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Efficient Catalytic Asymmetric Synthesis of *trans*-5-Aryl-2-substituted Cyclohexanones by Rhodium-Catalyzed Conjugate Arylation of Racemic 6-Substituted Cyclohexenones

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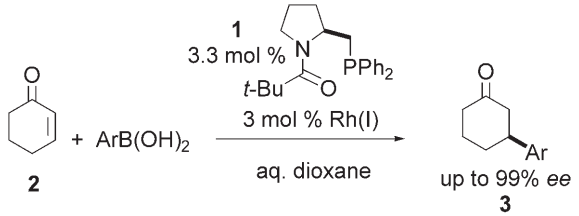
Abstract: Catalytic asymmetric conjugate arylation of racemic 6-substituted cyclohexenones with arylboronic acids was catalyzed by 3 mol% of chiral amidophosphane-$[RhCl(C_2H_4)]_2$ in a 10:1 mixture of 1,4-dioxane and water at 70°C to afford a nearly 1:1 mixture of *trans*- and *cis*-5-aryl-2-substituted cyclohexanones in high enantioselectivity, which was subsequently epimerized with sodium ethoxide in ethanol to give thermodynamically stable *trans*-5-aryl-2-substituted cyclohexanones with 99–97% *ee* in high two-step yields.

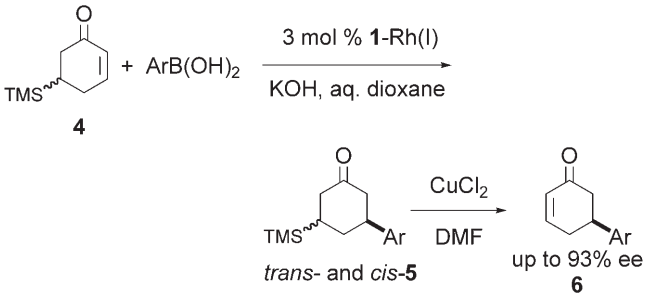
Keywords: arylation; asymmetric catalysis; conjugate addition; cyclohexanones; rhodium

Introduction

The catalytic asymmetric conjugate addition reaction of enones with metal-activated nucleophiles has been the significant historical milestone of modern asymmetric reactions.[1] Tremendous efforts have been devoted on the discovery of efficient chiral sources for the reaction with carbon and heteroatom nucleophiles. Chiral phosphorus compounds have been the recently established fruits of chiral sources for this purpose.[2] A familiar touchstone for the evaluation of chiral sources has been the asymmetric reaction of cyclohexenone **2** with diorganozinc-copper(I)[3] or arylboronic acid-rhodium(I)[4,5] reagent-catalyst combinations (Scheme 1). We have also engaged in this fascinating challenge and succeeded in the development of chiral amidophosphane **1**-based catalytic asymmetric conjugate addition reaction of **2** with organometallic reagents giving **3** (Scheme 1).[6,7] The advantage of conjugate addition reaction lies in the generation of a reactive enolate intermediate that upon treatment with an electrophile produces two new chiral centers in adjacent C2 and C3 positions of the cyclohexanone skeleton. This technology enables us to synthesize chiral disubstituted cyclohexanones with two chiral centers starting from achiral cyclohexenone. Although it is remarkable to know that chiral compounds bearing two chiral centers are produced from an achiral starting substrate by one-pot operation of an asymmetric reaction, it is much more interesting to develop a kind of asymmetric reaction which utilizes racemic substituted cyclohexenone as a substrate to produce chiral disubstituted cyclohexanones bearing two chiral centers in a single operation. It is important to remember that racemic substrates are usually considered as a substrate of kinetic resolution in which a chiral target is obtained as a recovery of the lesser reactive starting material among a pair of enantiomers by preferential consumption of more reactive other enantiomer.[8] We have already developed a two-step asymmetric synthesis of 5-arylcyclohexenones **6**, which utilized racemic 5-(trimethylsilyl)cyclohexenone **4** as a substrate in a chiral amidophosphane **1**-rhodium(I)-catalyzed asymmetric conjugate arylation with arylboronic acids to afford *trans*- and *cis*-3-aryl-5-(trimethylsilyl)cyclohexanones **5** both with high *ee* and subsequent dehydrosilylation of the mixture afforded 5-arylcylohexenones **6** with high *ee* in a reasonably high two-step yield (Scheme 2).[9] It should not be omitted to consider the work by Krause and



Scheme 1.



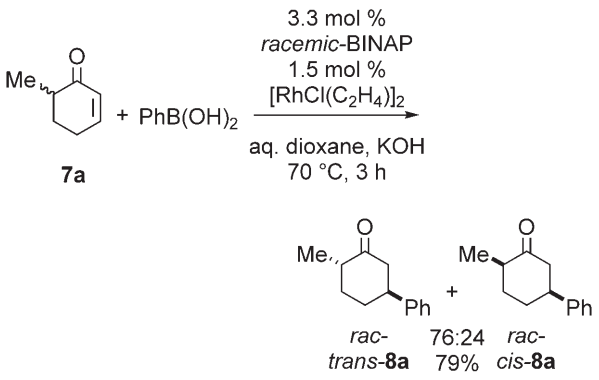
Scheme 2.

Alexakis who reported the asymmetric synthesis of *trans*-5-alkyl-2-methylcyclohexanones starting from 6-methylcyclohexenone **7a** by a chiral phosphoroamidite-copper(I)-catalyzed asymmetric conjugate alkylation with diorganozinc and subsequent epimerization.[10] Now we describe a general, two-step asymmetric synthesis of *trans*-5-aryl-2-substituted cyclohexanones **8** with sufficiently high *ee* starting from racemic 6-substituted cyclohexenones **7**.

Results and Discussion

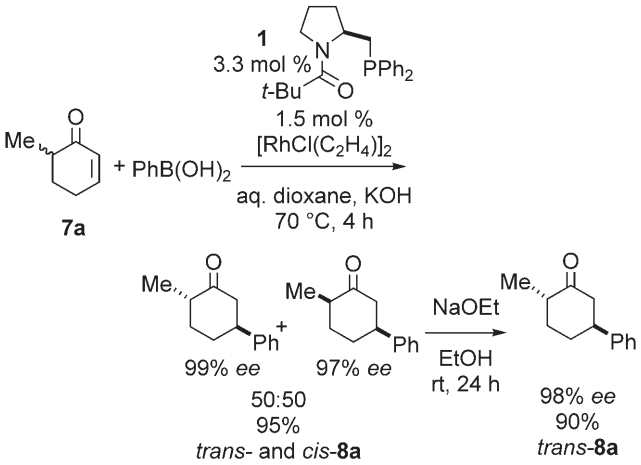
Catalytic Asymmetric Conjugate Arylation of 6-Substituted Cyclohexenones

Conjugate phenylation of racemic 6-methylcyclohexenone **7a** with phenylboronic acid was examined using 3 mol% of racemic-BINAP-rhodium(I)-catalyst in order to gather information on the stereochemical pathway (Scheme 3). The reaction gave a mixture of racemic *trans*- and *cis*-**8a** in a ratio of 76:24 in 79% isolated yield.[11] The similar *trans*-selectivity was also observed in 3-methoxyphenylation (76:24 in 92%) and 3-chlorophenylation (77:23 in 90%), indicating generality in the stereoselective production of *trans*-**8**. This *trans*-selectivity is complementary to that in the organocopper-mediated conjugate addition of **7a** in which the *cis* isomer is obtained as a major product.[12]



Scheme 3.

Chiral catalyst control changes the situation in which an enantiofacial selective arylation is operative over the *trans* control. Thus, the catalytic asymmetric conjugate phenylation of racemic 6-methylcyclohexenone **7a** with phenylboronic acid was conducted in the presence of 3.3 mol% of a chiral amidophosphane **1**, 1.5 mol% of $[RhCl(C_2H_4)_2]_2$ and 1 equivalent of potassium hydroxide in a 10:1 mixture of 1,4-dioxane and water at 70 °C for 4 h to give a 50:50 mixture of *trans*- and *cis*-**8a** both with high *ee* of 99% and 97%, respectively, in 95% combined isolated yield (Scheme 4). Subsequent epimerization of the mixture



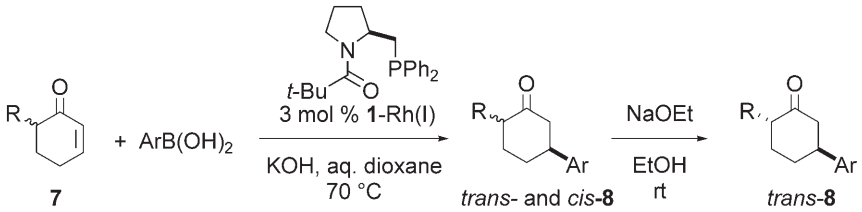
Scheme 4.

with 2 equivalents of sodium ethoxide in ethanol at room temperature for 24 h gave thermodynamically stable *trans*-(2*S*,5*S*)-**8a**[13] in 90% yield.[14] The enantioselectivity of *trans*-**8a** was determined to be 98% *ee* by a chiral stationary phase HPLC. The high yield production of highly enantioenriched *trans*-**8a** indicates that the new chiral centers of *trans*- and *cis*-**8a** were created in the same sense of enantiofacial selectivity. It is remarkable that nearly optically pure *trans*-**8a** was obtained in 86% total yield starting from racemic **7a**.

The two-step catalytic asymmetric synthesis of 5-aryl-2-methylcyclohexanones **8** from racemic **7a** was general to give a 50:50 mixture of *trans*- and *cis*-5-(3-methoxyphenyl)- and 5-(3-chlorophenyl)-2-methylcyclohexanones **8** that were then epimerized to *trans*-**8** with 98% and 99% *ee*, respectively, in high yields (Table 1, entries 1–3).

Other 6-substituted cyclohexenones **7b–d** bearing benzyl, phenyl, and *tert*-butyl group as 6-substituent were also converted to the corresponding nearly 50:50 mixture of *trans*- and *cis*-5-aryl-2-substituted cyclohexanones **8** with high *ee*s in high yields. Subsequent epimerization of these mixtures gave *trans*-**8** with high *ee* of over 97% *ee* in high yields (entries 4–9). It is important to note that the asymmetric conjugate arylation of **7** is general with regard to 6-substitu-

Table 1. Catalytic asymmetric conjugate arylation of racemic **7** and subsequent epimerization to *trans*-**8**.



7 *trans*- and *cis*-**8** *trans*-**8**

Entry	**7**	R	Ar	Time [h]	*trans*-**8** + *cis*-**8** yield [%]	*trans*:*cis*	*trans*-**8** yield [%]	*ee* [%]
1	**7a**	Me	Ph	4	95	50:50	90	98
2	**7a**	Me	3-$MeOC_6H_4$	4	90	51:49	92	98
3	**7a**	Me	3-ClC_6H_4	8	91	50:50	93	99
4	**7b**	Bn	Ph	4	97	50:50	98	98
5	**7b**	Bn	3-$MeOC_6H_4$	7	99	50:50	93	98
6	**7b**	Bn	3-FC_6H_4	4	99	50:50	91	98
7	**7c**	Ph	Ph	7	97	50:50	95	98
8	**7c**	Ph	4-$MeOC_6H_4$	4	96	50:50	88	97
9	**7d**	*t*-Bu	Ph	7	75	63:37	93	98

ent of **7** to afford the corresponding arylated products with high *ee* in high yields. This point is different from the copper(I)-catalyzed conjugate alkylation reaction reported by Alexakis and Krause in which 6-methylcyclohexenone **7a** is the substrate only applicable.[10]

Conclusions

A general, two-step catalytic asymmetric synthesis of 5-aryl-2-substituted cyclohexanones starting from racemic 6-substituted cyclohexenones was developed by applying a chiral amidophosphane-rhodium(I)-catalyzed asymmetric conjugate arylation with a variety of arylboronic acids. The enantioselectivity reached up to 99%.[15]

Experimental Section

All melting points are uncorrected. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$. Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. IR spectra were expressed in cm^{-1}. Purification was carried out by silica gel column chromatography. Racemic 6-substituted cyclohexenones **7** were prepared according to the procedure analogues to those reported.[16]

Catalytic Asymmetric Conjugate Phenylation of 6-Methylcyclohexenone (7a: R = Me) and Subsequent Epimerization to *Trans*-(2*S*,5*S*)-2-Methyl-5-phenylcyclohexanone (8a: R = Me, Ar = Ph) (Table 1, entry 1)

A mixture of 6-methylcyclohexenone (**7a**) (110 mg, 1.0 mmol), phenylboronic acid (610 mg, 5.0 mmol), ligand **1** (11.6 mg, 0.033 mmol) and $[RhCl(C_2H_4)]_2$ (5.8 mg, 0.015 mmol) in 0.25 mL of 4M aqueous KOH (1.0 mmol) and 1,4-dioxane (2.5 mL) was stirred at 70°C for 4 h. After dilution with AcOEt (40 mL), the mixture was washed with 10% NaOH (10 mL) and brine (20 mL), and then dried over sodium sulfate. Concentration and column chromatography (hexane/AcOEt = 40/1) gave a 50:50 mixture of *trans*- and *cis*-**8a** as a colorless oil; yield: 179 mg (95%). The ratio was determined by the integration area of ^1H NMR signals at 2.97 ppm for *trans*-**8a** and 3.26–3.31 ppm for *cis*-**8a**.

A solution of the 50:50 mixture of *trans*- and *cis*-**8a** (112 mg, 0.6 mmol) in 6 mL of 0.2 M sodium ethoxide (1.2 mmol) in ethanol was stirred at room temperature for 24 h. The mixture was diluted with diethyl ether (10 mL), and successively washed with saturated ammonium chloride (10 mL), satd sodium bicarbonate (10 mL) and brine (10 mL), and then dried over sodium sulfate. Concentration and column chromatography (hexane/Et_2O = 20/1) gave *trans*-**8a** as a white solid; yield: 101 mg (90%); 98% *ee*; mp 65–66°C; $[\alpha]_D^{20}$: −28.5 (*c* 1.0, $CHCl_3$). The% *ee* was determined to be 98% by HPLC (Daicel Chiralpak AD-H, hexane/2-propanol = 100/1, 254 nm, 0.5 mL min^{-1}, 20 and 21 min for major and minor). ^1H NMR: δ = 1.08 (d, *J* = 6.4 Hz, 3H), 1.50 and 1.94 (dddd, *J* = 13.1, 13.1, 13.1, 3.4 Hz, each 1H), 2.07 (m, 1H), 2.20 (m, 1H), 2.43–2.56 (m, 2H), 2.61 (ddd, *J* = 13.1, 3.8, 2.0 Hz, 1H), 2.97 (m, 1H), 7.22–7.26 (m, 3H), 7.33 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR: δ = 14.3, 33.2, 35.1, 44.6, 45.8, 49.1, 126.5, 126.7, 128.7, 144.4, 212.1; IR (KBr): ν = 1705 cm^{-1}; EI-MS: *m*/*z* = 188 (M^+); HR-MS-EI *m*/*z* = 188.1204, calcd. for $C_{13}H_{16}O$ (M^+): 188.1201.

(2*S*,5*S*)-5-(3-Methoxyphenyl)-2-methylcyclohexanone (*trans*-8: R = Me, Ar = 3-$MeOC_6H_4$) (Table 1, entry 2)

A 49:51 mixture of *trans*- and *cis*-**8** (determined by the integration area of ^1H NMR signals at 2.95 ppm for *trans*-**8** and 3.22–3.27 ppm for *cis*-**8**) was epimerized to give, after chromatography (hexane/Et_2O = 25/1), *trans*-**8** as a colorless oil; $[\alpha]_D^{20}$: −21.0 (*c* 1.2, $CHCl_3$); 98% *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 100/1, 254 nm, 0.5 mL min^{-1}, 38 and 41 min for major and minor); ^1H NMR: δ = 1.08 (d, *J* =

6.4 Hz, 3H), 1.49 and 1.93 (dddd, $J=13.0$, 13.0, 13.0, 3.7 Hz, each 1H), 2.07 (m, 1H), 2.20 (m, 1H), 2.45–2.54 (m, 2H), 2.60 (ddd, $J=13.0$, 3.7, 2.2 Hz, 1H), 2.95 (m, 1H), 3.81 (s, 3H), 6.77–6.83 (m, 3H), 7.24 (m, 1H); ^{13}C NMR: $\delta=14.3$, 33.1, 35.0, 44.7, 45.8, 49.1, 55.1, 111.6, 112.7, 118.9, 129.7, 146.0, 159.9, 212.1; IR (neat): $\nu=1682\ cm^{-1}$; EI-MS: $m/z=218$ (M^+); HR-MS-EI: $m/z=218.1300$; calcd. for $C_{14}H_{18}O_2$ (M^+): 218.1307.

(2*S*,5*S*)-5-(3-Chlorophenyl)-2-methylcyclohexanone (*trans*-8: R = Me, Ar = 3-ClC$_6$H$_4$) (Table 1, entry 3)

A 50:50 mixture of *trans*- and *cis*-**8** (determined by the integration area of ^{1}H NMR signals at 2.95 ppm for *trans*-**8** and 3.23–3.28 ppm for *cis*-**8**) was epimerized to give, after chromatography (hexane/Et$_2$O = 25/1), *trans*-**8** as a white solid; mp 70–72 °C; $[\alpha]_D^{20}$: −19.3 (*c* 1.1, $CHCl_3$); 99% *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 100/1, 254 nm, 0.5 mL min^{-1}, 20 and 22 min for major and minor); ^{1}H NMR: $\delta=1.09$ (d, $J=6.4$ Hz, 3H), 1.49 and 1.92 (dddd, $J=13.0$, 13.0, 13.0, 3.4 Hz, each 1H), 2.07 (m, 1H), 2.21 (m, 1H), 2.43–2.53 (m, 2H), 2.59 (ddd, $J=13.1$, 4.0, 2.2 Hz, 1H), 2.95 (m, 1H), 7.10 (d, $J=7.6$ Hz, 1H), 7.21–7.28 (m, 3H); ^{13}C NMR: $\delta=14.2$, 33.0, 34.8, 44.6, 45.4, 48.8, 124.8, 126.7, 126.9, 130.0, 134.4, 146.3, 211.6; IR (KBr): $\nu=1713\ cm^{-1}$; EI-MS: $m/z=222$ (M^+); anal. calcd. for $C_{13}H_{15}ClO$: C 70.11, H 6.79; found: C 70.19, H 6.89.

(2*R*,5*S*)-2-Benzyl-5-phenylcyclohexanone (*trans*-8: R = Bn, Ar = Ph) (Table 1, entry 4)

A 50:50 mixture of *trans*- and *cis*-**8** (determined by the integration area of ^{1}H NMR signals at 3.00 ppm for *trans*-**8** and 3.15–3.21 ppm for *cis*-**8**) was epimerized to give, after chromatography (hexane/Et$_2$O = 50/1), *trans*-**8** as a white solid; mp 75–77 °C; $[\alpha]_D^{20}$: +4.5 (*c* 1.0, $CHCl_3$); 98% *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 100/1, 254 nm, 0.5 mL min^{-1}, 46 and 39 min for major and minor); ^{1}H NMR: $\delta=1.47$ and 1.84 (dddd, $J=13.0$, 13.0, 13.0, 3.6 Hz, each 1H), 2.04 (m, 1H), 2.14 (m, 1H), 2.45 (dd, $J=14.0$, 8.7 Hz, 1H), 2.54–2.68 (m, 3H), 3.00 (m, 1H), 3.31 (dd, $J=14.0$, 4.6 Hz, 1H), 7.19–7.34 (m, 10H); ^{13}C NMR: $\delta=32.4$, 33.1, 35.2, 46.0, 49.4, 51.8, 126.0, 126.5, 126.7, 128.4, 128.7, 129.2, 140.3, 144.2, 211.1; IR (KBr): $\nu=1705\ cm^{-1}$; EI-MS: $m/z=264$ (M^+); HR-MS-EI: $m/z=264.1510$, calcd. for $C_{19}H_{20}O$ (M^+): 264.1514.

(2*R*,5*S*)-2-Benzyl-5-(3-methoxyphenyl)cyclohexanone (*trans*-8: R = Bn, Ar = 3-MeOC$_6$H$_4$) (Table 1, entry 5)

A 50:50 mixture of **8** was epimerized to give, after chromatography (hexane/Et$_2$O = 25/1), *trans*-**8** as a white solid; mp 64–66 °C; $[\alpha]_D^{20}$: +4.7 (*c* 1.2, $CHCl_3$); 98% *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 100/1, 254 nm, 0.5 mL min^{-1}, 37 and 32 min for major and minor); ^{1}H NMR: $\delta=1.46$ and 1.83 (dddd, $J=13.0$, 13.0, 13.0, 3.5 Hz, each 1H), 2.04 (m, 1H), 2.13 (m, 1H), 2.45 (dd, $J=14.0$, 8.8 Hz, 1H), 2.56 (ddd, $J=13.0$, 13.0, 1.3 Hz, 1H), 2.60–2.67 (m, 2H), 2.97 (m, 1H), 3.30 (dd, $J=14.0$, 4.6 Hz, 1H), 3.80 (s, 3H), 6.75–6.81 (m, 3H), 7.18–7.31 (m, 6H); ^{13}C NMR: $\delta=32.4$, 33.0, 35.1, 46.0, 49.4, 51.8, 55.1, 111.7, 112.6, 118.8, 126.0, 128.4, 129.2, 129.7, 140.3, 145.9, 159.9, 211.1; IR (KBr): $\nu=1705\ cm^{-1}$; EI-MS: $m/z=294$ (M^+); anal. calcd. for $C_{20}H_{22}O$: C 81.60, H 7.53; found: C 81.32, H 7.55.

(2*R*,5*S*)-2-Benzyl-5-(3-fluorophenyl)cyclohexanone (8: R = Bn, Ar = 3-FC$_6$H$_4$) (Table 1, entry 6)

A 50:50 mixture of **8** (determined by the integration area of ^{1}H NMR signals at 3.00 ppm for *trans*-**8** and 3.15–3.19 ppm for *cis*-**8**) was epimerized to give, after chromatography (hexane/Et$_2$O = 25/1), *trans*-**8** as a white solid; mp 65–67 °C; $[\alpha]_D^{20}$: +8.7 (*c* 1.0, $CHCl_3$); 98% *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 100/1, 254 nm, 0.5 mL min^{-1}, 24 and 20 min for major and minor); ^{1}H NMR: $\delta=1.46$ and 1.82 (dddd, $J=13.0$, 13.0, 13.0, 3.5 Hz, each 1H), 2.04 (m, 1H), 2.14 (m, 1H), 2.45 (dd, $J=14.0$, 8.6 Hz, 1H), 2.54 (dd, $J=13.3$, 13.3 Hz, 1H), 2.61–2.67 (m, 2H), 3.00 (m, 1H), 3.30 (dd, $J=14.0$, 4.9 Hz, 1H), 6.90–6.94 (m, 2H), 6.98 (d, $J=7.6$ Hz, 1H), 7.18–7.31 (m, 6H); ^{13}C NMR: $\delta=32.2$, 32.9, 35.1, 45.6, 49.2, 51.7, 113.4 (d, $J=21.7$ Hz), 113.6 (d, $J=20.7$ Hz), 122.2 (d, $J=3.1$ Hz), 126.1, 128.4, 129.2, 130.1 (d, $J=8.2$ Hz), 140.2, 146.7 (d, $J=7.2$ Hz), 163.0 (d, $J=245$ Hz), 210.6; IR (KBr): $\nu=1713\ cm^{-1}$; EI-MS: $m/z=282$ (M^+); anal. calcd. for $C_{19}H_{19}FO$: C 80.82, H 6.78; found: C 80.80, H 6.98.

(2*R*,5*S*)-2,5-Diphenylcyclohexanone (*trans*-8: R = Ar = Ph) (Table 1, entry 7)

A 50:50 mixture of *trans*- and *cis*-**8** (determined by the integration area of ^{1}H NMR signals at 3.17 ppm for *trans*-**8** and 3.30–3.36 ppm for *cis*-**8**) was epimerized to give, after chromatography (hexane/Et$_2$O = 30/1), *trans*-**8** as a white solid; mp 150–152 °C; $[\alpha]_D^{20}$: +27.2 (*c* 1.2, $CHCl_3$); 98% *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, 254 nm, 0.5 mL min^{-1}, 18 and 20 min for major and minor); ^{1}H NMR: $\delta=2.08$–2.25 (m, 3H), 2.41 (m, 1H), 2.69–2.78 (m, 2H), 3.17 (m, 1H), 3.68 (dd, $J=12.6$, 5.6 Hz, 1H), 7.18 (d, $J=7.0$ Hz, 2H), 7.25–7.31 (m, 4H), 7.35–7.39 (m, 4H); ^{13}C NMR: $\delta=33.4$, 34.3, 45.7, 49.5, 56.9, 126.5, 126.8, 127.1, 128.4, 128.7, 128.8, 138.5, 144.1, 208.9; IR (KBr): $\nu=1713\ cm^{-1}$; EI-MS: $m/z=250$ (M^+); HR-MS-EI: $m/z=250.1355$, calcd. for $C_{18}H_{18}O$ (M^+): 250.1358.

(2*R*,5*S*)-5-(4-Methoxyphenyl)-2-phenylcyclohexanone (*trans*-8: R = Ph, Ar = 4-MeOC$_6$H$_4$) (Table 1, entry 8)

A 50:50 mixture of *trans*- and *cis*-**8** (determined by the integration area of ^{1}H NMR signals at 3.11 ppm for *trans*-**8** and 3.28–3.34 ppm for *cis*-**8**) was epimerized to give, after chromatography (hexane/Et$_2$O = 20/1), *trans*-**8** as a white solid; mp 131–133 °C; $[\alpha]_D^{20}$: +24.7 (*c* 1.0, $CHCl_3$); 97% *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, 254 nm, 0.5 mL min^{-1}, 23 and 26 min for major and minor); ^{1}H NMR: $\delta=2.01$–2.22 (m, 3H), 2.39 (m, 1H), 2.67 (dd, $J=13.1$, 13.1 Hz, 1H), 2.73 (ddd, $J=13.1$, 4.2, 1.6 Hz, 1H), 3.11 (m, 1H), 3.68 (dd, $J=12.6$, 5.4 Hz, 1H), 3.81 (s, 3H), 6.90 (d, $J=8.2$ Hz, 2H), 7.17–7.21 (m, 4H), 7.28 (m, 1H), 7.35–7.38 (m, 2H); ^{13}C NMR: $\delta=33.6$, 34.3, 44.9, 49.8, 55.2, 56.9, 114.1, 127.1, 127.4, 128.4, 128.7, 136.3, 138.5, 158.4, 209.0; IR (KBr): $\nu=1705\ cm^{-1}$; EI-MS: $m/z=280$ (M^+); anal. calcd. for $C_{19}H_{20}O_2$: C 81.40, H 7.19; Found: C 81.10; H 7.42.

(2*R*,5*S*)-2-*tert*-Butyl-5-phenylcyclohexanone (*trans*-8: R = *t*-Bu, Ar = Ph) (Table 1, entry 9)

A 63:27 mixture of *trans*- and *cis*-**8** (determined by the integration area of ^{1}H NMR signals at 2.99 ppm for *trans*-**8** and 3.28–3.33 ppm for *cis*-**8**) was epimerized to give, after chromatography (hexane/Et_2O = 50/1), *trans*-**8** as a white solid; mp 85–87 °C, $[\alpha]_D^{20}$: −4.5 (*c* 1.0, $CHCl_3$), 98 % *ee* (Daicel Chiralpak AD-H, hexane/2-propanol = 100/1, 254 nm, 0.5 mL min^{-1}, 12 and 13 min for major and minor), ^{1}H NMR: δ = 1.04 (s, 9H), 1.59 and 1.89 (dddd, J = 12.8, 12.8, 12.8, 3.7 Hz, each 1H), 2.12 (m, 1H), 2.23–2.31 (m, 2H), 2.47–2.57 (m, 2H), 2.99 (m, 1H), 7.21–7.24 (m, 3H), 7.32 (t, J = 7.4 Hz, 2H); ^{13}C NMR: δ = 27.6, 28.6, 31.7, 33.9, 46.6, 51.1, 59.6, 126.5, 126.7, 128.7, 144.3, 211.3; IR (KBr): ν = 1713 cm^{-1}; EI-MS: m/z = 230 (M^+); anal. calcd. for $C_{16}H_{22}O$: C 83.43, H 9.63; found: C 83.13, H 9.83.

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