Kinetic Resolutions by Enantioselective Pauson–Khand-Type Reaction

Dong Eun Kim,[a] Jaesung Kwak,[a] In Su Kim,[a] and Nakcheol Jeong[a,*]

[a] Department of Chemistry, Korea University, Seoul 136-701, Korea
Fax: (+82) 2-3290-3121; phone: (+82) 2-3290-3136; e-mail: njeong@korea.ac.kr

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Abstract: A kinetic resolution of 1-arylallyl propargyl ethers by enantioselective Pauson–Khand-type reaction catalysts was successfully carried out. While cationic rhodium(I) with a BINAP-based ligand having an electron-deficient phosphine is the choice for the slow reacting substrates, neutral iridium(I) with a BINAP-based ligand possessing an electron-rich phosphine provided excellent results for the more reactive substrates.

Keywords: allyl propargyl ethers; atropisomerism; iridium; kinetic resolution; Pauson–Khand reaction; rhodium

Kinetic resolution has been established as a useful tool for the preparation of an optically active compound from a racemic mixture. Enzymatic kinetic resolution has a long history, but transition metal-mediated kinetic resolution has become popular over the last two decades due to the progress made in the development of chiral catalysts for asymmetric reactions.[1] In this communication, we would like to report the first kinetic resolution by a catalytic asymmetric Pauson–Khand-type reaction.[2]

The study was initiated with the racemic substrate 1-arylallyl propargyl ether, **1a-1**. Either Rh(I) or Ir(I) catalysts under thermal conditions originally developed by us[3] and Shibata,[4] respectively, were tested. The results were confusing and indicated that this reaction might require much effort for optimization. For example, under the conditions employing Rh(I) (conditions a in Table 1), the reaction was too fast for its halfway point to be judged precisely. Thus the data initially obtained were inconsistent. On the other hand, the Ir(I)-catalyzed reaction was too slow for practical use, resulting in an unsatisfactory chemical yield of the PKR product even after a prolonged reaction time (conditions b in Table 1). Better and more reliable results were obtained by employing the newly developed reaction conditions utilizing a Rh(I) catalyst at ambient temperature.[5c] The reaction of racemic **1a-1** at ambient temperature under a reduced pressure of CO (0.1 atm) afforded an efficient kinetic resolution (conditions c in Table 1).[5]
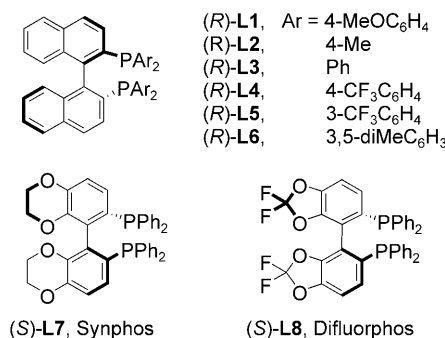
The following characteristics of the reaction are worth mentioning. First, it was easy to determine the termination point of the reaction. Once the reaction reached 50% conversion, its progress became noticeably slower. Second, the reaction provided the PKR product **2a-1** as a single diastereomer.[6] The absolute configuration of **2a-1** was [R(C1), R(C2)] as shown in

Table 1. Preliminary experiments of the kinetic resolution through asymmetric Pauson–Khand type reaction.

Conditions[a]	t [h]	1a-1 Yield [%]/ee [%]	2a-1 Yield [%]/ee [%]	3a-1 Yield [%]
a	0.5	48/60	50/82	–
b	12	70/27	20/92	–
c	1.5	56/40	33/85	10

[a] *Condtions a:* [Rh(CO)$_2$Cl]$_2$ (3 mol%), (R)-BINAP (9 mol%), AgOTf (12 mol%) in THF at 80°C under CO (1 atm); *conditions b:* [Ir(COD)$_2$Cl]$_2$ (15 mol%), (R)-4-tol-BINAP (30 mol%), toluene, CO (1 atm), reflux; *conditions c:* [Rh(CO)$_2$Cl]$_2$ (3 mol%), (R)-BINAP (9 mol%), AgOTf (12 mol%), Ar:CO (10:1, 1 atm), THF, 18–20°C.

Table 2. Ligand effects on the kinetic resolution of (±) **1a-1**.

(R)-**L1**, Ar = 4-MeOC$_6$H$_4$
(R)-**L2**, 4-Me
(R)-**L3**, Ph
(R)-**L4**, 4-CF$_3$C$_6$H$_4$
(R)-**L5**, 3-CF$_3$C$_6$H$_4$
(R)-**L6**, 3,5-diMeC$_6$H$_3$

(S)-**L7**, Synphos

(S)-**L8**, Difluorphos

Entry[a]	Lig.	δ (^{31}P, ppm)[c]	Dihedral angle (°)[d]	1a-1[f] Yield [%]/ee [%]	2a-1[g] Yield [%]/ee [%]	3a-1 Yield [%]
1	(R)-**L1**	−16.9	78.3	42/40	25/59	20
2	(R)-**L2**	−15.8	[e]	48/37	23/67	20
3	(R)-**L3**	−14.4	78.3	56/40	32/85	10
4[b]	(R)-**L4**	−13.8	78.0	**50/71**	**40/91**	5
5[b]	(R)-**L5**	−13.7	[e]	58/50	36/89	–
6	(R)-**L6**	−13.6	[e]	62/27	31/58	5
7	(S)-**L7**	−14.3	73.0	40/56[h]	23/66^i	25
8	(S)-**L8**	−12.3	72.2	**43/99**[h]	**45/83**[i]	<2

[a] [Rh(CO)$_2$Cl]$_2$ (3 mol%), L* (6 mol%), AgOTf (9 mol%), Ar:CO (10:1, 1 atm), THF, 18–20 °C.
[b] Reactions at 40 °C.
[c] We correlated the electron density on phosphorus through the ^{31}P NMR spectra of the free ligands.[5a]
[d] Structures minimized by Molecular Mechanics calculations (CAChe MM2 program).[5]
[e] This number has not been calculated, but is assumed to be similar to that of **L3**.
[f] The absolute configuration of ent-**1** was (S).
[g] The absolute configuration at C-1 and C-2 of ent-**2** was (R,R).
[h] The absolute configuration of **1a-1** is (R).
[i] The absolute configuration at C-1 and C-2 of **2a-1** is (S,S).

Table 1, when (R)-BINAP was employed as a chiral ligand.[7] Third, compound **3**, a rearranged product of **1**, was obtained sporadically because of the intrinsic Lewis acidity of the catalyst.[8] Fourth, the efficiency of the reaction and its stereoselectivity depended sensitively not only on the electronic and steric characters of the ligands, but also on the electron density of the alkyne.[9] The ligand effects are summarized in Table 2. From Table 2, we learned that (S)-Difluorphos (**L8**) and (R)-4-trifluorotolyl-BINAP (**L4**) are the best choices of ligand.[9]

In an earlier study, we were able to summarize the ligand effects on this reaction.[9] Ligands possessing the more electron-rich phosphorus atom accelerated the reaction. In addition, for ligands having similar electron density to that of phosphorus, those ligands having a narrower dihedral angle in the metal-bound Rh(I) complex accelerated the reaction substantially. However, this acceleration is often tainted by side reactions, resulting in a decrease of the chemical yield. In this light, ligand **L8**, whose dihedral angle in the metal-bound ligand is smaller than those of BINAP derivatives and for which phosphorus is significantly deshielded (12.3 ppm), provides a good compromise in terms of the chemical yield and enantioselectivity. The reaction proceeded smoothly at ambient temperature and thus a significantly improved combined chemical yield of the PKR product **2a** and the remaining **1a** was obtained. Although this rate acceleration provided the isomer **3** noticeably in several cases (**1a-3** and **1a-4** in Table 3), where the electron density of the alkyne was rich, the combined chemical yield in most cases was normally excellent. Furthermore, excellent enantioselectivities were obtained especially for the remaining starting materials, but the enantioselectivities of PKR product need to be improved.

Meanwhile, the reaction by the catalyst possessing **L4**, which has a relatively wider dihedral angle in the metal complex together with the electron-deficient phosphorus, was slowed down substantially and thus required slight warming (40 °C) for the reliable initiation of the reaction.

However, this condition provided excellent ees (> 90%) for the PKR products with chemical yields uniformly greater than 40%. The only exceptions were those substrates having an electron-deficient alkyne, which gave a relatively inferior result (80% ee).

Table 3. Kinetic resolution of **1a** and **1b** by cationic chiral Rh(I) catalysts.

| Substrates | | Reaction by a catalyst with (S)-L8 | | | | | Reaction by a catalyst with (R)-L4 | | | | |
R¹	R²	t [h]	ent-1[a] Yield [%]/ ee [%]	ent-2[b] Yield [%]/ ee [%]	3 Yield [%]	S[1d,10]	t [h]	ent-1[c] Yield [%]/ ee [%]	ent-2[d] Yield [%]/ ee [%]	3 Yield [%]	S[1d,10]
O Ph (**1a**)	C₆H₅ (**1**)	1.7	**44/99**	45/80	<2	41	1.2	48/84	**41/90**	<5	83
	2-(CH₃O)C₆H₄ (**2**)	1.5	**38/99**	61/65	0	17	1.0	48/90	**49/90**	–	69
	4-(CH₃O)C₆H₄ (**3**)	1.5	**40/99**	45/76	10	24	1.0	58/53	**40/94**	–	66
	4-CH₃C₆H₄ (**4**)	1.2	**40/91**	49/75	8	12	1.0	52/83	**44/92**	–	65
	(3,5-diCH₃)C₆H₃ (**5**)	2.0	**42/95**	51/70	<5	19	0.8	48/76	**40/83**	<5	33
	4-ClC₆H₄ (**6**)	3.0	**40/96**	59/63	–	17	1.0	52/60	**46/85**	–	29
	4-CF₃C₆H₄ (**7**)	4.0	**42/90**	55/75	–	13	1.0	48/71	**46/80**	–	25
	2-ClC₆H₄ (**8**)	2.5	**46/73**	54/60	–	9	3.0	52/61	**44/82**	–	23
Naphth (**1b**)	4-(CH₃O)C₆H₄ (**1**)	1.0	50/90	**42/80**	–	58	1.0	56/77	**33/90**	–	36
	C₆H₅ (**2**)	1.0	54/84	**40/92**	–	200	1.0	57/56	**38/91**	–	44
	4-CF₃C₆H₄ (**3**)	1.0	50/84	48/80	–	30	1.0	56/65	41/80	–	17

[a] The absolute configuration of ent-**1** was (R).
[b] The absolute configuration at C-1 and C-2 of ent-**2** was (S,S).
[c] The absolute configuration of ent-**1** was (S).
[d] The absolute configuration at C-1 and C-2 of ent-**2** was (R,R).

The bigger naphthyl group was introduced in place of phenyl (substrate **1a-1** *vs.* **1b-2**) to exaggerate the steric factor at the pre-existing stereogenic centre C-2. This modification gave rise to a considerable improvement in the optical purity of the PKR product (from 80% to 92% *ee*) when a catalyst bearing **L8** was used (**1b-2** in Table 3). However, under the conditions in which a catalyst bearing **L4** was used, its influence on the enantioselectivity was marginal and its effect on the chemical yield was slightly negative, since the steric congestion near the reaction site made the reaction less efficient.

The replacement of the aryl substituent on the alkyne with an alkyl substituent made a dramatic change of the reaction course. It is mainly attributed to the fact that the presence of an alkyl group on the alkyne expedited the PKR reaction substantially as well as side reactions, resulting in a kind of parallel kinetic resolution.[11]

The characteristics of this case are summarized as follows. The reaction of **1c-1** under the previously described conditions went on too fast to stop at the halfway point of completion. Instead, the reaction consumed **1c-1** completely in less than an hour even at ambient temperature and provided the desired PKR product **2c-1** together with a significant amount of a new product **4c-1**, which was present as an insepara-

ble mixture of diastereoemers and regioisomers of dimeric product[12] (entry 1 in Table 4). Product **4c-1** was presumably derived from the intermediate **8** in Scheme 1.[13] Since the binding of the remaining (±)-**1c-1** to **6′** to form **8** was non-stereoselective and the energy difference between the two competing transient intermediates **6** and **6′** seemed not to be significant, the optical purity of the PKR product was at a negligible level (10–20% *ee*).

Extensive optimization efforts have focused on the suppression of **4c-1** and the improvement of enantioselectivity of **2c-1**. However, all attempts employing Rh(I) catalysts for optimization so far were unsuccessful (entries 2 and 3 in Table 4).

Differing from the reactions with the slow reacting substrates such as **1a** and **1b** (conditions b in Table 1), the reactions of these intrinsically reactive substrates like **1c** proceeded nicely with the much less reactive Ir(I)-based catalyst (3 mol%).[4] Although it required significantly more forcing conditions (reflux in toluene, 12 hr) than the reaction with cationic Rh(I), much cleaner results, affording only the remaining starting material **1c-1** in 54% yield and 67% *ee* and PKR product **2c-1** in 36% with 96% *ee* after 12 h with (R)-**L3** (entry 6 in Table 4). The absolute stereochemistry of product is consistent with the previous study on Rh(I) catalyst; that is, (+)-[R(C1),R(C2)]-**2c-1** and

Table 4. Kinetic resolution of (±)-**1c** having alkyl substituents on the alkyne.

and their regioisomers
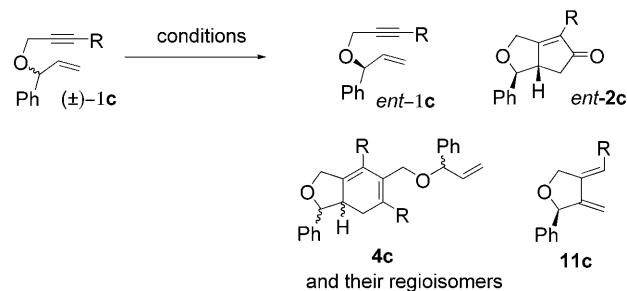
Entry	R²	C[a]	Lig.	t [h]	ent-**1c**[b] Yield [%]/ee [%]	ent-**2c**[c] Yield [%]/ee [%]	**4c**+**11c** Yield[f] [%]
1	Me (**1c-1**)	a	(R)-**L3**	1	0	35/8	50
2		b	(R)-**L3**	1	0	25/11	55
3		c	(R)-**L3**	1	0	44/14	45
4			(R)-**L1**	12	52/60	36/90	10
5			(R)-**L2**	12	55/63	32/91	10
6			(R)-**L3**	12	54/67	36/96	–
7			(R)-**L3**	24	46/78	**41/92**	<5
8		d	(R)-**L4**	12	**42/91**	40/82	10[g]
9			(R)-**L5**	12	48/76	40/82	8
10			(R)-**L6**	12	80/26	20/97	–
11			(S)-**L7**	12	88/8[d]	12/88[e]	–
12			(S)-**L8**	12	74/33[d]	20/92[e]	10
13	Allyl (**1c-2**)	d	(R)-**L3**	28	53/75	**40/90**	–
14			(R)-**L4**	24	**49/94**	42/81	–

[a] *Conditions a:* [Rh(CO)₂Cl]₂ (3 mol%), (R)-BINAP (9 mol%), AgOTf (12 mol%), Ar:CO (10:1, 1 atm), THF, 18–20°C; *conditions b:* same as conditions a, but slow addition of **1c-1** in THF into a solution of the catalyst to maintain the high dilution; *conditions c:* [Rh(CO)₂Cl]₂ (3 mol%), (R)-BINAP (9 mol%), AgOTf (12 mol%), CO (1 atm), THF, 18–20°C; *conditions d:* [Ir(COD)₂Cl]₂ (3 mol%), ligand (9 mol%), toluene, CO (1 atm), reflux.

[b] The absolute configuration of ent-**1c** was (R).

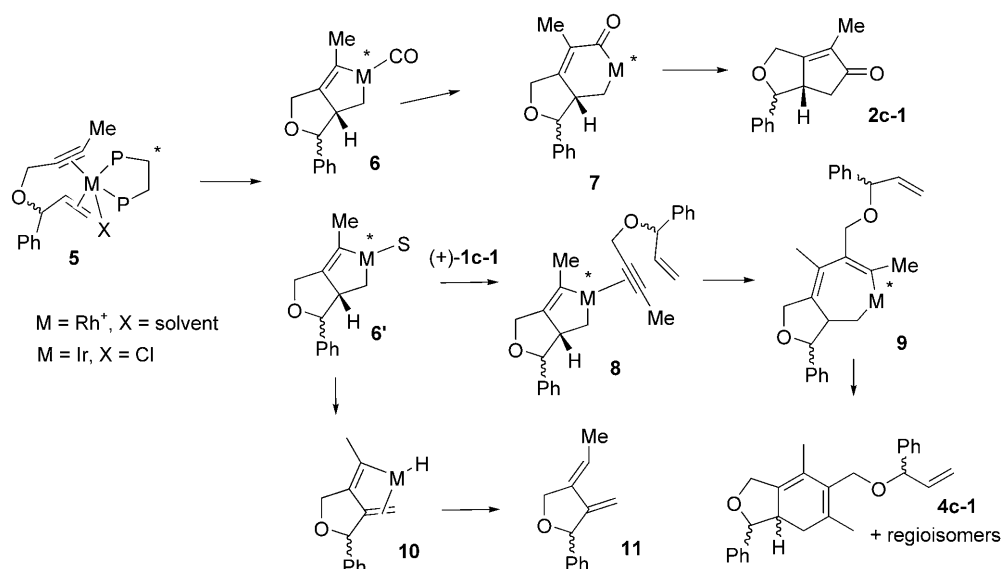[c] The absolute configuration at C-1 and C-2 of ent-**2c** was (S,S).

[d] The absolute configuration of ent-**1c** was (S).

[e] The absolute configuration at C-1 and C-2 of ent-**2c** was (R,R).

[f] **4c** is obtained.

[g] **4c** is contaminated by **11c**.

Scheme 1. Competing pathways in the enantioselective PKR.

(−)-(*S*)-**1c-1** were obtained when (*R*)-BINAP was employed.[7]

The ligand effect on the chemical yields and stereoselectivies was also evident, but less explicable than the reaction of the Rh(I) catalyst. The catalysts having (*R*)-BINAP (**L3**) gave rise to a better enantioselectivity for the PKR product, up to 92% *ee* in 41% yield after optimization with 24 h reaction time (entry 7 in Table 4) and the catalyst having (*R*)-**L4** yielded a better optical purity for the remaining **1c-1**, affording up to 91% *ee* in 42% yield, albeit the formation of **4c-1** was more considerable in the latter case (entries 7 and 8 in Table 4).

The substrate scope of this condition was examined with **1c-2** by employing catalysts having (*R*)-**L3** and (*R*)-**L4**. The recovered (+)-**1c-2** was obtained in 75% *ee* and 53% yield and PKR product **2c-2** in 90% *ee* and 41% yield by utilizing an Ir(I)-based catalyst bearing (*R*)-**L3**, respectively (entry 13 in Table 4).

In conclusion, we have developed a highly efficient kinetic resolution of (±)-1-arylallyl propargyl ethers (**1**) by an enantioselective Pauson–Khand-type reaction. The choice of catalyst depended on the substrates: a cationic Rh(I) catalyst for the substrates having aryl substituents on the alkyne and a neutral Ir(I) catalyst for the substrates having alkyl substituents. In addition, the optical purity of the recovered allyl propargyl ether **1** or PKR product **2** was found to be sensitive to the ligands employed and was fully optimized.

Experimental Section

General Procedure for Kinetic Resolution by Cationic Rh(I) under Reduced Pressure of CO

[Rh(CO)$_2$Cl]$_2$ (2.4 mg, 0.006 μmol, 3 mol%) and a ligand (12.4 mg for (*S*)-**L8**, 0.012 mmol, 6 mol%) were placed in THF (1 mL) and the mixture was stirred for 0.5 hour at 20 °C under an atmospheric pressure of argon. A solution of AgOTf (5.2 mg, 0.020 mmol, 10 mol%) in THF (1 mL) was added, and the resultant reaction mixture was stirred for another 0.5 hour at 20 °C. The argon atmosphere was replaced with a mixture of CO in argon (1:10, 1 atm), and then a solution of **1a-1** (50 mg, 0.201 mmol) in THF (1 mL) was introduced. The reaction mixture was stirred at 20 °C. The progress of the reaction was monitored by TLC and/or by HPLC. At the half-way point to completion, the reaction was stopped by removal of gas. The crude reaction mixture was concentrated under vacuum, and then the residue was purified by column chromatography on silica gel using an *n*-hexane/ethyl acetate mixture as an eluent to afford (+)-(*S*,*S*)-**2a-1**; yield: 25.0 mg (0.090 mmol, 45%) as well as (+)-(*R*)-**1a-1**; yield: 22.2 mg (0.089 mmol, 44%), respectively.

(+)-(*S*,*S*)-3,6-Diphenyl-3a,4-dihydro-1*H*,3*H*-cyclopenta[*c*]furan-5-one (2a-1): IR (KBr): ν = 1710 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.50 (dd, *J* = 18.0, 3.1 Hz, 1H), 2.81 (dd, *J* = 18.0, 6.3 Hz, 1H), 3.27 (m, 1H), 4.43 (d, *J* = 10.2 Hz,

1H), 4.81 (d, *J* = 16.1 Hz, 1H), 5.23 (d, *J* = 16.1 Hz, 1H), 7.37–7.58 (m, 10H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 40.1, 50.9, 67.4, 84.7, 126.3, 128.4, 128.7, 128.95, 128.98, 129.0, 130.7, 135.5, 139.2, 177.6, 206.6; HR-MS (FAB$^+$): *m/z* = 299.1045 [M+Na]$^+$, calcd. for C$_{19}$H$_{16}$O$_2$Na: 299.1048; [α]$_D^{21}$: +30.3 (*c* 7.0, CH$_2$Cl$_2$); the *ee* value was determined as 80% by HPLC analysis using a chiral column (DAICEL CHIRALPAK AS-H, *n*-hexane/*i*-PrOH = 9/1, flow 1.5 mL min^{-1}, detection at 254 nm): retention time: 11.92 min (major) and 14.11 min (minor).

(+)-(*R*)-4-[3-(1-phenyl-allyloxy)-prop-1-ynyl]benzene (1a-1): IR (KBr): ν = 2230 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 4.35 (d, *J* = 15.7 Hz, 1H), 4.43 (d, *J* = 15.7 Hz, 1H), 5.13 (d, *J* = 6.9 Hz, 1H), 5.30 (d, *J* = 10.1 Hz, 1H), 5.37 (d, *J* = 17.3 Hz, 1H), 6.00 (ddd, *J* = 17.3, 10.1, 6.9 Hz, 1H), 7.30–7.49 (m, 10H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 56.4, 81.6, 85.5, 86.5, 117.5, 123.0, 127.4, 128.1, 128.5, 128.7, 128.8, 132.0, 138.3, 140.4; HR-MS (EI$^+$): *m/z* = 248.1218 [M$^+$], calcd. for C$_{18}$H$_{16}$O: 248.1201; [α]$_D^{21}$: +63.4 (*c* 4.8, CH$_2$Cl$_2$); the *ee* value was determined as 99% by HPLC analysis using a chiral column (DAICEL CHIRALPAK OB-H, *n*-hexane/*i*-PrOH = 30/1, flow 0.7 mL min^{-1}, detection at 254 nm): retention time: 16.42 min (major).

4-[3-(3-Phenylallyloxy)-prop-1-ynyl]benzene (3a-1): This product was obtained as an inseparable mixture of *E*- and *Z*-isomers (3:1). IR (KBr): ν = 2233 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$, for *E*-isomer): δ = 4.33 (d, *J* = 6.0 Hz, 2H), 4.45 (s, 2H), 6.35 (dt, *J* = 16.0, 6.0 Hz, 1H), 6.69 (d, *J* = 16.0 Hz, 2H), 7.24–7.58 (m, 10H); ^{1}H NMR (300 MHz, CDCl$_3$, for *Z*-isomer): δ = 4.23 (d, *J* = 6.0 Hz, 2H), 4.45 (s, 2H), 6.35 (dt, *J* = 15.6, 6.0 Hz, 1H), 6.66 (d, *J* = 15.6 Hz, 1H), 7.24–7.58 (m, 10H); ^{13}C NMR (100 MHz, CDCl$_3$, mixture of *E*- and *Z*-isomers): δ = 58.2, 70.6, 71.0, 85.3, 86.6, 122.9, 125.5, 126.2, 126.76, 126.80, 128.0, 128.1, 128.6, 128.7, 128.8, 132.0, 132.8, 133.6, 136.8; HR-MS (EI$^+$): *m/z* = 248.1202 [M$^+$], calcd. for C$_{18}$H$_{16}$O: 248.1201.

General Procedure for Kinetic Resolution by Neutral Ir(I) under Atmospheric Pressure of CO

[Ir(COD)Cl]$_2$ (5.5 mg, 0.008 mmol, 3 mol%) and a ligand (12.0 mg for (*R*)-**L3**) were placed in toluene (1.5 mL) and the mixture was stirred for 0.5 hour at 40 °C under an atmospheric pressure of CO. A solution of **1c-1** (50 mg, 0.269 mmol) in toluene (1.5 mL) was introduced. The reaction mixture was stirred at reflux. The progress of the reaction was monitored by TLC and/or by HPLC. At the half-way point to completion, the reaction was stopped by removal of the gas. The crude reaction mixture was concentrated under vacuum, and then the residue was purified by column chromatography on silica gel using an *n*-hexane/ethyl acetate mixture as an eluent to afford (+)-(*R*,*R*)-**2c-1**; yield: 23.6 mg (0.110 mmol, 41%) and (−)-(*S*)-**1c-1**; yield: 23.1 mg (0.124 mmol, 46%).

(+)-(*R*,*R*)-6-Methyl-3-phenyl-3a,4-dihydro-1H-cyclopenta[*c*]furan-5(3*H*)-one (2c-1): IR (KBr): ν = 1709 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.80 (s, 3H), 2.26 (dd, *J* = 17.8, 2.8 Hz, 1H), 2.63 (dd, *J* = 17.8, 6.3 Hz, 1H), 3.09 (m, 1H), 4.36 (d, *J* = 10.4 Hz, 1H), 4.69 (d, *J* = 15.4 Hz, 1H), 4.87 (d, *J* = 15.4 Hz, 1H), 7.31–7.40 (m, 5H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 9.1, 38.5, 50.9, 65.9, 85.1, 126.2, 128.6, 128.9, 133.4, 139.6, 176.4, 208.7; HR-MS (EI$^+$): *m/z* =

214.0988, [M$^+$], calcd. for C$_{14}$H$_{14}$O$_2$: 214.0994; found; [α]$_D^{25}$: +33.7 (c 7.6, CH$_2$Cl$_2$); the *ee* value was determined as 92% by HPLC analysis using a chiral column (DAICEL CHIR-ALPAK OD-H, *n*-hexane/*i*-PrOH = 9/1, flow 1.0 mL min^{-1}, detection at 254 nm): retention time: 14.35 min (major) and 16.34 min (minor).

(−)-(S)-[1-(But-2-ynyloxy)allyl]benzene (1c-1): IR (KBr): = 2227 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.87 (t, J = 2.2 Hz, 3H), 4.06 (dq, J = 15.2, 2.2 Hz, 1H), 4.13 (dq, J = 15.2, 2.5 Hz, 1H), 4.99 (d, J = 6.6 Hz, 1H), 5.24 (d, J = 10.2 Hz, 1H), 5.30 (d, J = 17.1 Hz, 1H), 5.96 (ddd, J = 17.1, 10.2, 6.6 Hz, 1H), 7.27–7.37 (m, 5H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 3.9, 56.2, 75.4, 81.4, 82.6, 117.2, 127.3, 128.0, 128.7, 138.4, 140.5; HR-MS (EI$^+$): m/z = 186.1061 [M$^+$], calcd. for C$_{13}$H$_{14}$O: 186.1045; [α]$_D^{25}$: −31.6 (c 5.0, CH$_2$Cl$_2$); The *ee* value was determined as 78% by HPLC analysis using a chiral column (DAICEL CHIRALPAK OJ-H, *n*-hexane/*i*-PrOH = 30/1, flow 1.0 mL min^{-1}, detection at 254 nm): retention time: 11.77 min (major) and 19.06 (minor).

References

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[7] The determination of the relative stereochemistry of **2a-1** and **2c-1** as well as the absolute stereochemistry is described in the Supporting Information. In fact, we determined the absolute stereochemistry of the remaining **1a-1** and **1c-1** by comparing of the optical purity of the remaining **1a-1** and **1c-1** with the corresponding enantiomers whose absolute stereochemistry is well established.

[8] Compound **3** was obtained as a mixture of the geometrical isomers.

[9] The electronic and steric characteristics of the ligands mentioned in this manuscript and their effects on the reaction rate and enantioselectivity are described in the literature; a) D. E. Kim, C. Choi, I. S. Kim, S. Jeulin, V. Ratovelomanana-Vidal, J.-P. Genêt, N. Jeong, *Synthesis* **2006**, *23*, 4053–4059; b) D. E. Kim, C. Choi, I. S. Kim, S. Jeulin, V. Ratovelomanana Vidal, J.-P. Genêt, N. Jeong, *Adv. Synth. Catal.* **2007**, *349*, 1999–2006.

[10] The *S* value, unless the yield of **3** is negligible, should be counted as an approximate measure. It was calculated based on the assumption that **3**, if it was formed, was formed from both enantiomers of **1** equally. However, this may not be the case and, since the possibility of a parallel kinetic resolution cannot be eliminated, these numbers are only intended as a rough estimation in these cases. The *S* value with emphasis on the recovered substrate was calculated using the equation $[(1−c)(1−ee)]/\ln[(1−c)(1+ee)]$ while the *S* value with emphasis on product was calculated using the equation $\ln[1−c(1+ee)]/\ln[1−c(1−ee)]$. See refs.[1a,d]

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[12] LC-MS analysis exhibited that this inseparable mixture consisted of seven isomers having the same molecular weight corresponding to the dimeric product of **1c-1** (MW: 372.2).

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