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# 铜催化格氏试剂的不对称烯丙基烷基化连续流反应

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**摘要** 基于连续流微通道反应器, 在温和条件下首次实现了铜催化格氏试剂的不对称烯丙基烷基化反应. 在−20～−10 ℃条件下, 用双流路不锈钢折线型连续流微通道反应器, 以极短的保留时间 0.6 s, 实现了铜催化的不同格氏试剂的不对称烯丙基烷基化反应, 获得的产物收率为 82%～99%, *ee* 值中等至良好. 此外, 在连续流反应条件下连续进料 34 min, 放大(*S*)-3-甲基-1-环己烯的合成规模, 获得 0.968 g 的(*S*)-3-甲基-1-环己烯, 收率为 98.7%, *ee* 值为 96.6%, 证明了在连续流条件下铜催化剂可以稳定地催化格氏试剂发生不对称烯丙基烷基化反应.

**关键词** 连续流; 微通道反应器; 铜催化; 不对称烯丙基烷基化; 克级制备

# Copper-Catalyzed Asymmetric Allyl Alkylation Using Grignard Reagents under Continuous Flow

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**Abstract** Continuous flow reactors were used to explore the copper-catalyzed asymmetric allyl alkylation (AAA) reactions of Grignard reagents under milder conditions for the first time. After continuous optimization, a 2-channel stainless steel broken-line continuous flow reactor was used to achieve a copper-catalyzed AAA reaction of various Grignard reagents at −20～−10 ℃ under very short reaction retention time of 0.6 s furnishing the corresponding products in 82%～99% yields with moderate to good enantioselectivity. Furthermore, the copper-catalyzed AAA reaction of 3-bromocyclohexene with methylmagnesium bromide was scaled up under a continuous flow process with continuous feeding for 34 min affording 0.968 g of (*S*)-3-methylcyclohex-1-ene with 98.7% yield and 96.6% *ee*.

**Keywords** continuous flow; micro reactors; copper-catalysis; asymmetric allyl alkylation; gram-scale preparation

## 1 Introduction

Asymmetric allyl alkylation (AAA) reactions play an important role in the construction of complex chiral molecules.[1] In the metal-catalyzed AAA reactions, where non-symmetric allylic alkylation is involved, regioselectivity is a challenge. As a result, the substrate scope of metal-catalyzed AAA reactions is usually restricted to simple symmetrical allyl ester species and stabilized nucleophile.[2-3] Many pioneers have made significant contribu-

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tions to the development of this chemistry. Van Koten[4] and Bäckvall *et al*.[5-6] developed an AAA reaction with good γ-regioselectivity by using Grignard reagent as nucleophiles in the presence of chiral thiophenol cuprous salt and the *ee* value of products was up to 60%. Based on Bäckvall's work, Alexakis' group[7] designed a series of chiral phosphite and phosphoramidite ligands to enhance the control of enantioselectivity generating the *ee* value of desired products up to 95%. Previous works have achieved the AAA reaction of non-stabilized nucleophiles with good to excellent stereoselectivity by using copper catalyst. However, the high activity and instability of the non-stabilized nucleophile reagents required the reaction to perform in a reactor with good airtightness. Furthermore, the precisely controlled dripping rate of the Grignard reagents and the ultra-low reaction temperature were also necessary. All of these factors may limit the application of copper-catalyzed AAA reactions of non-stabilized nucleophiles.

Unlike conventional tank reactors, continuous flow reactors have a larger surface area to volume ratio, higher mixing efficiency, and better heat and mass transfer functions,[8] which allow the continuous flow reactor to tolerate harsh reaction conditions, achieve precise and real-time control of the reaction process, and ensure excellent process safety and good airtightness.[9-11] This technology has been demonstrated as a powerful platform and used in coal chemical, fine chemical and pharmaceutical fields,[12] and shone in AI synthesis.[13] By integrating the components of the microreactor with heat exchange equipment, ultrasonic equipment, light sources, microwave generators, electrochemical devices, *etc*., continuous flow technology could be used to realize ultra-low temperature reactions, high temperature/high pressure reactions, photochemical reactions, microwave reactions, *etc*. Herein, the use of continuous flow technology to achieve copper-catalyzed AAA reaction was explored under shorter reaction time and milder reaction conditions for the first time. The copper-catalyzed AAA reactions were performed in the presence of various Grignard reagents as substrates furnishing the target products. The copper-catalyzed process exhibited a nearly quantitative yield with moderate to good enantioselectivity under a retention time of 0.6 s by using a 2-channels metal broken line reactor. In addition, the stability of this copper-catalyzed AAA reaction of 3-bromocyclohexene with methylmagnesium bromide was also evaluated with continuous feeding for 34 min under a continuous flow process and achieved the large-scale synthesis.

In preliminarily designed three material conveying flow paths (delivering copper salt and ligand, allyl halide, and Grignard reagent respectively) with the T-type mixers as the connection and mixing unit, and a syringe pump was equipped to realize the quantitative conveying of materials. The reactor was placed in an alcohol bath to control the temperature, and in which an ultrasonic module was added to promote the fully mixing of the materials.[14] The reaction mixture was quenched with methanol and following analyzed the yield and *ee* value directly by GC (Figure 1).

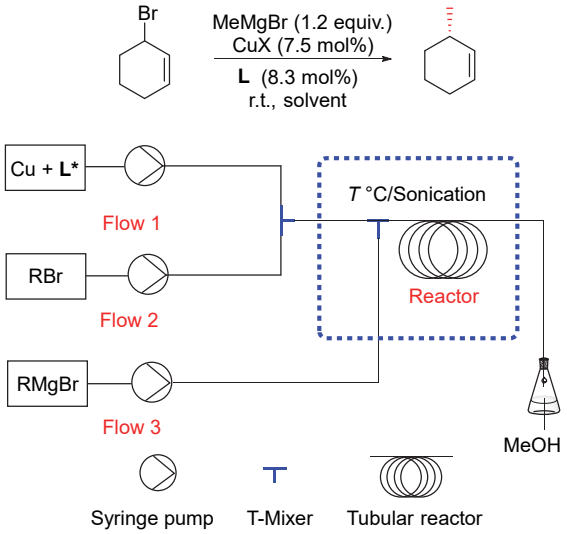


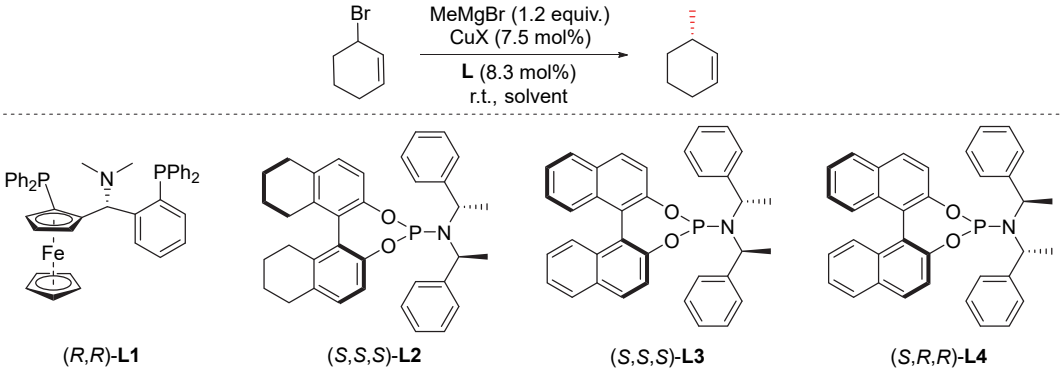

**Figure 1** Template reaction & 3-channel continuous flow reaction device

## 2 Results and discussion

Firstly, the residence time was optimized in the presence of a catalytic system of copper thiophene-2-carboxylate (I) and chiral ligand **L2** by using a polyfluoroalkoxy (PFA) tubular reactor. At the residence time of 64 s, the reaction was performed smoothly at room temperature furnishing desired product in 99% yield with a moderate *ee* value in the absence of the ultrasonic mixing module (Table 1, Entry 1). To our delight, the *ee* value of the reaction was significantly enhanced with an ultrasonic mixing module promoting the complete and uniform mixing of the reaction materials (Table 1, Entry 2). The *ee* value of the reaction increased slightly when the retention time was shortened to 32 s by raising the flow rate to two times (Table 1, Entry 3). However, the flow rate was further increased to get a retention time of 16 s resulting in a decrease in the *ee* value (Entry 4). Maintaining the best residence time, different types of copper salts were further screened, including copper trifluoromethanesulfonate (II), cuprous bromide, cuprous iodide, cuprous cyanide, and cuprous chloride (Table 1, Entries 5～9). Among these, the reaction of 3-bromocyclohex-1-ene and methyl magnesium bromide provided the corresponding product with the best *ee* value in the presence of cuprous chloride. In addition, the reaction using *n*-hexane or methyl *tert*-butyl ether (MTBE) as solvent was also evaluated with cuprous chloride as the catalyst furnishing the target product with a significant drop in the *ee* value. On the other hand, the slight solubility of CuCl and **L2** in dichloromethane (DCM) and the insolubility of CuCl in *n*-hexane or MTBE were a potential risk of clogging the continuous flow reactor. Thus, the reaction in the presence of cuprous bromide dimethyl sulfide was further examined, affording the desired product with good enantioselectivity (Table 1, Entry 12). Satisfactorily, cuprous bromide dimethyl sulfide has a good solubility in

**Table 1** Screening of retention time, copper salt, ligand and solvent[a]




(*R*,*R*)-**L1** (*S*,*S*,*S*)-**L2** (*S*,*S*,*S*)-**L3** (*S*,*R*,*R*)-**L4**

| Entry | Time/s | CuX | Ligand | Solvent | Yield[c]/% | *ee*[d]/% |
|---|---|---|---|---|---|---|
| 1[b] | 64 | CuTc | **L2** | DCM | ＞99 | 48 |
| 2[e] | 64 | CuTc | **L2** | DCM | ＞99 | 67 |
| 3[f] | 32 | CuTc | **L2** | DCM | ＞99 | 69 |
| 4[g] | 16 | CuTc | **L2** | DCM | ＞99 | 64 |
| 5[f] | 32 | $Cu(OTf)_2$ | **L2** | DCM | ＞99 | 61 |
| 6[f] | 32 | CuBr | **L2** | DCM | ＞99 | 69 |
| 7[f] | 32 | CuI | **L2** | DCM | ＞99 | 64 |
| 8[f] | 32 | CuCN | **L2** | DCM | ＞99 | 51 |
| 9[f] | 32 | CuCl | **L2** | DCM | ＞99 | 70 |
| 10[f] | 32 | CuCl | **L2** | MTBE | ＞99 | 53 |
| 11[f] | 32 | CuCl | **L2** | Hexane | ＞99 | 52 |
| 12[f] | 32 | CuBr•$SMe_2$ | **L2** | DCM | ＞99 | 70 |
| 13[f] | 32 | CuBr•$SMe_2$ | **L1** | DCM | ＞99 | 13 |
| 14[f] | 32 | CuBr•$SMe_2$ | **L3** | DCM | ＞99 | 42 |
| 15[f] | 32 | CuBr•$SMe_2$ | **L4** | DCM | ＞99 | 8 |

[a] Room temperature, flow 1 (copper salt-ligand, copper salt 0.019 mol/L, ligand 0.021 mol/L), flow 2 (3-bromocyclohexene, 0.5 mol/L), flow 3 (MeMgBr, 0.6 mol/L); PFA tubular reactor (0.8 mm×127 cm). [b] 0.15 mL/min of flow 2 and 3, 0.3 mL/min of flow 1; without ultrasonic mixing module. [c] NMR yield, $CH_2Br_2$ as internal standard. [d] Measured by gas-phase chiral column. [e] Ultrasonic module mixing. [f] Two times of flow rate, ultrasonic module mixing. [g] Four times of flow rate, ultrasonic module mixing.

DCM avoiding the reactor clogging and back pressure increasing. In addition, another ligand including **L1**, **L3** and **L4** by using cuprous bromide dimethyl sulfide as a catalyst was also evaluated and provided the target products with 8%～42% *ee* (Table 1, Entries 13～15). Through the screening of a series of different reaction conditions, the reaction of 3-bromocyclohex-1-ene and methyl magnesium bromide was performed in a PFA tubular reactor under a retention time of 32 s at room temperature by using CuBr-$Me_2S$-**L2** catalyst system and DCM as solvent giving the desired product with the best enantioselectivity.

However, the reaction involved Grignard reagent which is generally exothermic during the reaction process and the enantioselectivity of the copper-catalyzed AAA reaction was also sensitive to the temperature. Therefore, the use of a metal continuous flow reactor which has higher heat transfer efficiency than the PFA continuous flow reactor would enhance the enantioselectivity of the reaction. In the next step, the reaction temperature and the corresponding retention time were optimized by using a metal continuous flow reactor.

Compared with the PFA reactor, the stainless steel broken line reactor (hole size of 300 mm×500 mm, and the liquid holding capacity is about 18 μL; Figure 2, above) provided (*S*)-3-methylcyclohex-1-ene with a notable drop in enantioselectivity (59% *ee*) under a retention time of 32 s at room temperature (Table 2, Entries 1～2). Fortunately, when the flow rate was greatly increased to shorten the retention time to 0.6 s, the *ee* value was significantly enhanced to 74% (Table 2, Entry 3). At the same retention time, the *ee* value further raised to 82% while the reaction was performed at 0 ℃ (Table 2, Entry 4). Intriguingly, the *ee* value of the reaction was increased to 87% by increasing the material concentration. However, reducing the material concentration led to a drop in enantioselectivity (Table 2, Entries 5～6). Subsequently, the continuous flow system to 2 channels was simplified by mixing 3-bromocyclohexene and copper salt-ligand into a single solution (Figure 2, below) and the reaction was performed by keeping the concentration of each material unchanged to furnish the target product with 85% *ee* (Table 2, Entry 7). Satisfactorily, the *ee* value of the reaction was increased to 96% by decreasing the reaction temperature to －10 ℃ under the continuous flow system with 2 channels (Table

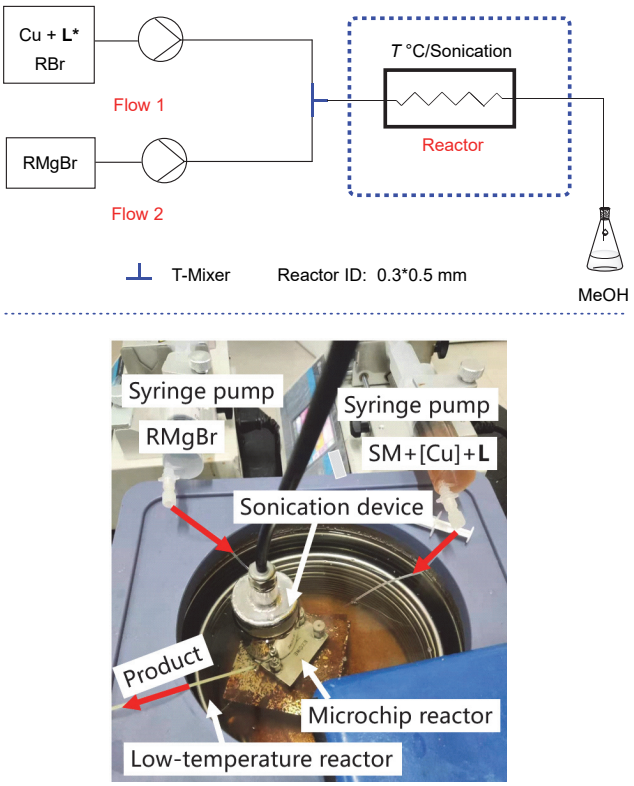



**Figure 2** Schematic and set-up diagram of 2-channels continuous flow reaction device

2, Entry 8). In addition, the reaction was performed at −20 ℃ providing the corresponding products with a slight increase in enantioselectivity (97% *ee*, Table 2, Entry 9).

**Table 2** Optimization of the reaction condition by using the stainless steel broken line reactor

| Entry[a] | $T^b$/℃ | Time/s | Yield[b]/% | *ee*[c]/% |
|---|---|---|---|---|
| 1[d] | r.t. | 32 | >99 | 70 |
| 2[a] | r.t. | 32 | >99 | 59 |
| 3[a] | r.t. | 0.6 | >99 | 74 |
| 4[a] | 0 | 0.6 | >99 | 82 |
| 5[e] | 0 | 0.6 | >99 | 71 |
| 6[f] | 0 | 0.6 | >99 | 87 |
| 7[f,g] | 0 | 0.6 | >99 | 85 |
| 8[f,g] | −10 | 0.6 | >99 | 96 |
| 9[f,g] | −20 | 0.6 | >99 | 97 |

[a] 3-Bromocyclohexene (0.5 mol/L), MeMgBr (0.6 mol/L), CuBr•$SMe_2$-$L_2$ (copper salt 0.019 mol/L, ligand 0.021 mol/L), broken line metal reactor, three channel. [b] NMR yield, $CH_2Br_2$ as internal standard. [c] Measured by gas-phase chiral column. [d] PFA tubular reactor. [e] Concentration double diluted. [f] Concentration doubled. [g] Two channle, catalyst and haloalkane combined.

Based on the above experimental results, it is believed that the 2-flow stainless steel broken liner continuous flow reactor combined with the ultrasonic mixing module would achieve a high yield and excellent enantioselectivity of copper-catalyzed AAA reaction in the temperature range of −20～−10 ℃ with a retention time of 0.6 s.

The application scope of the Grignard reagents was further investigated. Initially, the reaction of a series of various saturated linear aliphatic Grignard reagents was examined and the corresponding products were afforded with a nearly quantitative yield (Table 3, Entries 1～4). However, the *ee* value of the products decreased as the growth of the carbon chain of Grignard reagents (Table 3, Entries 1～3). Unexpectedly, the reaction of dodecane Grignard reagents showed a different tendency, which provided the target product with 71% *ee* (Table 3, Entry 5). To our delight, the carbon chain of Grignard reagents attaching a double bond or phenyl ring on *γ*-position generated the products with the *ee* value of more than 70% (Table 3, Entries 5～6). These results suggested that this strategy could use the long-chain saturated and unsaturated Grignard reagents modified by remote functionalization to achieve high enantioselective AAA reactions. However, the Grignard reagents bearing a substituent on *β*-position furnished the desired product with extremely poor enantioselectivity (Table 3, Entry 7) and the reaction produced (cyclohex-2-en-1-ylmethyl)benzene with no enantioselectivity by using benzyl Grignard reagent as substrate (Table 3, Entry 8). These results further proved that the Grignard reagents bearing a substituent on *β*-position would drastically erode the *ee* value of the corresponding product. In addition, the reaction could also react smoothly with 3-bromocyclohex-1-ene to provide desired products with poor to moderate enantioselectivity by using cyclopentyl or cyclohexyl Grignard reagent bearing a bulky substituent as reaction partners (Table 3, Entries 6～7). The enantioselectivity of the reaction generally had a slight increase while the reaction was performed at −20 ℃, as shown in Table 3.

To verify the stability of the copper-catalyzed AAA reaction under continuous flow conditions, the gram-scale reaction of 3-bromocyclohexene with methylmagnesium bromide. As shown in Figure 3, the large-scale synthesis of (*S*)-3-methylcyclohex-1-ene in excellent yield and high enantioselectivity via the copper-catalyzed AAA reaction under continuous flow conditions with a continuous feeding for 34 min. Starting from the 6th minute of the feed, the enantioselectivity and the yield of the reaction every 4 min and found that the reaction provided the corresponding product in more than 98% yield with more than 96% *ee* under continuous flow conditions. These tests showed that the continuous flow technology guaranteed the stable high yield and enantioselectivity of the copper-catalyzed AAA reaction.

## 3 Conclusions

In summary, the copper-catalyzed AAA reaction by using continuous flow technology for the first time at −20～−10 ℃ has been realized. The copper-catalyzed AAA reactions were performed in the presence of various Grignard reagents as substrates furnishing the target products in a nearly quantitative yield with moderate to good enantioselectivity under a retention time of 0.6 s by using a 2-channels metal broken line reactor. In addition, the stability of the copper-catalyzed AAA reaction of 3-bromo-

**Table 3** Substrate scope of the continuous flow reaction

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| -10 °C | 99% yield<br>96% *ee* | 99% yield<br>86% *ee* | 99% yield<br>33% *ee* | 99% yield<br>71% *ee* | 96% yield<br>70% *ee* |
| -20 °C | 99% yield<br>97% *ee* | 99% yield<br>87% *ee* | 99% yield<br>33% *ee* | 99% yield<br>73% *ee* | 95% yield<br>72% *ee* |
| | **6** | **7** | **8** | **9** | **10** |
| -10 °C | 92% yield<br>74% *ee* | 99% yield<br>13% *ee* | 99% yield<br>0% *ee* | 99% yield<br>56% *ee* | 99% yield<br>22% *ee* |
| -20 °C | 82% yield<br>75% *ee* | | | 84% yield<br>59% *ee* | 99% yield<br>24% *ee* |

[a] Flow 1: 3-bromocyclohexene (0.25 mol/L), copper salt (0.019 mol/L), ligand (0.021 mol/L), mixed solution, 1.2 mL/min; flow 2: RMgBr (0.6 mol/L), 0.6 mL/min; broken line metal reactor. [b] NMR yield, $CH_2Br_2$ as internal standard.

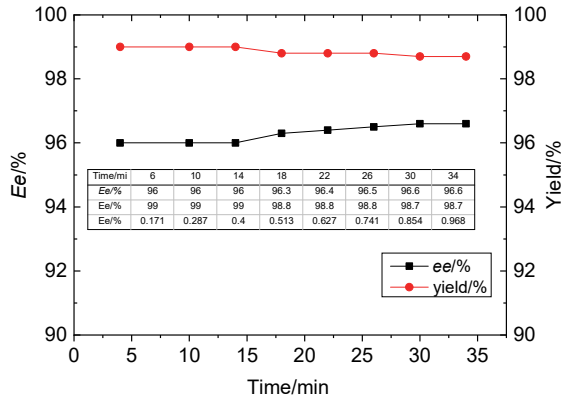



**Figure 3** Continuous flow scale-up of 3-bromocyclohexene

cyclohexene with methylmagnesium bromide was evaluated with continuous feeding for 34 min under a continuous flow process and achieved the large-scale synthesis of (*S*)-3-methylcyclohex-1-ene in 98.7% yield with 96.6% *ee*.

## 4 Experimental section

### 4.1 General experimental information

All reactions were carried out under argon atmosphere with flame-dried glassware. Solvents were redistilled with sodium hydride under nitrogen. All substrates and parts of Grignard reagents were prepared according to the published procedures. All chiral ligands were prepared according to the literature procedure. Other reagents were received from commercial sources. Flash chromatography was performed using 200～300 mesh silica gel with the indicated solvent system. $^1$H (400 MHz) and $^{13}$C (101 MHz) NMR spectra were recorded on a Quantum-I 400M in $CDCl_3$. Evolution of reaction was followed by GC-MS (EI mode) on an Agilent 7890B-5977B. Optical rotations were recorded on an IP-digi300/2 polarimeter at 25 ℃ in a 5 cm cell in the stated solvent. Enantiomeric excesses were determined by chiral GC measurement either on an Agilent 7890B ($H_2$ as vector gas) with the stated column or HPLC UltiMate 3000 with the stated column using isopropanol and *n*-hexane as mobile phase.

### 4.2 General method for continuous flow synthesis of the products **1**～**10**

In a flame-dried Schlenk tube under argon atmosphere, CuBr•$SMe_2$ (0.0375 mmol, 7.5 mol%) and the ligand **L2** (0.0415 mmol, 8.3 mol%) were dissolved in dry DCM (2 mL) and the solution was stirred for 15 min at room temperature. Then, the substrate (0.5 mmol) was added to the solution as the reactant of flow 1. In a separate Schlenk tube, the corresponding organomagnesium reagent (0.6 mmol, 1.2 equiv.) was diluted with dry DCM (combined volume of 1 mL) under nitrogen as the reactant of Flow 2. The two tubes of solution were drawn into two syringes respectively and connected to a predried system filled with nitrogen. The continuous flow system was cooled to the specified temperature in the low-temperature reactor in advance. The flow rates of flow 1 and flow 2 were set to 1.2 and 0.6 mL/min, respectively. The product was collected in MeOH and quenched *in situ*. The solution was diluted with DCM, washed with 1 mol/L HCl and then with brine, dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. The crude mixture was purified on silica gel chromatography column (pentane) to afford the product as a colorless liquid.

(*S*)-3-Methylcyclohex-1-ene (**1**): Colorless liquid (99% yield, 97% *ee*). $^1$H NMR (400 MHz, Chloroform-*d*) *δ*: 5.67～5.60 (m, 1H), 5.56～5.48 (m, 1H), 2.22～2.10 (m, 1H), 1.99～1.92 (m, 2H), 1.82～1.67 (m, 2H), 1.55～1.46 (m, 1H), 1.23～1.13 (m, 1H), 0.97 (d, *J*=7.0 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) *δ*: 133.55, 126.29, 31.32, 30.12, 25.10, 21.75, 21.44. The data are consistent with those reported in the literature.[7]

(*S*)-3-Ethylcyclohex-1-ene (**2**): Colorless liquid (99% yield, 87% *ee*). $^1$H NMR (400 MHz, Chloroform-*d*) *δ*: 5.63～5.71 (m, 1H), 5.63～5.53 (m, 1H), 2.02～1.91 (m,

3H), 1.83～1.68 (m, 2H), 1.46～1.56 (m, 1H), 1.38～1.18 (m, 3H), 0.92 (t, $J$=7.4 Hz, 3H); $^{13}$C NMR (100 MHz, Chloroform-*d*) $\delta$: 132.12, 126.73, 36.87, 29.04, 28.67, 25.43, 21.57, 11.44. The data are consistent with those reported in the literature [7].

(*S*)-3-Butylcyclohex-1-ene (**3**): Colorless liquid (99% yield, 87% *ee*). $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 5.69～5.62 (m, 1H), 5.62～5.56 (m, 1H), 2.10～1.92 (m, 3H), 1.83～1.66 (m, 2H), 1.58～1.45 (m, 1H), 1.36～1.16 (m, 7H), 0.94～0.87 (m, 3H); $^{13}$C NMR (100 MHz, Chloroform-*d*) $\delta$: 132.31, 126.49, 36.19, 35.23, 29.26, 29.21, 25.45, 23.00, 21.61, 14.06. The data are consistent with those reported in the literature [7].

(*S*)-3-Dodecylcyclohex-1-ene (**4**): Colorless liquid (99% yield, 73% *ee*). $[\alpha]_D^{25}$ −16.56 (*c* 1.000, $CHCl_3$); $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 5.69～5.62 (m, 1H), 5.62～5.55 (m, 1H), 2.10～1.94 (m, 3H), 1.83～1.68 (m, 2H), 1.55～1.47 (m, 1H), 1.32～1.26 (m, 23H), 0.91～0.88 (t, $J$=6.6 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta$: 132.42, 126.57, 36.44, 35.19, 31.94, 29.92, 29.70 (br. m, 6C), 29.37, 29.15, 26.98, 25.43, 22.70, 21.57. The data are consistent with those reported in the literature [15].

(*R*)-3-(4-Methylpent-3-enyl)cyclohex-1-ene (**5**): Colorless liquid (95% yield, 72% *ee*). $[\alpha]_D^{25}$ −16.09 (*c* 1.000, $CHCl_3$); $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 5.69～5.62 (m, 1H), 5.62～5.54 (m, 1H), 5.15～5.08 (m, 1H), 2.10～1.93 (m, 5H), 1.83～1.73 (m, 1H), 1.69 (s, 3H), 1.61 (s, 3H), 1.54～1.46 (m, 1H), 1.33～1.22 (m, 4H); $^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta$: 132.16, 131.29, 126.74, 124.73, 36.45, 34.73, 29.03, 25.72, 25.41, 21.52, 17.64. The data are consistent with those reported in the literature [7].

(*R*)-(2-(Cyclohex-2-en-1-yl)ethyl)benzene (**6**): Colorless liquid (82% yield, 75% *ee*). $[\alpha]_D^{25}$ −26.46 (*c* 1.000, $CHCl_3$); $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 7.31～7.23 (m, 2H), 7.21～7.15 (m, 3H), 5.73～5.67 (m, 1H), 5.67～5.60 (m, 1H), 2.70～2.63 (m, 2H), 2.16～2.05 (m, 1H), 2.02～1.96 (m, 2H), 1.88～1.80 (m, 1H), 1.80～1.70 (m, 1H), 1.68～1.47 (m, 4H), 1.29～1.24 (m, 1H); $^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta$: 142.82, 131.73, 128.36, 128.26, 127.10, 125.58, 38.20, 34.74, 33.26, 29.02, 25.39, 21.47. The data are consistent with those reported in the literature [7].

(*R*)-3-Isobutylcyclohex-1-ene (**7**): Colorless liquid (82% yield, 13% *ee*). $[\alpha]_D^{25}$ −22.83 (*c* 1.000, $CHCl_3$); $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 5.68～5.61 (m, 1H), 5.59～5.53 (m, 1H), 2.17～2.08 (d, $J$=2.4 Hz, 1H), 2.00～1.94 (m, 2H), 1.81～1.66 (m, 3H), 1.55～1.45 (m, 1H), 1.23～1.08 (m, 3H), 0.88 (t, $J$=6.8 Hz, 6H); $^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta$: 132.49, 126.59, 45.97, 32.72, 29.40, 25.51, 24.98, 23.11, 22.56, 21.50. The data are consistent with those reported in the literature [7].

(Cyclohex-2-en-1-ylmethyl)benzene (**8**): Colorless liquid (99% yield, 0% *ee*). $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 7.40～7.33 (m, 2H), 7.31～7.24 (m, 3H), 5.82～5.74 (m, 1H), 5.72～5.62 (m, 1H), 2.77～2.60 (m, 2H), 2.52～2.41 (m, 1H), 2.13～2.02 (m, 2H), 1.87～1.74 (m, 2H), 1.67～1.53 (m, 1H), 1.43～1.29 (m, 1H); $^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta$: 140.83, 131.28, 129.10, 128.11, 127.30, 125.72, 42.70, 37.17 28.87, 25.37, 21.27. The data are consistent with those reported in the literature [7].

(*R*)-3-Cyclopentylcyclohex-1-ene (**9**): Colorless liquid (84% yield, 59% *ee*). $[\alpha]_D^{25}$ −72.11 (*c* 1.000, $CHCl_3$); $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 5.72～5.63 (m, 2H), 2.01～1.86 (m, 3H), 1.83～1.70 (m, 4H), 1.66～1.56 (m, 3H), 1.56～1.45 (m, 3H), 1.31～1.12 (m, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta$: 131.27, 127.01, 45.67, 40.94, 30.68, 30.18, 28.50, 25.45, 25.41, 25.34, 21.79. The data are consistent with those reported in the literature [7].

(*R*)-3-Cyclohexylcyclohexene (**10**): Colorless liquid (99% yield, 24% *ee*). $[\alpha]_D^{25}$ −22.57 (*c* 1.000, $CHCl_3$); $^1$H NMR (400 MHz, Chloroform-*d*) $\delta$: 5.75～5.65 (m, 1H), 5.65～5.54 (m, 1H), 2.01～1.88 (m, 3H), 1.77～1.62 (m, 8H), 1.54～1.44 (m, 1H), 1.38～1.29 (m, 1H), 1.27～1.08 (m, 5H); $^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta$: 131.05, 127.17, 42.69, 40.94, 30.25, 30.16, 29.86, 26.89, 26.78, 25.77, 25.45, 22.22. The data are consistent with those reported in the literature [7].

**Supporting Information** $^1$H NMR, $^{13}$C NMR spectra and GC traces of products **1**～**10**, and the optical rotations data of parts of products **1**～**10**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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