Ru-Catalyzed Asymmetric Addition of Arylboronic Acids to Aliphatic Aldehydes via P-Chiral Monophosphorous Ligands

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Abstract: Chiral alcohols are among the most widely applied in fine chemicals, pharmaceuticals and agrochemicals. Herein, the Ru-monophosphine catalyst formed in situ was found to promote an enantioselective addition of aliphatic aldehydes with arylboronic acids, delivering the chiral alcohols in excellent yields and enantioselectivities and exhibiting a broad scope of aliphatic aldehydes and arylboronic acids. The enantioselectivities are highly dependent on the monophosphorous ligands. The utility of this asymmetric synthetic method was showcased by a large-scale transformation.

Keywords: Ru-catalyzed; asymmetric addition; P-chiral monophosphorous ligands; chiral alcohols

1. Introduction

Chiral alcohols are widely present in biologically active substances and pharmaceuticals [1–7]. Of these, chiral aryl alkyl alcohols are one important class of alcohols. The ubiquity of aryl alkyl alcohols as high-ranking intermediates makes them appealing precursors [8–10]. Thus, the invention of methods for the preparing of such chiral aryl alkyl alcohols features an important role in organic synthesis. Classic methods for constructing such chiral molecules include asymmetric hydrogenation of ketones [11–13], asymmetric hydrogen transfer reduction of ketones or unsaturated ketones [14–21], along with the asymmetric addition of organometallic reagents to aldehydes [22–24]. As an alternative, strategies via the asymmetric homologation reaction [25–28], tandem Michael–MPV reaction and subsequent reductive desulfurization [29], as well as the asymmetric addition of aldehydes with arylboronic acids were also established [30,31]. It is worth noting that the tandem α-alkylation/asymmetric reactions of ketones with alcohols [32] and the asymmetric Guerbet reaction of alcohols [33,34] are green and high-efficient strategies.

Similar to the organometallic reagents, the addition of organoborons to carbonyl compounds allows for the generation of chiral alcohols in direct and effective ways. Compared with the disadvantages of organometallic reagents [22–24], the organoborons feature the advantages of easy manipulation, low toxicity and good functional group tolerance [35], which has attracted great attention [36–38] since Miyaura reported the first Rh-catalyzed asymmetric addition of arylboronic acid to aldehydes in 1998 [39]. For example, metals including Rh [40–48], Ru [49], Ni [50], Co [51] and Pd [52–54] have been intensively explored in this regard recently. Additionally, miscellaneous carbonyl compounds, such as asisatins [55–58], ketoesters [59–63], diketones [64–66], trifluoroacetophenones [67–69], inactive ketones [70–72] and aldehydes [73–75] were successfully employed to couple with organoborons reagents.

Despite the fact that these remarkable achievements were created in the asymmetric addition of carbonyl compounds with organoboron reagents, efforts have been mainly devoted to the active ketones [55–69], inactive ketones [70–72], and aromatic aldehydes [73–75],
but studies on aliphatic aldehydes have been less reported [30]. In this regard, the development of new, high-efficient catalytic systems for the enantioselective addition of aliphatic aldehydes with arylboronic acids still is desirable.

L1–L8 (Scheme 1) represent one kind of phosphorus ligand featured with a P-chiral center, which is successfully utilized in asymmetric synthesis [76–82]. For example, the ligands L3 and L9 were discovered to realize the asymmetric addition of aromatic aldehydes and active ketones with arylboronic acids with excellent enantioselectivities [67,83]. Based on this, we envisioned to further extend the utility of these chiral phosphorous ligands in the asymmetric catalysis. Herein, we reported the Ru-catalyzed enantioselective addition of aliphatic aldehydes with arylboronic acids via P-chiral monophosphorous ligands to access chiral secondary alcohols (Scheme 2), delivering the desired aryl alkyl alcohols in excellent yields and enantioselectivities. The application for gram-scale synthesis of 3da was also disclosed.

Scheme 1. Chiral phosphorous ligands developed by Tang’s group.

This work:

\[
\begin{align*}
1, R &= \text{alkyl} \\
2, R &= \text{alkyl} \\
3, R &= \text{alkyl} \\
4, R &= \text{alkyl} \\
\end{align*}
\]

Scheme 2. Asymmetric addition of aliphatic aldehydes with arylboronic acids.

2. Results and Discussions

At the outset of the research, initial experimental results show that the monophosphine ligand L1 effectively promoted the Ru (II)-catalyzed asymmetric addition of phenylpropanal 1a with 4-methylphenylboronic acid 2a to access chiral alcohol 3aa in excellent yields and with good enantioselectivity; only a trace amount of 4aa was obtained as a byproduct (Table 1, entry 1). Further ligand investigations indicated that the ligands had a remarkable influence on enantioselectivity (Table 1, entries 2–5 and entry 11). For instance, good enantioselectivities can be afforded by using L3 or L5 as chiral phosphorous ligands (Table 1, entries 3 and 5), while a racemic or nearly racemic product was formed by employing L2, L4 and L11 (Table 1, entries 2, 4 and 11), indicating that the substituents on the carbon between the phosphorus and oxygen atom appear to have a negative influence on enantioselectivity.
d enantioselectivities are accomplished using rhodium and iridium.

while organic bases, such as 1, 4-diazabicyclo [2.2.2] octane (DABCO), afforded a lower yield than inorganic bases (Table 2, entry 17). Corresponding various bases also delivered providing the corresponding asymmetric addition product.

Solvent screening showcased that xylene/H$_2$O (3:1) at 80 ° C under N$_2$ atmosphere for 12 h. Determined by NMR with dimethyl terephthalate as internal standard.

Similar trends were also observed by using chiral bisphosphine ligands L6–L7 or L9–L10, which were connected via α-position of a P-chiral center (Table 1, entries 6–7 and 9–10). For example, only low enantioselectivity was shown when bisphosphine ligands L6–L7 and L9–L10 were utilized in the reaction, while a moderate enantioselective product could be afforded by using L8 as a bisphosphine ligand, which was coupled at the β-position (Table 1, entry 8). In general, the ruthenium precursors have no influence on the yields and enantioselectivities of this reaction (Table 1, entries 12 and 13). However, only low yields and enantioselectivities are accomplished using rhodium and iridium complexes as precursors (Table 1, entries 14 and 15).

The reaction was further assessed under various reaction conditions (Table 2). Solvent screening showcased that xylene/H$_2$O was the optimal reaction medium, providing the corresponding asymmetric addition product 3aa in full conversion and 91:9 er (Table 2, entry 7). Interestingly, full conversion and 93:7 er were obtained even when the reaction was conducted within 4 h (Table 2, entry 8). Corresponding various bases also delivered the desired chiral alcohol product 3aa in good enantioselectivities (Table 2, entries 9–16), while organic bases, such as 1, 4-diazabicyclo [2.2.2] octane (DABCO), afforded a lower yield than inorganic bases (Table 2, entry 17).

Table 1. Ligand and precursor screening of metal-catalyzed asymmetric additions of aliphatic aldehydes.

| Entry | Metal   | Ligands | Conv. (%) | NMR Yield of 3aa/4aa (%) | Isolated Yield of 3aa (%) | er of 3aa (%) |
|-------|---------|---------|-----------|--------------------------|---------------------------|--------------|
| 1     | [RuCl$_2$(cymene)$_2$] | L1      | >99       | 97/4                     | 92                        | 89:11        |
| 2     | [RuCl$_2$(cymene)$_2$] | L2      | >99       | 91/4                     | 80                        | 50:50        |
| 3     | [RuCl$_2$(cymene)$_2$] | L3      | >99       | 93/3                     | 83                        | 83:17        |
| 4     | [RuCl$_2$(cymene)$_2$] | L4      | 16        | 12/4                     | 10                        | 59:41        |
| 5     | [RuCl$_2$(cymene)$_2$] | L5      | 78        | 64/4                     | 54                        | 83:17        |
| 6     | [RuCl$_2$(cymene)$_2$] | L6      | –         | Trace                    | –                         | 26:74        |
| 7     | [RuCl$_2$(cymene)$_2$] | L7      | 53        | 29/3                     | 12                        | 30:70        |
| 8     | [RuCl$_2$(cymene)$_2$] | L8      | 66        | 41/4                     | 16                        | 77:23        |
| 9     | [RuCl$_2$(cymene)$_2$] | L9      | 69        | 39/2                     | 18                        | 61:39        |
| 10    | [RuCl$_2$(cymene)$_2$] | L10     | 65        | 30/2                     | 14                        | 48:52        |
| 11    | [RuCl$_2$(cymene)$_2$] | L11     | 70        | 36/3                     | 14                        | 57:43        |
| 12    | [RuCl$_2$(benzene)$_2$] | L1      | >99       | 94/5                     | 86                        | 89:11        |
| 13    | [RuCl$_2$(CO)$_2$] | L1      | >99       | 100/0                    | 96                        | 87:13        |
| 14    | [Rh(CH$_2$CH$_2$)$_2$Cl]$_2$ | L1      | >99       | 93/8                     | 80                        | 49:51        |
| 15    | [Ir(coe)$_2$Cl]$_2$ | L1      | –         | Trace                    | –                         | 61:39        |

*Performed with 1a (0.5 mmol), 2a (2.0 eq.), metal (1 mol%), ligand (2 mol%), K$_2$CO$_3$ (2.0 eq.), toluene (1.5 mL), H$_2$O (0.5 mL), at 80 ° C under N$_2$ atmosphere for 12 h. Determined by Chiral OJ H column.
Having established the optimal conditions, we next investigated the scope of the reaction substrates (Scheme 3).

Generally, para-substituted arylboronic acids bearing electron-donating or electron-drawing groups (2a–2h) reacted with phenyl propanal (1a) smoothly to form the relevant alcohol products (3aa, 3ac and 3ae–3ah) in excellent yields and enantioselectivities. However, only moderate yields and good enantioselectivities were observed when arylboronic acids bearing alkoxy substituents in the para position were introduced (3ab and 3ad). On the other hand, the position of the substituent on arylboronic acid has significant influence on enantioselectivity and yield. For instance, arylboronic acids bearing substituents in the ortho position resulted in low yields and enantioselectivities (3ai and 3aj), presumably due to ortho effects [83]. Gratifyingly, the meta-substituted phenylboronic acids are also well compatible under the standard conditions, giving the desired addition products excellent enantioselectivities and yields (3ak–3am). In addition, except for thiophene boronic acid (3ao), other different boronic acids, including 2-naphthalene boronic acid, phenyl boronic acid and disubstituted boronic acid, worked well in this catalytic system to yield the alcohols in excellent yields and enantioselectivities (3an, 3ap and 3aq). Unlike aryl boronic acid bearing alkoxy, phenyl propanal bearing 4-methoxy substituent on the phenyl group resulted in a low yield but with excellent enantioselectivities (3ba and 3be). To our satisfaction, excellent yields and enantioselectivities resulted when furan-substituted propionaldehyde was loaded in this Ru-monophosphine catalytic system (3ca and 3ce). Interestingly, aldehydes with electron-withdrawing substituents (1j) are also compatible with this catalytic system, giving desirable product 3ja in the yield of 74% and 91.9 er.

Table 2. Optimization of reaction conditions a.

| Entry | Solvent | Solvent | Conv. (%) b | NMR Yield of 3aa/4aa (%) b | Isolated Yield of 3aa (%) | er of 3aa (%) c |
|-------|---------|---------|-------------|-----------------------------|--------------------------|-----------------
| 1     | H2O     | K2CO3   | >99         | 91/4                        | 90                       | 86:14          |
| 2     | toluene | K2CO3   | >99         | 94/3                        | 89                       | 87:13          |
| 3     | toluene/H2O (3:1) | K2CO3 | >99         | 96/4                        | 92                       | 89:11          |
| 4     | dioxane | K2CO3   | >99         | 95/3                        | 86                       | 90:10          |
| 5     | dioxane/H2O (3:1) | K2CO3 | >99         | 92/2                        | 76                       | 89:11          |
| 6     | MTBE/H2O (5:1) | K2CO3 | >99         | 80/8                        | 67                       | 90:10          |
| 7     | xylen/H2O (3:1) | K2CO3 | >99         | 95/5                        | 91                       | 91:9           |
| 8     | xylen/H2O (3:1) | K2CO3 | >99         | 96/3                        | 95                       | 93:7           |
| 9     | THF     | K2CO3   | 85          | 64/4                        | 53                       | 76:24          |
| 10    | xylen/H2O (3:1) | K2PO4 | >99         | 93/4                        | 90                       | 89:11          |
| 11    | xylen/H2O (3:1) | Na2CO3 | >99         | 96/4                        | 88                       | 90:10          |
| 12    | xylen/H2O (3:1) | Li2CO3 | >99         | 95/5                        | 82                       | 90:10          |
| 13    | xylen/H2O (3:1) | Cs2CO3 | >99         | 96/5                        | 80                       | 89:11          |
| 14    | xylen/H2O (3:1) | KOH    | >99         | 87/3                        | 91                       | 89:11          |
| 15    | xylen/H2O (3:1) | KOBu   | >99         | 80/3                        | 55                       | 92:8           |
| 16    | xylen/H2O (3:1) | NaOMe  | 89          | 77/2                        | 67                       | 91:9           |
| 17    | xylen/H2O (3:1) | DABCO  | 88          | 78/5                        | 51                       | 90:10          |

a Performed with 1a (0.5 mmol), 2a (2.0 eq.), [RuCl2(cymene)]2 (1.0 mol%), L1 (2 mol%), base (2.0 eq.), solvent (2.0 mL), at 80 °C under N2 atmosphere for 12 h. b Determined by NMR with dimethyl terephthalate as internal standard. c Determined by Chiral OJ-H column. d reaction time: 4 h.
Scheme 3. Substrates of 3-arylpropanal for asymmetric addition with arylboronic acids. 

a, b Performed with 1 (0.5 mmol), 2 (2.0 eq.), [RuCl₃(cymene)]₂ (1.0 mol%), L₁ (2 mol%), K₂CO₃ (2.0 eq.), xylene (1.5 mL) and H₂O (0.5 mL), at 80 °C under N₂ atmosphere for 4 h. 

b The yield is isolated yield and ee is determined by CHIRAL column.

We next investigated the utility of this catalytic system for the substrate scope of aliphatic aldehydes bearing no aryl substituents (Scheme 4). Various common aliphatic aldehydes including cyclohexylformaldehyde, n-heptanal, isoaleraldehyde and propionaldehyde were also well tolerated in this catalytic system. Notably, the electron-withdrawing and electron-donating aryl boronic acids could be used as nucleophiles, generating chiral alcohols in 82%–93% yields and 93:7–95:5 er’s (3da–3ge). Due to the steric hindrance, only a moderate yield and good enantioselectivity were afforded (3ha) when t-BuCHO was employed as a substrate under standard conditions. In addition, cinnamaldehyde can also react with 2a, giving 3ia in 90% ee.
nic acids

In addition, the corresponding addition product of 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (2r) was severed as an organoboron reagent in this system (Scheme 5).

Additionally, in order to gain more insight into the versatility of nucleophilic reagents, other organoboron reagents were utilized under standard conditions. To our delight, potassium trifluoro(phenyl)borate (2s) could be compatible with this catalytic system, providing the desirable product in a moderate yield and with good ee. However, no desired product 3ar was afforded when 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (2r) was severed as an organoboron reagent in this system (Scheme 5).

In order to illustrate the practicability of the catalytic system, we carried out a large-scale reaction of cyclohexyl formaldehyde (1d) and p-methylphenyl boronic acid (2a). Indeed, the corresponding addition product 3da was successfully afforded on a 6.0 mmol scale from 1d in a 91% yield and 94:6 er (Scheme 6).

Scheme 4. Substrates of alkyl aldehyde for asymmetric addition with arylboronic acids $^a,b$.

$^a$ Performed with 1 (0.5 mmol), 2 (2.0 eq.), [RuCl$_2$(cymene)]$_2$ (1.0 mol%), L1 (2 mol%), K$_2$CO$_3$ (2.0 eq.), xylene (1.5 mL) and H$_2$O (0.5 mL), at 80 °C under N$_2$ atmosphere for 4 h. $^b$ The yield is isolated yield and ee is determined by CHIRAL column.

Scheme 5. Substrates and other organoboron reagents tested in the system.

Scheme 6. Large-scale experiment.
The model reaction was measured over time to know about details of this reaction (Scheme 7). To our surprise, the treatment of 1a with 2a under standard conditions within 4 min afforded the desirable alcohol product 3aa in the yield of 96% and 92:8 er, albeit with trace amounts of a ketone byproduct. The best enantioselectivity of product 3aa was observed in 4 h, after which the enantioselectivities of alcohol decreased slightly, and the byproduct ketone increased slightly as time went by. In addition, the racemization of enantioenriched product 3aa was monitored over time under the standard system, which showcased that the yield of 4aa increased gradually, and a slight loss of enantioselectivity was observed (Scheme 8).

Based on the experimental results, we proposed a possible mechanistic cycle described in Scheme 9 [84]. Firstly, the catalyst Ru-L1 was generated in situ with an Ru precursor and L1, followed by a transmetalation with aryl boronic acid to form Int-I under the condition of base. Subsequently, there was the coordination of aliphatic aldehydes with Int-I to generate the Int-II, followed by carbonyl insertion to produce Int-III. The β-H elimination
of Int-III produced byproduct 4. Finally, the addition of product 3 was released, and the catalyst was regenerated under the action of water and aryl boronic acid.

![Scheme 9. Proposed mechanism.](image)

In summary, we described a Ru-catalyzed asymmetric addition of aliphatic aldehydes with aryl boronic acids based on a monophosphorous ligand, providing the corresponding alcohol products in excellent yields and enantioselectivities. A large-scale experiment showcased the utility of this catalytic system, which provides a supplementary method on acquiring chiral aryl alky alcohols.

### 3. Materials and Methods

#### 3.1. General Information

Aliphatic aldehyde, arylboronic acids, dioxane, H$_2$O, MTBE, THF, xylene and toluene were commercially acquired and used directly without further purifications. Reactions were carried out under a nitrogen atmosphere. $^1$H and $^{13}$C NMR spectra were recorded using a 400 MHz NMR spectrometer (CDCl$_3$, $\delta$$_H$ = 7.26 ppm, $\delta$$_C$ = 77.23 ppm). The melting point was determined by a WRR melting point apparatus. The progress of the reaction was monitored by thin layer chromatography (TLC) or Agilent GC-7900. HPLC analyses were performed with an Agilent 1100 instrument using Chiralcel OD-H or OJ-H or Chiralpak AD-H, AS-H, IA or IB columns (0.46 cm diameter x 25 cm length). Optical rotations and MS spectra were recorded on a Perkin Elmer polarimeter (Model 341) and an ESI-ion trap mass spectrometer (Shimadzu LCMS-IT-TOF) separately.

#### 3.2. General Procedure for Asymmetric Addition of Aliphatic Aldehydes

A mixture of aliphatic aldehydes (0.5 mmol), boric acids (1.0 mmol, 2.0 equiv), [RuCl$_2$(cyrene)$_2$] (3.1 mg, 1.0 mol%), L1 (3.3 mg, 2.0 mol%) and K$_2$CO$_3$ (138.2 mg, 2.0 equiv) in $p$-xylene (1.5 mL)/H$_2$O (0.5 mL) was added to a 25.0 mL Schlenk tube successively. Then, the reaction was stirred at 80 °C under N$_2$ for 4h after which the reaction was diluted with H$_2$O (15.0 mL), neutralized with HCl, and extracted with EtOAc (10.0 mL x 3). The organic layer was washed with brine (10.0 mL x 3) and dried over anhydrous MgSO$_4$ after removal of the solvent under vacuum to afford the crude product, which was purified by column chromatography on silica gel with hexanes or petroleum ether/ethyl acetate (5:1 to 20:1) to deliver the desired product 3. The enantioselectivities were determined by OD-H, AD-H, OJ-H, AS-H, IA or IB columns.

3-phenyl-1-(p-tolyl)propan-1-ol (3aa) [85]

$[^1]D$ = +17.5 (c 0.29, CH$_2$Cl$_2$). Yield: 93% (105.1 mg) as yellow solid; m.p. 48–53 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.66–6.66 (m, 9H), 4.60 (dd, $J$ = 7.7, 5.5, 1H), 2.94–2.49 (m, 2H),
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2.32 (s, 3H) and 2.21–1.86 (m, 3H). 13C NMR (100 MHz, CDCl3) δ 141.94, 141.67, 137.33, 129.24, 128.51, 128.43, 125.98, 125.87, 73.75, 40.42, 32.15 and 21.18. The enantiomeric excess was determined by HPLC using Daicel Chiralpak OD-H column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, UV detection at 220 nm, tminor = 13.758 min, tmajor = 16.774 min, and 93.7% ee.

1-(4-methoxyphenyl)-3-phenylpropan-1-ol (3ab) [85]

[a]D 20 = +19.3 (c 0.66, CH2Cl2). Yield: 55% (66.6 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.35–7.08 (m, 7H), 6.86 (d, J = 8.3, 2H), 4.59 (dd, J = 6.7, 1H), 3.77 (s, 3H), 2.78–2.51 (m, 2H) and 2.19–1.89 (m, 3H). 13C NMR (100 MHz, CDCl3) δ 159.11, 141.91, 136.77, 128.49, 128.42, 127.27, 125.87, 113.92, 73.49, 55.32, 40.39 and 32.16. The enantiomeric excess was determined by HPLC using Daicel Chiralpak AD-H column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, UV detection at 220 nm, tminor = 19.320 min, tmajor = 21.773 min and 88:12% ee.

1-(4-(tert-butyl)phenyl)-3-phenylpropan-1-ol (3ac) [86]

[a]D 20 = +10.5 (c 0.32, CH2Cl2). Yield: 97% (130.2 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.54–6.94 (m, 9H), 4.63 (dd, J = 7.9, 5.4, 1H), 2.99–2.54 (m, 2H), 2.25–1.98 (m, 2H), 1.95 (s, 1H) and 1.31 (s, 9H). 13C NMR (100 MHz, CDCl3) δ 150.64, 141.94, 141.62, 128.50, 128.41, 125.85, 125.74, 125.46, 73.71, 40.32, 34.58, 32.18 and 31.42. The enantiomeric excess was determined by HPLC using Daicel Chiralpak OD-H column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, UV detection at 220 nm, tminor = 10.092 min, tmajor = 14.461 min and 93:7% ee.

1-(4-isopropoxyphenyl)-3-phenylpropan-1-ol (3ad) [87]

[a]D 20 = +12.1 (c 0.22, CH2Cl2). Yield: 45% (60.7 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.53–7.03 (m, 7H), 6.86 (d, J = 8.3, 2H), 4.61 (dd, J = 6.7, 1H), 4.53 (p, J = 6.0, 1H), 2.78–2.57 (m, 2H), 2.19–1.93 (m, 2H), 1.87 (s, 1H) and 1.33 (d, J = 6.0, 6H). 13C NMR (100 MHz, CDCl3) δ 157.45, 141.90, 136.51, 128.47, 128.39, 127.25, 125.83, 115.86, 73.55, 69.95, 40.32, 32.17 and 22.09. HRMS-ESI ([M+H]+): calculated for C18H23O2: [M+H]+: 271.1698, found 271.1701. The enantiomeric excess was determined by HPLC using Daicel Chiralpak AD-H column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, UV detection at 220 nm, tminor = 20.451 min, tmajor = 23.591 min and 92:8% ee.

1-(4-chlorophenyl)-3-phenylpropan-1-ol (3ae) [87]

[a]D 20 = +13.1 (c 1.17, CH2Cl2). Yield: 96% (118.3 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.53–6.94 (m, 9H), 4.60 (dd, J = 7.8, 5.3, 1H), 2.81–2.52 (m, 2H), 2.15 (s, 1H) and 2.12–1.88 (m, 2H). 13C NMR (100 MHz, CDCl3) δ 143.06, 141.54, 133.26, 128.67, 128.50, 128.46, 127.37, 126.02, 73.15, 40.51 and 31.95. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 20.117 min, tmajor = 23.060 min and 92:8% ee.

1-(4-bromophenyl)-3-phenylpropan-1-ol (3af) [88]

[a]D 20 = +10.0 (c 1.31, CH2Cl2). Yield: 91% (132.4 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.44 (d, J = 7.9, 2H), 7.35–7.03 (m, 7H), 4.59 (dd, J = 6.6, 1H), 2.75–2.56 (m, 2H), 2.12 (s, 1H) and 2.08–1.89 (m, 2H). 13C NMR (100 MHz, CDCl3) δ 143.58, 141.51, 131.62, 128.50, 128.46, 127.71, 126.02, 121.37, 73.18, 40.47 and 31.93. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 22.304 min, tmajor = 25.606 min and 92:8% ee.

1-(4-fluorophenyl)-3-phenylpropan-1-ol (3ag) [33]

[a]D 20 = +22.1 (c 0.99, CH2Cl2). Yield: 86% (98.8 mg) as a yellowish oil; 1H NMR (400 MHz, CDCl3) δ 7.60–7.09 (m, 7H), 7.01 (t, J = 8.6, 2H), 4.63 (dd, J = 7.8, 5.4, 1H), 2.77–2.57 (m, 2H) and 2.16–1.90 (m, 3H). 13C NMR (100 MHz, CDCl3) δ 162.24 (d, J = 245.4), 141.61, 140.33 (d, J = 3.1), 128.47, 128.44, 127.60 (d, J = 8.0), 125.97, 115.33 (d, J = 21.3), 73.22, 40.57 and 32.02. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 20.004 min, tmajor = 22.949 min and 92:8% ee.

3-phenyl-1-(4-(trifluoromethyl)phenyl)propan-1-ol (3ah) [33]

[a]D 20 = +17.1 (c 1.32, CH2Cl2). Yield: 94% (131.9 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.56 (d, J = 8.0, 2H), 7.39 (d, J = 8.0, 2H), 7.34–6.99 (m, 5H), 4.68 (dd, J = 7.9, 5.2,
1H), 2.77–2.57 (m, 2H), 2.36 (s, 1H) and 2.13–1.91 (m, 2H). 13C NMR (100 MHz, CDCl3) δ 148.98, 141.38, 129.78 (q, J = 32.3), 128.54, 128.45, 126.21, 126.09, 125.46 (q, J = 3.8), 124.32 (q, J = 272.0), 73.17, 40.56 and 31.86. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 210 nm, tminor = 21.798 min, tmajor = 24.466 min and 93.7 er.

1-(2-fluorophenyl)-3-phenylpropan-1-ol (3ai) [33]

[α]D20 = +20.8 (c 0.53, CH2Cl2). Yield: 49% (52.7 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.45 (t, J = 7.6, 1H), 7.39–6.89 (m, 8H), 5.01 (t, J = 6.5, 1H), 2.90–2.58 (m, 2H) and 2.19–1.98 (m, 3H). 13C NMR (100 MHz, CDCl3) δ 159.87 (d, J = 245.5), 141.64, 131.50 (d, J = 13.2), 128.93 (d, J = 8.3), 128.44, 128.43, 127.34 (d, J = 4.7), 125.92, 124.35 (d, J = 3.6), 115.37 (d, J = 21.9), 68.01 (d, J = 2.5), 39.42 and 32.02. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 17.583 min, tmajor = 19.992 min and 84.16 er.

1-(2-methoxyphenyl)-3-phenylpropan-1-ol (3aj) [89]

[α]D20 = +18.5 (c 0.19, CH2Cl2). Yield: 16% (19.4 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.38–7.11 (m, 7H), 6.96 (t, J = 7.4, 1H), 6.88 (d, J = 8.2, 1H), 4.88 (dd, J = 8.0, 5.1, 1H), 3.84 (3H), 2.89–2.57 (m, 3H) and 2.22–2.02 (m, 2H). 13C NMR (100 MHz, CDCl3) δ 156.65, 142.20, 132.27, 128.48, 128.39, 128.31, 127.02, 125.72, 120.80, 110.58, 70.71, 55.27, 38.68 and 32.38. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 19.673 min, tmajor = 24.260 min and 74:26 er.

1-(3-chlorophenyl)-3-phenylpropan-1-ol (3ak) [88]

[α]D20 = +15.0 (c 0.55, CH2Cl2). Yield: 91% (111.7 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.46–6.98 (m, 9H), 4.59 (dd, J = 7.9, 5.2, 1H), 2.85–2.53 (m, 2H), 2.26 (s, 1H) and 2.10–1.90 (m, 2H). 13C NMR (100 MHz, CDCl3) δ 146.74, 141.51, 134.43, 129.83, 128.51, 128.48, 127.73, 126.37, 126.03, 124.11, 73.20, 40.48, 31.94. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 21.487 min, tmajor = 27.495 min and 93.7 er.

3-phenyl-1-(m-tolyl)propan-1-ol (3al) [88]

[α]D20 = +21.0 (c 0.98, CH2Cl2). Yield: 87% (98.3 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.63–6.82 (m, 9H), 4.59 (dd, J = 7.8, 5.5, 1H), 2.84–2.53 (m, 2H), 2.23 (s, 3H) and 2.18–1.91 (m, 3H). 13C NMR (100 MHz, CDCl3) δ 144.64, 141.93, 138.19, 128.52, 128.47, 128.44, 128.42, 126.70, 125.89, 123.08, 73.94, 40.47, 32.17 and 21.53. The enantiomeric excess was determined by HPLC using Daicel Chiralpak IB column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 17.873 min, tmajor = 20.271 min and 92.8 er.

1-(3-isopropylphenyl)-3-phenylpropan-1-ol (3am) [90]

[α]D20 = +18.3 (c 1.14, CH2Cl2). Yield: 91% (102.8 mg) as a yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.35–7.02 (m, 9H), 4.62 (dd, J = 7.9, 5.3, 1H), 2.89 (hept, J = 6.9, 1H), 2.80–2.59 (m, 2H), 2.16–1.88 (m, 3H) and 1.24 (d, J = 7.0, 6H). 13C NMR (100 MHz, CDCl3) δ 149.23, 144.65, 141.96, 128.55, 128.45, 125.90, 125.77, 124.17, 123.47, 74.11, 40.51, 34.24, 32.23 and 24.12 (d, J = 3.0). HRMS-ESI (m/z): calculated for C18H22NaO, [M+Na]+: 277.1568, found 277.1574. The enantiomeric excess was determined by HPLC using Daicel Chiralpak OD-H column, hexane/i-PrOH 95:5, flow rate 0.5 mL/min, UV detection at 220 nm, tminor = 13.494 min, tmajor = 16.836 min and 92.8 er.

1-(napthalen-2-yl)-3-phenylpropan-1-ol (3ao) [91]

[α]D20 = +13.3 (c 1.31, CH2Cl2). Yield: 99% (130.2 mg) as a light-yellow solid; m.p. 81–83 °C; 1H NMR (400 MHz, CDCl3) δ 7.86–7.62 (m, 4H), 7.42 (dd, J = 12.0, 7.9, 3H), 7.23 (d, J = 7.1, 2H), 7.14 (d, J = 8.0, 3H), 4.74 (t, J = 6.6, 1H), 2.82–2.48 (m, 2H), 2.30 (s, 1H) and 2.22–1.98 (m, 2H). 13C NMR (100 MHz, CDCl3) δ 141.99, 141.86, 133.36, 133.10, 128.56, 128.50, 128.44, 128.04, 127.80, 126.26, 125.97, 125.95, 124.79, 124.17, 74.00, 40.38 and 32.12. The enantiomeric excess was determined by HPLC using Daicel Chiralpak OD-H column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, UV detection at 220 nm, tminor = 18.230 min, tmajor = 23.050 min and 92.8 er.
\[ \delta = 7.38 - 6.90 (m, 8H), 4.60 (dd, J = 7.9, 5.2, 1H), 6.82 (d, 2H), 4.63 (t, J = 6.7, 1H), 3.78 (s, 3H), 2.74 - 2.54 (m, 2H), 2.34 (s, 3H), 2.18 - 1.95 (m, 2H) \]

\[ \delta = 7.8, 5.5, 1H), 2.62 (t, J = 8.2, 2H), 2.33 (s, 3H), 2.23 (s, 3H) \]

\[ \delta = 7.29 (q, J = 8.3, 4H), 7.09 (d, J = 8.2, 2H), 6.82 (d, J = 8.3, 2H), 4.64 (dd, J = 7.9, 5.3, 1H), 3.78 (s, 3H), 2.75 - 2.54 (m, 2H) \]

\[ \delta = 7.3, 2.65 (h, J = 21.1), 2.18 - 1.94 (m, 2H) \]

\[ \delta = 7.2, 1.8, 1H) \]

\[ \delta = 7.3, 2.62 (t, J = 8.6, 8.1, 2H), 2.33 (s, 3H), 2.23 (s, 3H) \]

\[ \delta = 7.38 - 6.90 (m, 8H), 4.60 (dd, J = 7.9, 5.2, 1H), 6.82 (d, 2H), 4.63 (t, J = 6.7, 1H), 3.78 (s, 3H), 2.74 - 2.54 (m, 2H), 2.34 (s, 3H), 2.18 - 1.95 (m, 2H) \]
Molecules 2022, 128.53, 127.30, 73.97, 39.16, 31.76, 29.16, 25.67, 22.60 and 14.08. The enantiomeric excess was 1.42–1.15 (m, 8H) and 0.87 (t, J = 1.24–0.85 (m, 5H).

\[ \delta = 11.107 \text{ min} \text{ and } 93:7 \text{ er} \]

\[ \delta = +21.9 (\text{CDCl}_3) \]

\[ \delta = 11.2, 10.0, 5.5, 1H) \text{ and } 1.27–0.93 (m, 5H). \]

\[ \delta = 142.03, 132.99, 128.29, 127.99, 78.61, 45.00, 29.19, 28.65, 26.37, 26.05 \text{ and } 25.97. \]

\[ \delta = 7.44-7.09 (m, 4H), 4.33 (s, 1H), 1.91 (d, J = 12.9, 1H), 1.82–1.47 (m, 4H), 1.36 (d, J = 12.6, 1H) \text{ and } 0.93 (m, 5H). \]

\[ \delta = 117.1, 105.3, 54.84 (q, J = 32.3), 126.90, 125.08 (q, J = 3.9), 124.22 (q, J = 271.9), 78.63, 45.03, 29.22, 28.36, 26.31, 26.04 \text{ and } 25.94. \]

The enantiomeric excess was determined by HPLC using Daicel Chiralpak IA column, hexane/i-PrOH 98:2, flow rate 0.5 mL/min, UV detection at 220 nm, t\text{minor} = 25.489 min, \text{t} = 27.163 min and 95.5 er.

\[ \text{cyclohexyl}(p-tolyl)\text{methanol} (3\text{dh}) [94] \]

\[ \delta = +16.5 (c 1.06, \text{CH}_2\text{Cl}_2). \text{ Yield: } 83\% (107.1 \text{ mg}) \text{ as a white solid; m.p. } 55–57^\circ C; \]

\[ \delta = 142.07, 137.07, 129.10, 125.91, 74.53, 39.07, 31.82, 29.26, 25.88, 22.66, 21.13 \text{ and } 14.11. \]

The enantiomeric excess was determined by HPLC using Daicel Chiralpak AS-H column, hexane/i-PrOH 99:1, flow rate 1.0 mL/min, UV detection at 220 nm, t\text{minor} = 8.920 min, t\text{major} = 11.107 min and 93.7 er.

\[ 1-(p-tolyl)\text{heptan-1-ol} (3\text{ea}) [92] \]

\[ \delta = +21.7 (c 0.95, \text{CH}_2\text{Cl}_2). \text{ Yield: } 93\% (95.7 \text{ mg}) \text{ as a yellow solid; m.p. } 34–35^\circ C; \]

\[ \delta = 143.67, 139.37, 136.46, 133.44, 128.53, 127.30, 73.97, 39.16, 31.76, 29.16, 25.67, 22.60 \text{ and } 14.08. \]

The enantiomeric excess was determined by HPLC using Daicel Chiralpak OJ-H column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, UV detection at 220 nm, t\text{minor} = 17.151 min and 91.9 er.

\[ \text{HRMS-ESI} (m/z): \text{ calc for } C_{18}H_{18}\text{OF}: [M+H]: 245.1342, \text{ found } 245.1335. \]

\[ \text{cyclohexyl}(4-(trifluoromethyl)(phenyl)\text{methanol} (3\text{dh}) [94] \]

\[ \delta = +16.5 (c 1.06, \text{CH}_2\text{Cl}_2). \text{ Yield: } 83\% (107.1 \text{ mg}) \text{ as a white solid; m.p. } 55–57^\circ C; \]

\[ \delta = 142.07, 137.07, 129.10, 125.91, 74.53, 39.07, 31.82, 29.26, 25.88, 22.66, 21.13 \text{ and } 14.11. \]

The enantiomeric excess was determined by HPLC using Daicel Chiralpak IA column, hexane/i-PrOH 98:2, flow rate 0.5 mL/min, UV detection at 220 nm, t\text{minor} = 23.564 min and 93.7 er.

\[ 1-(p-tolyl)\text{heptan-1-ol} (3\text{ea}) [92] \]

\[ \delta = +21.7 (c 0.95, \text{CH}_2\text{Cl}_2). \text{ Yield: } 93\% (95.7 \text{ mg}) \text{ as a yellow solid; m.p. } 34–35^\circ C; \]

\[ \delta = 143.67, 139.37, 136.46, 133.44, 128.53, 127.30, 73.97, 39.16, 31.76, 29.16, 25.67, 22.60 \text{ and } 14.08. \]

The enantiomeric excess was determined by HPLC using Daicel Chiralpak AS-H column, hexane/i-PrOH 99:1, flow rate 1.0 mL/min, UV detection at 220 nm, t\text{minor} = 8.920 min, t\text{major} = 11.107 min and 93.7 er.

\[ 1-(4-chlorophenyl)\text{heptan-1-ol} (3\text{ee}) [95] \]

\[ \delta = +21.1 (c 0.97, \text{CH}_2\text{Cl}_2). \text{ Yield: } 86\% (97.4 \text{ mg}) \text{ as a yellow solid; m.p. } 50–52^\circ C; \]

\[ \delta = 142.07, 137.07, 129.10, 125.91, 74.53, 39.07, 31.82, 29.26, 25.88, 22.66, 21.13 \text{ and } 14.11. \]

The enantiomeric excess was determined by HPLC using Daicel Chiralpak OJ-H column, hexane/i-PrOH 99:1, flow rate 0.5 mL/min, UV detection at 220 nm, t\text{minor} = 28.980 min, t\text{major} = 32.669 min and 94.6 er.

\[ 3\text{-methyl-1-((p-tolyl)butan-1-ol} (3\text{fa}) [96] \]

\[ \delta = +35.0 (c 0.78, \text{CH}_2\text{Cl}_2). \text{ Yield: } 88\% (78.3 \text{ mg}) \text{ as a yellow solid; m.p. } 40–43^\circ C; \]

\[ \delta = 143.67, 139.37, 136.46, 133.44, 128.53, 127.30, 73.97, 39.16, 31.76, 29.16, 25.67, 22.60 \text{ and } 14.08. \]

The enantiomeric excess was determined by HPLC using Daicel Chiralpak OJ-H column, hexane/i-PrOH 99:1, flow rate 0.5 mL/min, UV detection at 220 nm, t\text{minor} = 17.151 min and 91.9 er.
(100 MHz, CDCl₃) δ 142.30, 137.14, 129.16, 125.88, 72.60, 48.28, 24.84, 23.10, 22.36 and 21.13. The enantiomeric excess was determined by HPLC using Daicel Chiralpak AS-H column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, UV detection at 220 nm, t_major = 5.628 min and 93.7 er.

1-(4-chlorophenyl)-3-methylbutan-1-ol (3fe) [97]

[α]D²⁰ = +37.9 (c 0.81, CH₂Cl₂). Yield: 82% (81.4 mg) as a light-yellow oil; 1H NMR (400 MHz, CDCl₃) δ 7.27 (q, J = 8.5, 4H), 4.69 (dd, J = 8.1, 5.3, 1H), 2.08 (s, 1H), 1.73–1.57 (m, 2H), 1.50–1.38 (m, 1H) and 0.93 (dd, J = 6.4, 2.0, 6H). 13C NMR (100 MHz, CDCl₃) δ 143.70, 133.06, 128.58, 127.27, 72.09, 48.39, 24.75, 23.09 and 22.22. The enantiomeric excess was determined by HPLC using Daicel Chiralpak AS-H column, hexane/i-PrOH 99:1, flow rate 0.5 mL/min, UV detection at 210 nm, t_minor = 24.966 min, t_major = 28.431 min and 95.5 er.

1-(p-tolyl)propan-1-ol (3ga) [98]

[α]D²⁰ = +37.2 (c 0.44, CH₂Cl₂). Yield: 88% (66.0 mg) as a light-yellow oil; 1H NMR (400 MHz, CDCl₃) δ 7.21 (d, J = 8.1, 2H), 7.14 (d, J = 7.4, 2H), 4.53 (t, J = 6.7, 1H), 2.34 (s, 3H), 1.94 (s, 1H), 1.88–1.64 (m, 2H) and 0.90 (t, J = 6.4, 3H). 13C NMR (100 MHz, CDCl₃) δ 141.67, 137.14, 129.09, 125.96, 75.89, 31.81, 21.12 and 10.20. The enantiomeric excess was determined by HPLC using Daicel Chiralpak AS-H column, hexane/i-PrOH 98:2, flow rate 1.0 mL/min, UV detection at 220 nm, t_minor = 10.091 min, t_major = 12.376 min and 94.6 er.

1-(4-chlorophenyl)propan-1-ol (3ge) [98]

[α]D²⁰ = +32.9 (c 0.54, CH₂Cl₂). Yield: 83% (70.5 mg) as a light-yellow oil; 1H NMR (400 MHz, CDCl₃) δ 7.39–7.14 (m, 4H), 4.53 (t, J = 6.7, 1H), 2.29 (s, 1H), 1.81–1.61 (m, 2H) and 0.87 (t, J = 8.3, 3H). 13C NMR (100 MHz, CDCl₃) δ 143.03, 133.05, 128.49, 127.37, 75.24, 31.91 and 9.97. The enantiomeric excess was determined by HPLC using Daicel Chiralpak OD-H column, hexane/i-PrOH 98:2, flow rate 1.0 mL/min, UV detection at 210 nm, t_major = 13.033 min, t_major = 14.609 min and 93.7 er.

2,2-dimethyl-1-(p-tolyl)propan-1-ol (3ha) [30]

[α]D²⁰ = +30.0 (c 0.23, CH₂Cl₂). Yield: 45% (40.1 mg) as a light-yellow oil; 1H NMR (400 MHz, CDCl₃) δ 7.20 (d, J = 8.1, 2H), 7.13 (d, J = 8.0, 2H), 4.37 (d, J = 2.2, 1H), 2.35 (s, 3H), 1.83 (s, 1H) and 0.92 (s, 3H). 13C NMR (101 MHz, CDCl₃) δ = 139.25, 136.89, 128.27, 127.51, 82.30, 35.62, 25.94 and 21.11. The enantiomeric excess was determined by HPLC using Daicel Chiralpak AS-H column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, UV detection at 220 nm, t_minor = 4.778 min, t_major = 6.400 min and 97.3 er.

(E)-3-phenyl-1-(p-tolyl)prop-2-en-1-ol (3ia) [99]

[α]D²⁰ = +33.9 (c 1.03, CH₂Cl₂). Yield: 92% (102.7 mg) as a yellow solid; m.p. 65–68 °C; 1H NMR (400 MHz, CDCl₃) δ 7.54–6.99 (m, 9H), 6.62 (d, J = 15.8, 1H), 6.33 (dd, J = 15.8, 6.4, 1H), 5.28 (d, J = 6.4, 1H), 2.35 (s, 1H) and 2.32 (s, 3H). 13C NMR (100 MHz, CDCl₃) δ 139.98, 137.55, 136.71, 131.79, 130.52, 129.37, 128.62, 127.77, 126.69, 126.43, 74.97 and 21.23. The enantiomeric excess was determined by HPLC using Daicel Chiralpak OD-H column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, t_minor = 16.002 min, t_major = 22.736 min and 95.5 er.

4'-Methyl-3-phenylpropophene (4aa) [100]

Yellow oil; 1H NMR (400 MHz, CDCl₃) δ 7.85 (d, J = 8.3, 2H), 7.35–7.15 (m, 7H), 3.26 (t, 2H), 3.05 (t, J = 7.8, 2H) and 2.39 (s, 3H). 13C NMR (100 MHz, CDCl₃) δ 198.98, 143.92, 141.45, 134.36, 129.34, 128.57, 128.49, 128.22, 126.16, 40.42, 30.23 and 21.72.

Ru-L1

Yield: 85% (35 mg) as a red solid. 1H NMR (400 MHz, CDCl₃) δ 7.36 (t, J = 7.9 Hz, 1H), 7.19 (t, J = 8.3 Hz, 1H), 6.93 (dd, J = 7.6, 1.1 Hz, 1H), 6.88–6.77 (m, 3H), 5.38 (d, J = 10.9 Hz, 1H), 4.49 (d, J = 10.9 Hz, 1H), 3.96 (s, 3H), 3.77 (s, 3H) and 0.87 (d, J = 14.0 Hz, 9H). 13C NMR (100 MHz, CDCl₃) δ 161.80, 157.76, 157.17, 136.47, 131.00, 127.61, 125.59, 124.43, 118.32, 110.68, 108.49, 70.53, 63.47, 55.94, 36.42 and 27.25. 31P NMR (162 MHz, CDCl₃) δ 72.32. HRMS-ESI (m/z): calculated for C₃₈H₄₇O₆Cl₂RuP₂ [M+H]: 833.1268, found 833.1254.
21. Ramasamy, B.; Gangwar, M.K.; Ghosh, P. Asymmetric transfer hydrogenation of α,β-unsaturated carbonyl compounds to saturated alcohols as catalyzed by iridium complexes of tricyclic bioxazoline-fused imidazole-derived N-heterocyclic carbene ligands. *ChemistrySelect* **2019**, *4*, 357–365. [CrossRef]

22. Bolm, C.; Muniz, K. Catalytic enantioselective aryl transfer: Asymmetric addition of diphenylzinc to aldehydes. *Chem. Commun.* **1999**, *14*, 1295–1296. [CrossRef]

23. Chaumont-Olive, P.; Rouen, M.; Barozzino-Consiglio, G.; Ben Abdeladhim, A.; Maddaluno, J.; Harrison-Marchand, A. Chiral lithium amido aryl zincates: Simple and efficient chemo- and enantio-selective aryl transfer reagents. *Angew. Chem. Int. Ed.* **2019**, *58*, 3193–3197. [CrossRef]

24. Liu, Y.; Da, C.S.; Yu, S.L.; Yin, X.G.; Wang, J.R.; Fan, X.Y.; Li, W.P.; Wang, R. Catalytic highly enantioselective alkylation of aldehydes with deactivated grignard reagents and synthesis of bioactive intermediate secondary arylpropanols. *J. Org. Chem.* **2010**, *75*, 6869–6878. [CrossRef]

25. OH, O. Lithiated primary alkyl carbanates for the homologation of boronic esters. *Org. Synth.* **2011**, *88*, 247–259.

26. Larouche-Gauthier, R.; Fletcher, C.J.; Couto, I.; Aggarwal, V.K. Use of Alkyl 2,4,6-trisopropylbenzoates in the asymmetric homologation of challenging boronic esters. *Chem. Commun.* **2011**, *47*, 12592–12594. [CrossRef] [PubMed]

27. Barsamian, A.L.; Wu, Z.; Blakemore, P.R. Enantioselective synthesis of α-phenyl- and α-(dimethylphenylsilyl)alkylboronic esters by ligand mediated stable inductive reagent-controlled homologation using configurationally labile carbenebonds. *Org. Biomol. Chem.* **2015**, *13*, 3781–3786. [CrossRef] [PubMed]

28. Binanzer, M.; Fang, G.Y.; Aggarwal, V.K. Asymmetric synthesis of aldehydes and α-ketoesters. *Total Synthesis of (-)-decaestrinactone* D. *Angew. Chem. Int. Ed.* **2010**, *49*, 4264–4268. [CrossRef] [PubMed]

29. Nishide, K.; Shigeta, Y.; Obata, K.; Node, M. Asymmetric 1,7-hydride shift: The highly asymmetric reduction of α, β-unsaturated ketones to secondary alcohols via a novel tandem michael addition Meerwein-Ponndorf-Verley reduction. *J. Am. Chem. Soc.* **1996**, *118*, 13103–13104. [CrossRef]

30. Yamamoto, Y.; Shiraishi, T.; Watanabe, M.; Kurihara, K.; Miyaura, N. Ru/Me-BIPAM-catalyzed asymmetric addition of arylboronic acids to aldehydes. *Org. Lett.* **2010**, *12*, 5020–5023. [CrossRef]

31. Abadie, M.-A.; MacIntyre, K.; Bouho, C.; Hoggan, P.; Capet, F.; Agbossou-Niedercorn, F.; Michon, C. Development of chiral C2-symmetric N-heterocyclic carbene Rh(I) catalysts through control of their steric properties. *Organoal metallitics* **2019**, *38*, 536–543. [CrossRef]

32. Margafel, J.; Slagbrand, T.; Tannis, F.; Adolfsson, H.; Dieuguez, M.; Pamies, O. Third-generation amino acid furanoside-based ligands from [2.2] paracyclophane and their application in ultrasound assisted asymmetric addition reactions of organoboronic acids to aliphatic aldehydes and α-ketoesters. *Org. Lett.* **2012**, *14*, 12941–12944. [CrossRef] [PubMed]

33. Wang, K.; Zhang, L.; Tang, W.; Sun, H.; Xue, D.; Lei, M.; Xiao, J.; Wang, C. Asymmetric guerbet reaction to access chiral alcohols. *Angew. Chem. Int. Ed.* **2020**, *132*, 11505–11512. [CrossRef]

34. Ng, T.W.; Liao, G.; Lau, K.K.; Pan, H.J.; Zhao, Y. Room-temperature guerbet reaction with unprecedented catalytic efficiency and enantioselectivity. *Angew. Chem. Int. Ed.* **2020**, *59*, 11384–11389. [CrossRef]

35. Wang, G.; Gan, Y.; Liu, Y. Nickel-catalyzed direct coupling of allylic alcohols with organoboron reagents. *Chin. J. Chem.* **2018**, *36*, 916–920. [CrossRef]

36. West, M.J.; Fyfe, J.W.; Vantourout, J.C.; Watson, A.J. Mechanistic development and recent applications of the Chan-Lam amination. *Chem. Rev.* **2019**, *119*, 12491–12523. [CrossRef] [PubMed]

37. Corpas, J.; Mauleón, P.; Arrayays, F.G.; Carretero, J.C. Transition-metal-catalyzed functionalization of alkenes with organoboron reagents: New trends, mechanistic insights, and applications. *ACS Catal.* **2021**, *11*, 7513–7551. [CrossRef]

38. Dimitrijevic, E.; Taylor, M.S. Organoboron reagents and their derivatives as catalysts for organic synthesis. *ACS Catal.* **2013**, *3*, 945–962. [CrossRef]

39. Sakai, M.; Ueda, M.; Miyaura, N. Rhodium-catalyzed addition of organoboron acids to aldehydes. *Angew. Chem. Int. Ed.* **1998**, *37*, 3279–3281. [CrossRef]

40. Duan, H.-F.; Xie, J.-H.; Shi, W.-J.; Zhang, Q.; Zhou, Q.-L. Enantioselective rhodium-catalyzed addition of arylboronic acids to aldehydes using chiral spiro monophosphite ligands. *Org. Lett.* **2006**, *8*, 1479–1481. [CrossRef]

41. Noel, T.; Vandyck, K.; Van der Eycken, J. Some new C2-symmetric bicyclo[2.2.1]heptadiene ligands: Synthesis and catalytic activity in rhodium(I)-catalyzed asymmetric 1,4- and 1,2-Additions. *Tetrahedron* **2007**, *63*, 12961–12967. [CrossRef]

42. Nishimura, T.; Kumatomo, H.; Nagaosa, M.; Hayashi, T. The concise synthesis of chiral tbf ligands and their application to the Rhodium-catalyzed asymmetric arylation of aldehydes. *Chem. Commun.* **2009**, *38*, 5713–5715. [CrossRef]

43. Morikawa, S.; Michigami, K.; Amii, H. Novel axially chiral phosphine ligand with a fluoro alcohol moiety for Rh-catalyzed asymmetric arylation of aromatic aldehydes. *Org. Lett.* **2010**, *12*, 2520–2523. [CrossRef]

44. Duan, W.; Ma, Y.; Qu, B.; Zhao, L.; Chen, J.; Song, C. Synthesis of new alkoxy/sulfonate-substituted carbene precursors derived from [2.2] paracyclophane and their application in the asymmetric arylation of aldehydes. *Tetrahedron Asymmetry* **2012**, *23*, 1369–1375. [CrossRef]

45. Duan, W.; Ma, Y.; He, F.; Zhao, L.; Chen, J.; Song, C. Synthesis of novel planar chiral Ag and Rh N-heterocyclic carbene complexes derived from [2.2] paracyclophane and their application in ultrasound assisted asymmetric addition reactions of organoboron acids to aldehydes. *Tetrahedron Asymmetry* **2013**, *24*, 241–248. [CrossRef]
46. Chen, J.; Yang, S.; Chen, Z.; Song, C.; Ma, Y. Synthesis of novel macrocyclic planar chiral carbene-Ag complexes derived from [2.2] paracyclophane for Rh-catalyzed asymmetric 1, 2-additions of arylboronic acids to aromatic aldehydes. *Tetrahedron Asymmetry* 2015, 26, 288–295. [CrossRef]

47. He, W.-F.; Zhou, B.-H.; Zhou, Y.-L.; Li, X.-R.; Fan, L.-M.; Shou, H.-W.; Li, J. Synthesis of new benzimidazolium salts and their application in the asymmetric arylation of aldehydes. *Tetrahedron Lett.* 2016, 57, 3152–3155. [CrossRef]

48. Kamikawa, K.; Tseng, Y.-Y.; Jian, J.-H.; Takahashi, T.; Ogasawara, M. Planar-chiral phosphine-olefin ligands exploiting a (cyclopentadienyl) manganese (I) scaffold to achieve high robustness and high enantioselectivity. *J. Am. Chem. Soc.* 2017, 139, 1545–1553. [CrossRef] [PubMed]

49. Lu, Z.; Zhang, H.; Yang, Z.; Ding, N.; Meng, L.; Wang, J. Asymmetric hydrophosphination of heterobicyclic alkenes: Facile access to phosphine ligands for asymmetric catalysis. *ACS Catal.* 2019, 9, 1457–1463. [CrossRef]

50. Aaro, T.; Kondo, K.; Aoyama, T. Nickel-catalyzed 1, 2-addition of arylboroxines to aromatic aldehydes. *Tetrahedron Lett.* 2007, 48, 4115–4117. [CrossRef]

51. Karthikeyan, J.; Jeganmohan, M.; Cheng, C.H. Cobalt-catalyzed addition reaction of organoboronic acids with aldehydes: Highly enantioselective synthesis of diarylmethanols. *Chem. Eur. J.* 2010, 16, 8989–8992. [CrossRef]

52. Suzuma, Y.; Hayashi, S.; Yamamoto, T.; Oe, Y.; Ohta, T.; Ito, Y. Asymmetric 1, 2-addition of organoboronic acids to α, β-unsaturated ketones and 1, 2-addition to aldehydes catalyzed by a palladium complex with a ferrocene-based phosphine ligand. *Tetrahedron Asymmetry* 2009, 20, 2751–2758. [CrossRef]

53. Loxq, P.; Debono, N.; Gülcemal, S.; Daran, J.-C.; Manoury, E.; Poli, R.; Çetinkaya, B.; Labande, A. Palladium(II) complexes with planar chiral ferrocenyl phosphane-(benz) imidazol-2-ylidene ligands. *New J. Chem.* 2014, 38, 338–347. [CrossRef]

54. (c) Zhang, R.; Xu, Q.; Zhang, X.; Zhang, T.; Shi, M. Axially chiral C2-symmetric N-heterocyclic carbene (NHC) palladium complexes-catalyzed asymmetric arylation of aldehydes with arylboronic acids. *Tetrahedron Asymmetry* 2010, 21, 1928–1935. [CrossRef]

55. Shintani, R.; Ioue, M.; Hayashi, T. Rhodium-catalyzed asymmetric addition of aryl-and alkylenoboronic acids to isatins. *Angew. Chem. Int. Ed.* 2006, 118, 3431–3434. [CrossRef]

56. Toullec, P.Y.; Jagt, R.B.; de Vries, J.G.; Feringa, B.L.; Minnaard, A.J. Rhodium-catalyzed addition of arylboronic acids to isatins: An entry to diversity in 3-aryl-3-hydroxyxindoles. *Org. Lett.* 2006, 8, 2715–2718. [CrossRef] [PubMed]

57. Zhuang, Y.; He, Y.; Zhou, Z.; Xia, W.; Cheng, C.; Wang, M.; Chen, B.; Zhou, Z.; Pang, J.; Qiu, L. Synthesis of a class of chiral-bridged phosphoramidite ligands and their applications in the first iridium-catalyzed asymmetric addition of arylboronic acids to isatins. *J. Org. Chem.* 2015, 80, 6968–6975. [CrossRef] [PubMed]

58. Marques, C.S.; Burke, A.J. Enantioselective rhodium(I)-catalyzed additions of arylboronic acids to N-1,2,3-triazole-isatin derivatives: Accessing N-(1,2,3-triazolomethyl)-3-hydroxy-3-aryloxindoles. *ChemCatChem* 2016, 8, 3518–3526. [CrossRef]

59. Duan, H.F.; Xie, J.H.; Qin, X.C.; Wang, L.X.; Zhou, Q.L. Enantioselective rhodium-catalyzed addition of arylboronic acids to α-ketoesters. *Angew. Chem. Int. Ed.* 2008, 120, 4423–4425. [CrossRef]

60. Cai, F.; Pu, X.; Qi, X.; Lynch, V.; Radha, A.; Ready, J.M. Chiral allene-containing phosphines in asymmetric catalysis. *J. Am. Chem. Soc.* 2011, 133, 18066–18069. [CrossRef]

61. Zhu, T.S.; Jin, S.S.; Xu, M.H. Rhodium-catalyzed, highly enantioselective 1, 2-addition of aryl boronic acids to α-ketoesters and α-diketones using simple, chiral sulfur-olene ligands. *Angew. Chem. Int. Ed.* 2012, 124, 804–807. [CrossRef]

62. Chang, C.A.; Uang, T.Y.; Jian, J.H.; Zhou, M.Y.; Chen, M.L.; Kuo, T.S.; Wu, P.Y.; Wu, H.L. Efficient and enantioselective rhodium(I)-catalyzed arylation of aldehydes with arylboronic acids to phosphine ligands for asymmetric catalysis. *Adv. Synth. Catal.* 2010, 352, 1297–1302. [CrossRef]

63. Bartlett, S.L.; Keiter, K.M.; Johnson, J.S. Synthesis of complex tertiary glycolates by enantioconvergent arylation of stereochemically atropos is better than tropos. *Org. Lett.* 2016, 18, 3911–3916. [CrossRef] [PubMed]

64. Feng, X.; Nie, Y.; Yang, J.; Du, H. Rh(I)-Catalyzed asymmetric 1, 2-addition to α-diketones with chiral sulfur-alke ne hybrid ligands. *Org. Lett.* 2012, 14, 624–627. [CrossRef]

65. Chen, J.; Yang, S.; Chen, Z.; Song, C.; Ma, Y. Synthesis of novel macrocyclic planar chiral carbene-Ag complexes derived from [2.2] paracyclophane for Rh-catalyzed asymmetric 1, 2-additions of arylboronic acids to aromatic aldehydes. *Tetrahedron Asymmetry* 2015, 26, 288–295. [CrossRef]

66. Zhang, Z.-F.; Zhu, D.-X.; Chen, W.-W.; Xu, B.; Xu, M.-H. Enantioselective synthesis of gem-diaryl benzofuran-3(2H)-ones via one-oct asymmetric rhodium/palladium relay catalysis. *Org. Lett.* 2017, 19, 2726–2729. [CrossRef] [PubMed]

67. Martina, S.L.; Jagt, R.B.; de Vries, J.G.; Feringa, B.L.; Minnaard, A.J. Enantioselective rhodium-catalyzed arylation of arylboronic acids to trifluoromethyl ketones. *Chem. Commun.* 2006, 39, 4093–4095. [CrossRef] [PubMed]

68. Jumde, V.R.; Fachetti, S.; Iuliano, A. A chiral Rh-phosphate complex displaying high activity in the enantioselective Rh-catalyzed addition of arylboronic acids to carbonyl compounds: When and why atropos is better than tropos. *Tetrahedron Asymmetry* 2010, 21, 2775–2781. [CrossRef]

69. Luo, R.; Li, K.; Hu, Y.; Tang, W. Enantioselective rhodium-catalyzed addition of arylboronic acids to trifluoromethyl ketones. *Adv. Synth. Catal.* 2013, 355, 1297–1302. [CrossRef]

70. Korenaga, T.; Ko, A.; Uotani, K.; Tanaka, Y.; Sakai, T. Synthesis and application of 2, 6-Bis (trifluoromethyl)-4-pyridyl phosphines: The most electron-poor aryl phosphines with moderate bulkiness. *Angew. Chem. Int. Ed.* 2011, 50, 10703–10707. [CrossRef]

71. Liao, Y.-X.; Xing, C.-H.; Hu, Q.-S. Rhodium (I)/Diene-catalyzed addition reactions of arylborons with ketones. *Org. Lett.* 2012, 14, 1544–1547. [CrossRef]
72. Huang, L.; Zhu, J.; Jiao, G.; Wang, Z.; Yu, X.; Deng, W.P.; Tang, W. Highly enantioselective rhodium-catalyzed addition of arylboroxines to simple aryl ketones: Efficient synthesis of escitalopram. Angew. Chem. Int. Ed. 2016, 55, 4527–4531. [CrossRef]
73. Richard, B.; àde Vries, J.G. Rhodium/Phosphoramidite-Catalyzed asymmetric arylation of aldehydes with arylboronic acids. Org. Biomol. Chem. 2006, 4, 773–775.
74. Ma, Q.; Ma, Y.; Liu, X.; Duan, W.; Qu, B.; Song, C. Planar chiral imidazolium salts based on [2.2] paracyclophane in the asymmetric rhodium-catalyzed 1, 2-addition of arylboronic Acids to Aldehydes. Tetrathrad Asymmetry 2010, 21, 292–298. [CrossRef]
75. Wang, D.; Ma, Y.; He, F.; Duan, W.; Zhao, L.; Song, C. Synthesis of planar chiral [2.2] paracyclophanilimidazo [1, 5-a] pyridinium salts for the rhodium-catalyzed asymmetric arylation. Synth. Commun. 2013, 43, 810–825. [CrossRef]
76. Wu, T.; Zhou, Q.; Tang, W. Enantioselective α-carbonylative amination for facile construction of chiral spirocyclic β, β′-diketones. Angew. Chem. Int. Ed. 2021, 60, 9978–9983. [CrossRef] [PubMed]
77. Tian, D.; Xu, R.; Zhu, J.; Huang, J.; Dong, W.; Claverie, J.; Tang, W. Asymmetric hydrosterification of diarylmethyl carbinols. Angew. Chem. Int. Ed. 2021, 60, 6305–6309. [CrossRef] [PubMed]
78. Li, K.; Nie, M.; Tang, W. Synthesis of a-tertiary allylsilanes by palladium-catalyzed hydroisilylation of 1, 1-disubstituted allenes. Green Synth. Catal. 2020, 1, 171–174. [CrossRef]
79. Xu, R.H.; Yang, H.; Tang, W. Efficient enantioselective syntheses of chiral natural products facilitated by ligand design. Chin. J. Org. Chem. 2020, 40, 1409–1422. [CrossRef]
80. Wu, T.; Xu, G.; Tang, W. P-Chiral Phosphorus Ligands for Cross-Coupling and Asymmetric Hydrogenation Reactions. Aldrichimica Acta 2020, 53, 27–35.
81. Xu, G.; Senanayake, C.H.; Tang, W. P-Chiral phosphorus ligands based on a 2,3-dihydrobenzo [á] azepine motif for asymmetric catalysis. Acc. Chem. Res. 2019, 52, 1101–1112. [CrossRef]
82. Yang, H.; Tang, W. Efficient enantioselective syntheses of chiral natural products catalyzed by ligand design. Chem. Rec. 2019, 19, 1–19.
83. Li, K.; Hu, N.; Luo, R.; Yuan, W.; Tang, W. A chiral ruthenium-monophosphine catalyst for asymmetric addition of arylboronic acids to aryl aldehydes. J. Org. Chem. 2013, 78, 6330–6355. [CrossRef]
84. Barkow, A.; Pilotek, S.; Grützmacher, H.-F. Ortho effects: A mechanistic study. Eur. Mass Spectrom. 1995, 6, 525–537. [CrossRef]
85. Kaur, M.; Reshi, N.U.D.; Patra, K.; Bhattacherya, A.; Kunnikuruvan, S.; Bera, J.K. A proton-responsive pyridyl (benzamide)-functionalized NHC ligand on Ir complex for alkylation of ketones and secondary alcohols. Chem. Eur. J. 2021, 27, 10732–10748. [CrossRef]
86. El-Sepelgy, O.; Matador, E.; Brzozowska, A.; Rueping, M. C-alkylation of secondary alcohols by primary alcohols through manganese-catalyzed double hydrogen autotransfer. ChemSusChem 2019, 12, 3099–3102. [CrossRef] [PubMed]
87. Wang, D.; Guo, X.Q.; Wang, C.X.; Wang, Y.N.; Zhong, R.; Zhu, X.H.; Cai, L.H.; Gao, Z.W.; Hou, X.F. An efficient and recyclable carbene iridium complex. Adv. Synth. Catal. 2013, 3099–3102. [CrossRef] [PubMed]
88. Liu, J.; Liu, W.; Li, Y.; Liu, Y.; Ke, Z. Selective C-alkylation between alcohols catalyzed by N-heterocyclic carbene iridium complex. Org. Lett. 2021, 23, 3124–3128. [CrossRef] [PubMed]
89. Liu, T.; Wang, L.; Wu, K.; Yu, Z. Manganese-catalyzed β-alkylation of secondary alcohols with primary alcohols under phosphine-free conditions. ACS Catal. 2018, 8, 7201–7207. [CrossRef]
90. Kaya, U.; Tran, U.P.; Enders, D.; Ho, J.; Nguyen, T.V. N-Heterocyclic olefin catalyzed silylation and hydrosilylation reactions of hydroxyl and carbonyl compounds. Org. Lett. 2017, 19, 1398–1401. [CrossRef]
91. Xu, Q.; Chen, J.; Tian, H.; Yuan, X.; Li, S.; Zhou, C.; Liu, J. Catalyst-free dehydroytic α-alkylation of ketones with alcohols: Green and selective autocatalyzed synthesis of alcohols and ketones. Angew. Chem. Int. Ed. 2014, 126, 229–233. [CrossRef]
92. Babu, R.; Subaramanian, M.; Midya, S.P.; Balaraman, E. Nickel-catalyzed guerbet type reaction: C-alkylation of secondary alcohols via double (de) hydrogenation. Org. Lett. 2021, 23, 3320–3325. [CrossRef]
93. Kabalka, G.W.; Wu, Z.; Trotman, S.E.; Gao, X. Alkylation of aromatic aldehydes with boron halide derivatives. Org. Lett. 2000, 2, 255–256. [CrossRef]
94. Shailaja, J.; Kaanumalle, L.S.; Sivasubramanian, K.; Natarajan, A.; Ponchot, K.J.; Pradhan, A.; Ramamurthy, V. Asymmetric induction during electron transfer mediated photoreduction of carbonyl compounds: Role of zeolites. Org. Biomol. Chem. 2006, 4, 1561–1571. [CrossRef]
95. Hirao, Y.; Katayama, Y.; Mitsunuma, H.; Kanai, M. Chromium-catalyzed linear-selective alkylation of aldehydes with alkenes. Org. Lett. 2020, 22, 8584–8588. [CrossRef]
96. Liao, Y.-X.; Xing, C.-H.; He, P.; Hu, Q.-S. Orthoplatinated Triarylphosphite as a highly efficient catalyst for addition reactions of arylboronic acids with aldehydes: Low catalyst loading catalysis and a new tandem reaction sequence. Org. Lett. 2008, 10, 2509–2512. [CrossRef] [PubMed]
97. Asada, M.; Iwahashi, M.; Obitsu, T.; Kinoshita, A.; Nakai, Y.; Onoda, T.; Nagase, T.; Tanaka, M.; Yamaura, Y.; Takizawa, H. 3-(2-Aminocarbonylphenyl) propanoic acid analogs as potent and selective EP3 receptor antagonists. Part 2: Optimization of the side chains to improve in vitro and in vivo potencies. Bioorg. Med. Chem. 2010, 18, 1641–1658. [CrossRef] [PubMed]
98. Irrgang, T.; Friedrich, D.; Kempe, R. Highly enantioselective amidobrid catalysts for the hydrogenation of simple ketones. Angew. Chem. Int. Ed. 2011, 50, 2183–2186. [CrossRef] [PubMed]
99. Keinan, E.; Peretz, M. Organotin nucleophiles. Palladium-catalyzed allylic propargylation with allenylstannane. *J. Org. Chem.* **1983**, *48*, 5302–5309. [CrossRef]

100. Ma, Z.; Wang, Y. Dirhodium(ii)/P(t-Bu)3 catalyzed tandem reaction of alpha, beta-unsaturated aldehydes with arylboronic acids. *Org. Biomol. Chem.* **2018**, *16*, 7470–7476. [CrossRef] [PubMed]