dd, $J=12.7$, 5.4 Hz, 1H), 4.27 (dd, $J=7.9$, 7.7 Hz, 1H), 5.07 (d, $J=17.1$ Hz, 1H), 5.11 (d, $J=9.4$ Hz, 1H), 5.73 (dddd, $J=17.1$, 9.4, 6.3, 5.4 Hz, 1H), 6.09 (s, 1H), 6.90 (d, $J=8.8$ Hz, 2H), 7.53 (d, $J=8.8$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=40.6$, 44.2, 55.5, 69.7, 70.6, 99.0, 113.8, 118.3, 122.5, 130.8, 133.7, 137.6, 160.2, 172.7, 208.0; HR-MS (EI^+): $m/z=286.1203$ [M^+], calcd. for $C_{17}H_{18}O_4$: 286.1205; $[\alpha]_D^{23}$: −38.1 (*c* 8.0, CH_2Cl_2); HPLC: The *ee* value was determined as 80% by HPLC analysis using a chiral column (DAICEL CHIRALPAK AS-H, *n*-hexane/2-PrOH = 9/1, flow 1.0 mL min^{-1}, detection at 254 nm); retention time: 14.41 min (minor) and 25.71 min (major).

Hydrolysis of the PKR Products

A mixture of 1-(allyloxy)-6-(4-methoxyphenyl)-3a,4-dihydro-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (**2-1-a**) (16 mg, 0.056 mmol) and *p*-toluenesulfonic acid (1.3 mg, 0.007 mmol, 3 mol%) in THF/water (3 mL/0.5 mL) was stirred at 80 °C for 6 h. The reaction mixture was quenched with a saturated aqueous solution of sodium bicarbonate (3 mL) and extracted with ethyl acetate (2 mL × 3). The combined organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. After filtration of the insoluble materials, the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography of silica gel with *n*-hexane/ethyl acetate (3/1, v/v) as an eluent to give **3-1** as an oil; yield: 11.3 mg (0.046 mmol, 82% yield). The *ee* was determined by HPLC analysis using a chiral column specified. IR (KBr): $\nu=3437$, 1712, 1670 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.54$ (dd, $J = 19.3$, 1.9 Hz, 1H), 2.81 (dd, $J = 19.3$, 7.2 Hz, 1H), 3.40–3.44 (m, 1H), 3.81–3.89 (m, 2H), 3.86 (s, 3H), 6.99 (d, $J = 8.6$ Hz, 2H), 7.40 (d, $J = 8.6$ Hz, 2H), 10.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 39.6$, 39.7, 55.7, 64.2, 114.5, 120.7, 132.1, 152.6, 157.7, 161.7, 193.4, 208.0; HR-MS (EI^+): $m/z = 246.0870$ [M^+], calcd. for $C_{14}H_{14}O_4$: 246.0892; $[\alpha]_D^{23}$: +60.5 (*c* 3.8, CH_2Cl_2); HPLC: The *ee* value was determined as 74% by HPLC analysis using a chiral column (DAICEL CHIRALPAK AS-H, *n*-hexane/2-PrOH = 2/1, flow 1.5 mL min^{-1}, detection at 254 nm); retention time: 7.84 min (minor) and 11.41 min (major).

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[7] CCDC 696219 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

[8] The absolute configuration at C*(1) of **2-3b** obtained with (*R*)-L2 was determined as *R* by comparison of the retention time of **2-3b** in HPLC analysis with the data previously reported in ref.[4c]

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