Tetrahedron: *Asymmetry* 19 (2008) 1804–1809

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

# Chiral phosphinoazomethinylate salts as new 'one-step available' ligands for copper-catalyzed asymmetric conjugate addition

Joanna Wencel, Diane Rix, Thomas Jennequin, Stéphane Labat, Christophe Crévisy *, Marc Mauduit *

*UMR CNRS 6226 'Sciences Chimiques de Rennes', Equipe Chimie Organique et Supramoléculaire, Ecole Nationale Supérieure de Chimie de Rennes, Av. du Général Leclerc, 35700 Rennes, France*

ARTICLE INFO

*Article history:*
Received 27 May 2008
Accepted 8 July 2008
Available online 9 August 2008

ABSTRACT

Herein, we report the use of phosphinoazomethinylate salts as chiral efficient ligands for the copper-catalyzed asymmetric conjugate addition (ACA) of dialkylzinc to various enones. These tridentate P,N,O ligands are straightforwardly obtained in a one-step procedure from commercially available enantiopure α-aminoacids. Performing the conjugate addition in the greener AcOEt solvent, high enantioselectivities were reached for both cyclic and acyclic enones ranging between 72% to 98% ee and 96% to >99%, respectively. The 2/1 Cu/ligand ratio required to obtain high enantioselectivities, led us to envisage a copper–copper bi-metallic catalytic system for this transformation.



## 1. Introduction

Copper-catalyzed Asymmetric Conjugate Addition is a fundamental method for the formation of C–C bonds.[1] This reaction has been extensively studied over the last decade, and most efforts have been realized through the development of copper[2] and rhodium[3] asymmetric conjugate addition of various alkylmetal (organozinc reagents,[4] organoaluminum reagents,[5] and Grignard reagents[6]) and arylboronic acids[7] to cyclic and acyclic unsaturated carbonyls. Moreover, various chiral ligands have been evaluated on both cyclic and acyclic Michael acceptors and proven to be efficient, giving full conversions and very high ee's.[7] As examples, peptidic phosphane ligands developed first by Hoveyda[8] and more recently by Tomioka[9] have proven to be highly efficient in this reaction with various Michael acceptors. Nevertheless, in a general way, many chiral ligands, are synthesized through lengthy and expensive routes, which compromises any possible industrial development. In the context of sustainable chemistry, there is a need for chiral ligands which are not only very efficient, but also available via step (transformation and purification) economy and costless processes.[10] Phosphoramidites are representative examples of a family of ligands that partly fulfills these criteria.[11] In the area of the Hoveyda's peptidic phosphane ligands[8] **A** (Fig. 1) and the P,N,O Schiff base ligands **B** (Fig. 1) recently reported by Gau,[12] we report here a novel family of ligands, the diphenylphosphinoazomethinylate salts **1** (Scheme 1).

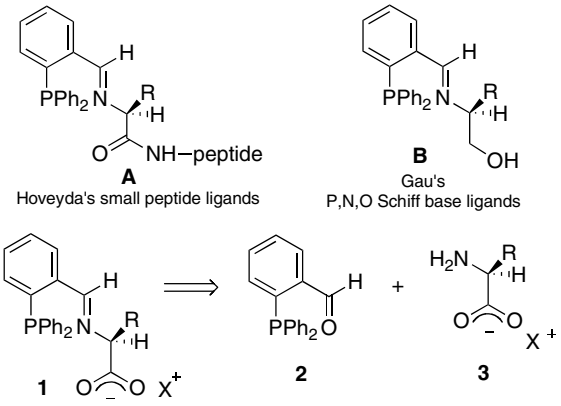



**Figure 1.** Easily available phosphino-azomethinylate salts **1**.

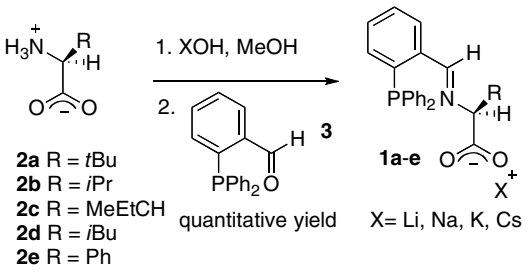
These ligands, which are a simplified version of Hoveyda's peptide ligands, can be readily obtained from α-aminoacids in a one-step procedure and do not require any purification. Diphenylphosphinoazomethinylate salts **1** are thus compatible with the concept of sustainable chemistry but have also proven to be very efficient in the copper-catalyzed conjugate addition of dialkylzinc reagents. Their synthesis and their evaluation in the above-mentioned reaction are reported herein.

## 2. Results and discussion

Ligands **1** bear a diphenylphosphinoaryl and a chiral iminocarboxylate chelating groups. They are readily accessible from

* Corresponding authors. Tel.: +33 (0) 2 23 23 81 12; fax: +33 (0) 2 23 23 81 08 (M.M.); tel.: +33 (0) 2 23 23 80 74; fax: +33 0 2 23 23 81 08 (C.C.).
*E-mail addresses:* christophe.crevisy@ensc-rennes.fr (C. Crévisy), marc.mauduit@ensc-rennes.fr (M. Mauduit).

0957-4166/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2008.07.011

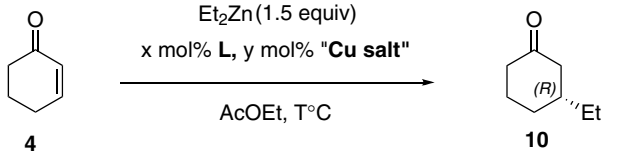



**Scheme 1.** Synthesis of ligands **1a**–**e**.

*o*-diphenylphosphinobenzaldehyde **3** and the carboxylate salt of α-aminoacid **2** (Scheme 1). Eight different ligands were obtained, varying both the nature of the cation and the nature of the amino acid. Amino acids **2a**–**e** were first converted to the corresponding carboxylate salts, which were then condensed with aldehyde **3** to give ligands **1a**–**e** in quantitative yields (Scheme 1).[13] Crude product **1** was sufficiently pure enough for catalytic applications and no purification was required.

The ligands were then examined in the copper-catalyzed conjugate addition of dialkylzinc to enones. Firstly, search for optimal conditions was carried out using diethylzinc and cyclohexenone **4** as model reagents (Table 1). For the first experiments, reactions were performed with $(CuOTf)_2{\cdot}C_7H_8$ at rt for 2 h. As AcOEt is considered as a green solvent,[14] it was chosen for the preliminary experiments. Unexpectedly, it was observed that a 2/1 Cu/ligand ratio was necessary to have good results. When the ratio was changed to 2/2 (mol %) and 2/4 (mol %), respectively, 53% and 25% conversions along with 80% and 50% ee were obtained (Table 1, entries 1–3). It should be noted that the Cu/ligand ratio employed in the case of Hoveyda's small peptide ligands **A** (Fig. 1), a ratio of 1/1 is required, which may suggest differences in the mechanisms between these two classes of ligands.

**Table 1**
Optimization of the reaction conditions with ligand **1a**

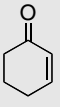
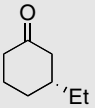
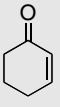
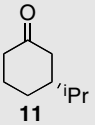
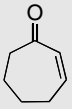
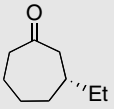
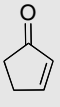
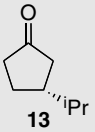
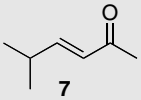
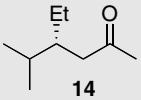
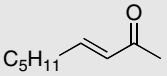
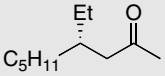
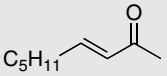
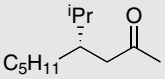
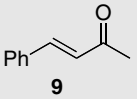
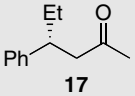



| Entry | Ligand | Cu salt | Ratio *x*/*y* | Temp | Time (h) | Conv.[a] | ee[a](%) |
|---|---|---|---|---|---|---|---|
| 1 | **1a-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 4/1 | rt | 2 | 25 | 50 |
| 2 | **1a-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 2/1 | rt | 2 | 53 | 80 |
| 3 | **1a-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | >99 | 89 |
| 4 | **1b-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | 85 | 72.5 |
| 5 | **1c-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | 98 | 74.5 |
| 6 | **1d-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | 87 | 51 |
| 7 | **1e-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | 90 | 22 |
| 8 | **1a-Li** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | >99 | 85 |
| 9 | **1a-K** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | >99 | 87 |
| 10 | **1a-Cs** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | rt | 2 | >99 | 86 |
| 11 | **1a-Na** | CuCl | 1/2 | rt | 2 | 51 | 44 |
| 12 | **1a-Na** | $CuCl_2$ | 1/2 | rt | 2 | 53 | 26.5 |
| 13 | **1a-Na** | $Cu(OTf)_2$ | 1/2 | rt | 2 | >99 | 75 |
| 14 | **1a-Na** | CuTC | 1/2 | rt | 2 | >99 | 34 |
| 15 | **1a-Na** | $Cu(acac)_2$ | 1/2 | rt | 2 | 83 | 34 |
| 16 | **1a-Na** | CuMes | 1/2 | rt | 2 | 64 | 27.5 |
| 17 | **1a-Na** | $CuBr{-}SMe_2$ | 1/2 | rt | 2 | 69 | 53 |
| 18 | **1a-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | 0 °C | 4 | >99 | 94.5 |
| 19 | **1a-Na** | $(CuOTf)_2{\cdot}C_7H_8$ | 1/1 | −18 °C | 6 | 94 | 98 |
| 20 | Isolated Cu-**1a** complex | | | 18 °C | 6 | 97 | 97 |

[a] Determined by chiral GC analysis (Lipodex E).

It was then observed that the nature of the stereogenic R-group has a great influence on the enantioselectivity (Table 1, entries 3–7), with the best ee (89%) being obtained with *tert*-Leu-derived ligand (R = *t*Bu) **1a**. Consequently, the following experiments were performed using **1a** as the ligand. On the contrary, the nature of the counter-cation has no noticeable influence on both the conversion and the enantioselectivity (entries 3 and 8–10). Sodium salts were used in the following experiments. It was observed that the nature of the copper source was critical for obtaining an efficient catalysis. Either Cu(I) or Cu(II) salts can be used in the reaction, since Cu(II) salts are in situ reduced by dialkyzinc.[15] So, both Cu(I) and Cu(II) salts were tested, and while many copper salts gave poor to fairly good results (entries 11–17), high ee (89%) and conversion (>99%) were obtained when $(CuOTf)_2{\cdot}C_7H_8$ was used (entry 3). Various solvents were also screened; AcOEt, THF,

**Table 2**
Enantioselective Copper-catalyzed conjugate addition of diethylzinc to cyclic and acyclic enones **4**–**9** with ligand **1a-Na** catalyzed by $(CuOTf)_2{\cdot}C_7H_8$ complex[a]

| Entry | Substrate | Product | *T* (°C) | Time (h) | Conv.[b] (%) | ee[b] (%) |
|---|---|---|---|---|---|---|
| 1[c] |  **4** |  **10** | −18 | 6 | 94 | 98 (*R*) |
| 2[c] |  **4** |  **11** | −18 | 14 | 83 | 88 (*R*) |
| 3[c] |  **5** |  **12** | −18 | 14 | 90 | 87 (R) |
| 4[d] |  **6** |  **13** | −18 | 14 | 96 | 72 (*R*) |
| 5[d] |  **7** |  **14** | rt | 14 | >99 | >99 (*R*) |
| 6[c] |  **8** |  **15** | 30 | 4 | >99 | 96 (*S*) |
| 7[d] |  **8** |  **16** | rt | 14 | >99 | 97 (*S*) |
| 8[d] |  **9** |  **17** | rt | 6 | >99 | 98 (*R*) |

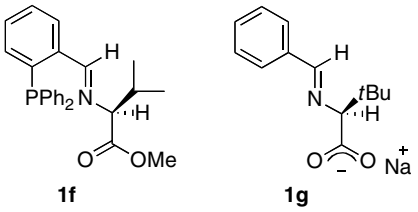
[a] All reactions were performed in AcOEt using 1.5–3 equiv of $R_2Zn$.
[b] Determined by chiral GC analysis (chiraldex GTA).
[c] 1 mol % of $(CuOTf)_2{\cdot}C_7H_8$ and 1 mol % of **1a-Na** were used.
[d] 2 mol % of $(CuOTf)_2{\cdot}C_7H_8$ and 2 mol % of **1a-Na** were used.

and $Et_2O$ gave quite similar results, while solubility problems were observed in toluene.

Finally, we observed a noticeable influence of the temperature (Table 1, entries 3, 18, and 19) on the enantiocontrol, but it is worth noting that a very high ee was obtained at only moderately low temperatures (94.5% ee at 0 °C and 98% ee at −18 °C). At this temperature, a nearly full conversion was obtained in 6 h. Nevertheless, it should be noted that the Cu/**1a**-**Na** complex could be isolated as a deep green powder; however, no clear cut difference was noticed in the result (entry 20). For practical reasons, the following experiments were performed with an in situ prepared catalyst.

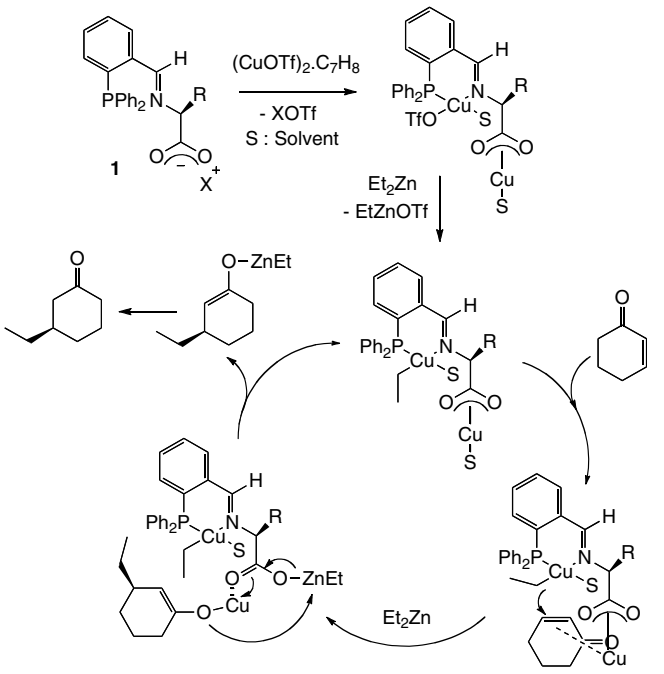
Having established the optimum reaction conditions in the use of diphenyphosphinoazomethinylate ligand **1a**, the addition of diethyl- and diisopropylzinc on various cyclic **4**–**6** and acyclic **7**–**9** Michael acceptors was examined (Table 2). High ee's (87–98%, entries 1 and 3) and nearly full conversions were reached with $Et_2Zn$ and cyclic enones. Lower enantioselectivities were observed when $iPr_2Zn$ was used (72–88%, entries 2 and 4). It should be noted that, with acyclic enones, very high ee's (96–99%) could be reached at room temperature both with $Et_2Zn$ and $iPr_2Zn$ (entries 5–8). Particularly noteworthy are the results observed with $Et_2Zn$ and acyclic enones **7** and **8** (>99% obtained at rt and 96% ee obtained at 30 °C, respectively, entries 5 and 6) since these results are similar to the best result reported to date by Nakamura (98.1% and 97.9% ee, respectively, obtained at 0 °C).[16] It is noteworthy that an excellent result was obtained when $iPr_2Zn$ and enone **8** were used (entry 7). This result is far better than the copper-catalyzed addition of isopropylgrignard reagent to **8**, as reported by Feringa[17] (48% ee).

Finally, some experiments were carried out in order to obtain information on the mechanism (Scheme 2). We have already noted that the cation is not involved in the determining steps of the mechanism, and that 2 mol of copper for one mole of ligand is required for the reaction to proceed. The latter result, which is very unusual, is consistent with the involvement of a bimetallic catalytic system[18] where two copper entities are linked to the same ligand, with the second copper atom being coordinated with the carboxylate.




**Scheme 2.** Mechanistic studies.

This is confirmed by the experiment carried out with ligand **1f**, which exhibits a methyl ester group instead of the carboxylate. In this case, using cyclohexenone and $Et_2Zn$ as the reagents, the product was obtained in low enantioselectivity (30% ee, >99% conv. with 1 mol % $(CuOTf)_2{\cdot}C_7H_8$ and 1 mol % of **1f**), which may arise from the impossibility of the enone to coordinate to the carboxylate-copper complex. Such a chelation might activate the enone and also increase the rigidity of the system. The presence of the phosphino chelating group is also critical since no reaction was observed when ligand **1g** was used (0% conv. with 1 mol % $(CuOTf)_2{\cdot}C_7H_8$ and 1 mol % **1g**). The activity is restored by the addition of extra $PPh_3$, but the enantioselectivity remains nil (41% conv. with 1 mol % $(CuOTf)_2{\cdot}C_7H_8$, 1 mol % **1g** and 1 mol % $Ph_3P$). This demonstrates that the P atom is important to have not only a high activity, but also an appropriate organization in the enantiodetermining step. From all these results, a proposal of mechanism was attempted (Scheme 3). The phosphino and the imine first coordinate to the copper forming a six-membered metallacycle while the carboxylate coordinates to the second Cu atom. The approach of the enone is *anti* to the stereogenic group, allowing for excellent control during the transfer of the ethyl group. Then a transmetallation occurs, leading to the regeneration of the starting copper–copper bi-metallic species. The second copper entity may act as a Lewis acid toward the enone.




**Scheme 3.** Proposal mechanism for the conjugate addition of diethylzinc to enones with phosphinoazomethinylate salt **1**.

## 3. Conclusion

In conclusion, phosphinoazomethinylate salts have been evaluated in the copper-catalyzed Michael addition of organozinc reagents to cyclic and acyclic enones. Excellent results were obtained, particularly with acyclic enones. A proposal of mechanism has been attempted and, to the best of our knowledge, the involvement of a copper–copper bimetallic catalytic system is proposed for the first time in this reaction. This behavior opens up a new field of investigation for this new type of ligands.

## 4. Experimental

### 4.1. General

$^1H$ (400 MHz), $^{13}C$ (100 MHz), $^{19}F$ (376.5 MHz), and $^{31}P$ (162 MHz) NMR spectra were recorded on a Bruker ARX400 spectrometer with complete proton decoupling for nucleus other than $^1H$. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (MeOD, $^1H$: $\delta$ 3.31 ppm, $^{13}C$: $\delta$ 49.05 ppm). Data are reported as follows: chemical shift ($\delta$ in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, sept = septuplet, m = multiplet), coupling constants (Hz), integration and attribution. Optical rotations were recorded using a polarimeter Perkin–Elmer 341. Elemental analyses were performed at Service centrale d'analyse S.C.A.—U.S.R.—59/C.N.R.S. Solaize, France, and at the Centre Régional de Mesures Physiques de l'Ouest (CRMPO), Université de Rennes 1. The conversions and enantiomeric excesses of

conjugate additions were measured using gas chromatography (capillary column—Chiraldex GTA, 0.12 μm, 30 m, 0.25 mm) with cyclododecane as internal standard. The products of conjugate additions were identified according to the literature.

### 4.2. Materials

All non-aqueous reactions were performed under an argon atmosphere using oven-dried glassware. Toluene was distilled from sodium metal under nitrogen. Methanol was distilled from sodium metal under argon. Tetrahydrofuran and diethyl ether were desiccated on alumina column under nitrogen. Ethyl acetate was distilled from calcium hydride under nitrogen. All other chemical reagents and solvents were obtained from commercial sources and used without further purification.

### 4.3. General experimental procedure for ligand's synthesis 1a–g

A flame-dried Schlenk tube was charged with amino acid **2** (1 mmol, 1 equiv), metal hydroxide (1 mmol, 1 equiv), molecular sieves 4 Å, and 5 mL of MeOH. The mixture was stirred under an argon atmosphere at room temperature for 15 min. 2-(Diphenylphosphino)-benzaldehyde **3** (297 mg, 1 mmol, 1 equiv) was added to the resulting solution. The reaction was allowed to stir at 40 °C for 3 h. Filtration of molecular sieves and removal of volatiles in vacuo left behind a yellow solid.

#### 4.3.1. Sodium *tert*-leucine phosphinoazomethinylate 1a-Na

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.86 (d, *J* (H,P) = 5.19 Hz, 1H, CHN), 8.25–8.19 (m, 1H, C*H*$_{ar}$CCHN), 7.36–7.02 (m, 12H, CH$_{ar}$), 6.78–6.72 (m, 1H, C*H*$_{ar}$CP), 3.33 (s, 1H, CH), 0,79 (s, 9H, CH$_3$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.63 (s, 1P). $^{13}$C NMR (101 MHz, MeOD): $\delta$ 179.13 (s, 1C, COO), 159.84 (d, *J* (C,P) = 25.92 Hz, 1C, CHN), 140.83 (d, *J* (C,P) = 17.90 Hz, 1C, C$_{ar}$), 138.53 (d, *J* (C,P) = 18.61 Hz, 1C, C$_{ar}$), 137.46 (d, *J* (C,P) = 9.46 Hz, 1C, C$_{ar}$), 137.13 (d, *J* (C,P) = 10.11 Hz, 1C, C$_{ar}$), 135.05 (d, *J* (C,P) = 2.97 Hz, 2C, C$_{ar}$), 134.85 (d, *J* (C,P) = 3.35 Hz, 2C, C$_{ar}$), 133.77 (s, 1C, C$_{ar}$), 131.08 (s, 1C, C$_{ar}$), 129.96 (s, 2C, C$_{ar}$), 129.84 (s, 1C, C$_{ar}$), 129.60 (d, *J* (C,P) = 7.17 Hz, 4C, C$_{ar}$), 128.64 (d, *J* (C,P) = 4.34 Hz, 1C, C$_{ar}$), 88.72 (s, 1C, NC), 35.07 (s, 1C, C(CH$_3$)$_3$), 27.66 (s,3C, CH$_3$). $[\alpha]_D^{20} = -11.4$ (*c* 1, methanol). Anal. Calcd for $C_{25}H_{27}NNaO_3P$: C, 67.71; H, 6.14; N, 3.16. Found: C, 67.74; H, 5.95; N, 3.15.

#### 4.3.2. Potassium *tert*-leucine phosphinoazomethinylate 1a-K

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.92 (d, *J* (H,P) = 5.20 Hz, 1H, CHN), 8.30 (ddd, *J* (H,H) = 7.78, 4.03, 1.28 Hz, 1H, C*H*$_{ar}$CCHN), 7.37–7.18 (m, 12H, H$_{ar}$), 6.81 (ddd, *J* (H,H) = 7.73, 4.79, 0.93 Hz, 1H, C*H*$_{ar}$CP), 3.38 (s, 1H, CH), 0.85 (s, 9H, CH$_3$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.60 (s, 1P). $^{13}$C NMR (101 MHz, *MeOD*) : $\delta$ 179.12 (s, 1C, COO), 159.71 (d, *J* (C,P) = 25.75 Hz, 1C, CN), 140.87 (d, *J* (C,P) = 17.56 Hz, 1C, C$_{ar}$), 138.51 (d, *J* (C,P) = 18.59 Hz, 1C, C$_{ar}$), 137.48 (d, *J* (C,P) = 9.49 Hz, 1C, C$_{ar}$), 137.16 (d, *J* (C,P) = 10.14 Hz, 1C, C$_{ar}$), 135.03 (d, *J* (C,P) = 4.31 Hz, 2C, C$_{ar}$), 134.85 (d, *J* (C,P) = 4.31 Hz, 2C, C$_{ar}$), 133.76 (s, 1C, C$_{ar}$), 131.06 (s, 1C, C$_{ar}$), 129.96 (s, 2C, C$_{ar}$), 129.83 (s, 1C, C$_{ar}$), 129.56 (d, *J* (C,P) = 7.20 Hz, 4C, C$_{ar}$), 128.63 (d, *J* (C,P) = 4.36 Hz, 1C, C$_{ar}$), 88.70 (s, 1C, NC), 35.07 (s, 1C, C(CH$_3$)$_3$), 27.67 (s, 3C, CH$_3$). $[\alpha]_D^{20} = -11.0$ (*c* 1, methanol). Anal. Calcd for $2C_{25}H_{25}NKO_2P$, $H_2O$: C, 66.64; H, 5.82; N, 3.11. Found: C, 66.56; H, 5.72; N, 3.06.

#### 4.3.3. Cesium *tert*-leucine phosphinoazomethinylate 1a-Cs

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.88 (d, *J* (H,P) = 5.20 Hz, 1H, CHN), 8.23 (ddd, *J* (H,H) = 7.78, 4.03, 1.21 Hz, 1H, C*H*$_{ar}$CCHN), 7.31–7.19 (m, 12H, H$_{ar}$), 6.78 (ddd, *J* (H,H) = 7.71, 4.74, 0.92 Hz, 1H, CHCP), 3.34 (s, 1H, CH), 0.81 (s, 9H, CH$_3$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.59 (s, 1P). $^{13}$C NMR (101 MHz, *MeOD*): $\delta$ 179.31 (s, 1C, COO), 159.85 (d, *J* (C,P) = 25.60 Hz, 1C, CN), 141.09 (d, *J* (C,P) = 17.58 Hz, 1C, C$_{ar}$), 138.73 (d, *J* (C,P) = 18.21 Hz, 1C, C$_{ar}$), 137.72 (d, *J* (C,P) = 9.49 Hz, 1C, C$_{ar}$), 137.39 (d, *J* (C,P) = 10.33 Hz, 1C, C$_{ar}$), 135.27 (d, *J* (C,P) = 5.40 Hz, 2C, C$_{ar}$), 135.07 (d, *J* (C,P) = 5.36 Hz, 2C, C$_{ar}$), 133.97 (s, 1C, C$_{ar}$), 131.26 (s, 1C, C$_{ar}$), 130.17 (s, 2C, C$_{ar}$), 130.04 (s,1C, C$_{ar}$), 129.82 (d, *J* (C,P) = 6.97 Hz, 4C, C$_{ar}$), 128.85 (d, *J* (C,P) = 4.34 Hz, 1C, C$_{ar}$), 88.90 (s, 1C, NC), 35.30 (s, 1C, C(CH$_3$)$_3$), 27.91 (s, 3C, CH$_3$). $[\alpha]_D^{20} = -7.4$ (*c* 1, methanol). Anal. Calcd for $C_{25}H_{25}NCsO_2P$: C, 56.09; H, 4.71; N, 2.62. Found: C, 56.52; H, 5.01; N, 2.56.

#### 4.3.4. Lithium *tert*-leucine phosphinoazomethinylate 1a-Li

$^1$H NMR (400 MHz, MeOD): $\delta$ 8.89 (d, *J* (H,P) = 5.35 Hz, 1H, CHN), 8.22 (ddd, *J* (H,H) = 7.79, 4.04, 1.31 Hz, 1H, C*H*CCHN), 7.35–7.15 (m, 12H, H$_{ar}$), 6.80 (ddd, *J* (H,H) = 7.74, 4.74, 0.87 Hz, 1H, CHCP), 3.36 (s, 1H, CH), 0.83 (s, 9H, CH$_3$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.60 (s, 1P). $^{13}$C NMR (101 MHz, *MeOD*): $\delta$ 179.35 (s, 1C, COO), 160.27 (d, *J* (*C,P*) = 25.91 Hz, 1C, CN), 140.93 (d, *J* (*C,P*) = 17.57 Hz, 1C, C$_{ar}$), 138.86 (d, *J* (*C,P*) = 18.50 Hz, 1C, C$_{ar}$), 137.66 (d, *J* (*C,P*) = 9.52 Hz, 1C, C$_{ar}$), 137.31 (d, *J* (*C,P*) = 10.13 Hz, 1C, C$_{ar}$), 135.27 (d, *J* (*C,P*) = 5.13 Hz, 2C, C$_{ar}$), 135.07 (d, *J* (*C,P*) = 5.39 Hz, 2C, C$_{ar}$), 134.04 (s, 1 C, C$_{ar}$), 131.40 (s, 1C, C$_{ar}$), 130.20 (s, 2C, C$_{ar}$), 130.08 (s, 1C, C$_{ar}$), 129.83 (d, *J* (*C,P*) = 7.07 Hz, 4C, C$_{ar}$), 128.83 (d, *J* (*C,P*) = 4.34 Hz, 1C, C$_{ar}$), 88.75 (s, 1C, CH), 35.34 (s, 1C, C(CH$_3$)$_3$), 27.90 (s, 3C, CH$_3$). $[\alpha]_D^{20} = -11.5$ (*c* 1, methanol). Anal. Calcd for $C_{25}H_{25}NCsO_2P$, $H_2O$: C, 70.25; H, 6.37; N, 3.28. Found: C, 70.37; H, 6.31; N, 3.32.

#### 4.3.5. Sodium valine-phosphinoazomethinylate 1b

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.93 (d, *J* (H,P) = 5.38 Hz, 1H, CHN), 8.12 (ddd, *J* (H,H) = 7.79, 4.04, 1.30 Hz, 1H, C*H*CCHN), 7.38–7.14 (m, 12H, H$_{ar}$), 6.81 (ddd, *J* (H,H) = 7.72, 4.66, 0.93 Hz, 1H, CHCP), 3.33 (s, 0.5H, NCH), 3.27 (s, 0.5H, NCH), 2.18–2.06 (m, 1H, CH(CH$_3$)$_2$), 0.79 (d, *J* = 6.76 Hz, 3H, CH$_3$), 0.51 (d, *J* = 6.72 Hz, 3H, CH$_3$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.73 (s, 1P). $^{13}$C NMR (101 MHz, *MeOD*) : $\delta$ 179.93 (s, 1C, COO), 160.86 (d, *J* (C,P) = 25.99 Hz, 1C, CN), 140.89 (d, *J* (C,P) = 17.61 Hz, 1C, C$_{ar}$), 139.01 (d, *J* (C,P) = 18.65 Hz, 1C, C$_{ar}$), 137.61 (d, *J* (C,P) = 9.40 Hz, 1C, C$_{ar}$), 137.28 (d, *J* (C,P) = 10.11 Hz, 1C, C$_{ar}$), 135.30 (d, *J* (C,P) = 3.58 Hz, 2C, C$_{ar}$), 135.10 (d, *J* (C,P) = 3.65 Hz, 2C, C$_{ar}$), 134.01 (s, 1C, C$_{ar}$), 131.42 (s, 1C, C$_{ar}$), 130.21 (s, 2C, C$_{ar}$), 130.06 (s, 1C, C$_{ar}$), 129.84 (d, *J* (C,P) = 7.06 Hz, 4C, C$_{ar}$), 128.74 (d, *J* (C,P) = 4.30 Hz, 1C, C$_{ar}$), 86.68 (s, 1C, NCH), 32.75 (s, 1C, CH), 20.34 (s, 1C, CH$_3$), 19.33 (s, 1C, CH$_3$). $[\alpha]_D^{20} = -11.7$ (*c* 1, methanol). Anal. Calcd for $C_{24}H_{23}NNaO_2P$, $H_2O$: C, 67.13; H, 5.87; N, 3.26. Found: C, 66.63; H, 5.70; N, 3.46.

#### 4.3.6. Sodium *iso*-leucine-phosphinoazomethinylate 1c

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.90 (d, *J (H,P)* = 5.45 Hz, 1H, CHN), 8.07 (ddd, *J (H,H)* = 7.69, 4.02, 1.18 Hz, 1H, CHCCHN), 7.33–7.08 (m, 12H, H$_{ar}$), 6.76 (ddd, *J (H,H)* = 7.71, 4.68, 0.86 Hz, 1H, CHCP), 3.33 (d, *J (H,H)* = 8.33 Hz, 1H, NCH), 1.93–1.82 (m, 1H, CH(CH$_3$)(CH$_2$)), 1.04–0.97 (m, 1H, CH$_2$), 0.75 (d, *J (H,H)* = 6.77 Hz, 3H, CH$_3$), 0.59 (dd, *J (H,H)* = 6.62, 3.54 Hz, 4H, CH$_3$, CH$_2$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.76 (s, 1P). $^{13}$C NMR (101 MHz, MeOD): $\delta$ 179.89 (s, 1C, COO), 160.92 (d, *J* (*C,P*) = 26.03 Hz, 1C, CHN), 140.94 (d, *J* (*C,P*) = 17.94 Hz, 1C, C$_{ar}$), 138.97 (d, *J* (*C,P*) = 18.37 Hz, 1C, C$_{ar}$), 137.68 (d, *J* (*C,P*) = 9.41 Hz, 1C, C$_{ar}$), 137.29 (d, *J* (*C,P*) = 10.26 Hz, 1C, C$_{ar}$), 135.30 (d, *J* (*C,P*) = 8.71 Hz, 2C, C$_{ar}$), 135.10 (d, *J* (*C,P*) = 8.89 Hz, 2C, C$_{ar}$), 133.96 (s, 1C, C$_{ar}$), 131.41 (s, 1C, C$_{ar}$), 130.22 (s, 1C, C$_{ar}$), 130.19 (s, 1C, C$_{ar}$), 130.06 (s, 1C, C$_{ar}$), 129.86 (d, *J* (*C,P*) = 1.16 Hz, 2C, C$_{ar}$), 129.79 (d, *J* (*C,P*) = 1.25 Hz, 2C, C$_{ar}$), 128.75 (d, *J* (*C,P*) = 4.29 Hz, 1C, C$_{ar}$), 85.63 (s, 1C, NCH), 38.90 (s, 1C, CH(CH$_3$)(CH$_2$)), 26.07 (s, 1C, CH$_2$), 16.30 (s, 1C, CHCH$_3$), 11.31 (s, 1C, CH$_2$CH$_3$). $[\alpha]_D^{20} = -15.0$ (*c* 1, methanol). Anal. Calcd for $C_{25}H_{25}NNaO_2P$, $0.5H_2O$: C, 69.12; H, 6.03; N, 3.22. Found: C, 68.67; H, 6.02; N, 3.32.

#### 4.3.7. Sodium leucine-phosphinoazomethinylate 1d

$^1$H NMR (400 MHz, MeOD): $\delta$ 8.91 (d, $J$ (*H,P*) = 5.48 Hz, 1H, CHN), 8.07 (ddd, $J$ (*H,H*) = 7.78, 4.03, 1.31 Hz, 1H, CHCCN), 7.33–7.05 (m, 12H, $H_{ar}$), 6.74 (ddd, $J$ (*H,H*) = 7.72, 4.71, 0.85 Hz, 1H, CHCP), 3.71 (dd, $J$ (H,H) = 9.70, 4.39 Hz, 1H, NCH), 1.63–1.44 (m, 2H, $CH_2$), 0.88 (m, 1H, CH), 0.65 (d, $J$ (*H,H*) = 6.66 Hz, 3H, $CH_3$), 0.53 (d, $J$ (*H,H*) = 6.51 Hz, 3H, $CH_3$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.81 (s, 1P). $^{13}$C NMR (101 MHz, *MeOD*) : $\delta$ 180.35 (s, 1C, COO), 160.93 (d, $J$ (*C,P*) = 26.02 Hz, 1C), 140.72 (d, $J$ (*C,P*) = 17.68 Hz, 1C, $C_{ar}$), 138.66 (d, $J$ (*C,P*) = 18.21 Hz, 1C, $C_{ar}$), 137.34 (d, $J$ (*C,P*) = 9.21 Hz, 1C, $C_{ar}$), 137.06 (d, $J$ (*C,P*) = 10.15 Hz, 1C, $C_{ar}$), 135.09 (d, $J$ (*C,P*) = 20.24 Hz, 2C, $C_{ar}$), 134.82 (d, $J$ (*C,P*) = 20.18 Hz, 2C, $C_{ar}$), 133.77 (s, 1C, $C_{ar}$), 131.31 (s, 1C, $C_{ar}$), 130.07 (s, 1C, $C_{ar}$), 129.94 (d, $J$ (*C,P*) = 5.67 Hz, 2C, $C_{ar}$), 129.66 (d, $J$ (*C,P*) = 2.75 Hz, 2C, $C_{ar}$), 129.59 (d, $J$ (*C,P*) = 2.87 Hz, 2C, $C_{ar}$), 128.53 (d, $J$ (*C,P*) = 3.96 Hz, 1C, $C_{ar}$), 76.40 (s, 1C, NCH), 43.99 (s, 1C, CH), 25.14 (s, 1C, $CH_2$), 23.76 (s, 1C, $CH_3$), 21.36 (s, 1C, $CH_3$). $[\alpha]_D^{20} = -12.3$ ($c$ 1 in methanol). Anal. Calcd for $C_{25}H_{25}NNaO_2P$, $0.5H_2O$: C, 69.12; H, 6.03; N, 3.22. Found: C, 69.19; H, 6.00; N, 3.36.

#### 4.3.8. Sodium phenylglycine-phosphinoazomethinylate 1e

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.95 (d, $J$ (*H,P*) = 5.41 Hz, 1H, CHN), 8.16 (ddd, $J$ (*H,H*) = 7.74, 3.94, 1.13 Hz, 1H, C*H*CCHN), 7.31–7.08 (m, 17H, $H_{ar}$), 6.77 (ddd, $J$ (*H,H*) = 7.71, 4.80, 0.91 Hz, 1H, CHCP), 4.83 (s, 1H, NCH). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −15.31 (s, 1P). $^{13}$C NMR (101 MHz, *MeOD*): $\delta$ 178.55 (s, 1C, COO), 161.34 (d, $J$ (*C,P*) = 25.80 Hz, 1C, CHN), 141.90 (s, 1C, $C_{ar}$), 140.77 (d, $J$ (*C,P*) = 17.25 Hz, 1C, $C_{ar}$), 139.30 (d, $J$ (*C,P*) = 18.40 Hz, 1C, $C_{ar}$), 137.51 (d, $J$ (*C,P*) = 9.42 Hz, 1C, $C_{ar}$), 137.22 (d, $J$ (*C,P*) = 9.99 Hz, 1C, $C_{ar}$), 135.26 (d, $J$ (*C,P*) = 9.42 Hz, 2C, $C_{ar}$), 135.06 (d, $J$ (*C,P*) = 9.51 Hz, 2C, $C_{ar}$), 133.95 (s, 1C, $C_{ar}$), 131.58 (s, 1C, $C_{ar}$), 130.20 (d, $J$ (*C,P*) = 2.84 Hz, 2C, $C_{ar}$), 130.08 (s, 1C, $C_{ar}$), 129.83 (d, $J$ (*C,P*) = 7.23 Hz, 2C, $C_{ar}$), 129.43 (s, 1C, $C_{ar}$), 129.14 (d, $J$ (*C,P*) = 13.87 Hz, 2C, $C_{ar}$), 128.80 (s, 1C, $C_{ar}$), 128.77 (s, 1C, $C_{ar}$), 128.26 (s, 1C, $C_{ar}$), 127.98 (s, 2C, $C_{ar}$), 81.80 (s, 1C, NCH). $[\alpha]_D^{20} = +4.5$ ($c$ 1, methanol). Anal. Calcd for $C_{27}H_{21}NNaO_2P$, $0.25H_2O$: C, 72.08; H, 4.82; N, 3.11. Found: C, 72.11; H, 4.79; N, 3.20.

#### 4.3.9. Valine-phosphinoazomethinylate methyl ester 1f

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.85 (d, $J$ (*H,P*) = 5.27 Hz, 1H, CHN), 7.92 (dd, $J$ (*H,H*) = 7.09, 3.53 Hz, 1H, C*H*CCHN), 7.35–7.12 (m, 12H, $H_{ar}$), 6.81 (dd, $J$ (*H,H*) = 7.16, 4.79 Hz, 1H, CHCP), 3.57 (s, 3H, $OCH_3$), 3.47 (d, $J$ (*H,H*) = 7.39 Hz, 1H, NCH), 2.09 (qd, $J$ (*H,H*) = 13.68, 6.77, 6.77, 6.75 Hz, 1H, CH), 0.72 (d, $J$ (*H,H*) = 6.77 Hz, 3H, $CH_3$), 0.60 (d, $J$ (*H,H*) = 6.75 Hz, 3H, $CH_3$). $^{31}$P NMR (162 MHz, *MeOD*): $\delta$ −14.64 (s, 1P). $^{13}$C NMR (101 MHz, *MeOD*): $\delta$ 173.43 (s, 1C, COO), 164.07 (d, $J$ (*C,P*) = 23.14 Hz, 1C, CHN), 139.79 (d, $J$ (*C,P*) = 17.43 Hz, 1C, $C_{ar}$), 139.50 (d, $J$ (*C,P*) = 19.44 Hz, 1C, $C_{ar}$), 137.28 (d, $J$ (*C,P*) = 8.89 Hz, 1C, $C_{ar}$), 137.14 (d, $J$ (*C,P*) = 9.48 Hz, 1C, $C_{ar}$), 135.13 (d, $J$ (*C,P*) = 1.53 Hz, 2C, $C_{ar}$), 134.92 (d, $J$ (*C,P*) = 1.55 Hz, 2C, $C_{ar}$), 134.00 (s, 1C, $C_{ar}$), 131.85 (s, 1C, $C_{ar}$), 130.07 (d, $J$ (*C,P*) = 3.76 Hz, 2C, $C_{ar}$), 129.92 (s, 1C, $C_{ar}$), 129.70 (d, $J$ (*C,P*) = 2.91 Hz, 2C, $C_{ar}$), 129.63 (d, $J$ (*C,P*) = 2.90 Hz, 2C, $C_{ar}$), 128.85 (d, $J$ (*C,P*) = 3.79 Hz, 1C, $C_{ar}$), 81.05 (s, 1C, NCH), 52.21 (s, 1C, $OCH_3$), 32.49 (s, 1C, $CH(CH_3)_2$), 19.44 (s, 1C, $CH_3$), 18.63 (s, 1C, $CH_3$) $[\alpha]_D^{20} = -9.1$ (c 1, methanol).

#### 4.3.10. Sodium *tert*-leucine azomethinylate 1g

$^1$H NMR (400 MHz, *MeOD*): $\delta$ 8.12 (s, 1H, CHN), 7.74–7.70 (m, 2H, $H_{ar}$), 7.32–7.29 (m, 1H, $H_{ar}$), 3.44 (s, 1H, NCH), 0.94 (s, 9H, $CH_3$). $^{13}$C NMR (101 MHz, *MeOD*): $\delta$ 179.56 (s, 1C, COO), 162.16 (s, 1C, CHN), 137.98 (s, 1C, $C_{ar}$), 131.50 (s, 1C, Car), 129.57 (s, 2C, $C_{ar}$), 129.54 (s, 2C, $C_{ar}$), 88.55 (s, 1C, NCH), 35.36 (s, 1C, $C(CH_3)_3$), 27.97 (s, 3C, $CH_3$). $[\alpha]_D^{20} = -3.2$ ($c$ 1, methanol).

### 4.4. General experimental procedure for complex syntheses

A flame-dried Schlenk tube was charged with $(CuOTf)_2{\cdot}C_7H_8$ (52.8 mg, 0.1 mmol, 0.1 equiv) and ligand **1a-Na** (42.5 mg, 0.1 mmol, 0.1 equiv). Dry ethyl acetate (20 mL) was added and the resulting green mixture was stirred at room temperature for 30 min. The resulting solution was concentrated in vacuo to afford a green powder in quantitative yield. $[\alpha]_D^{20} = +10.5$ ($c$ 1 in methanol). Anal. Calcd for $C_{27}H_{25}Cu_2F_6NNaO_8PS_2$: C, 38.12; H, 2.96; N, 1.65. Found: C, 37.85; H, 3.18; N, 1.44.

### 4.5. Representative experimental proceudre for Cu-catalyzed conjugate addition of dialkylzinc reagents to cyclic and acyclic enones

A flame-dried Schlenk tube was charged with copper source (0.02 mmol, 0.02 equiv) and ligand (0.01 mmol, 0.01 equiv). Next 3 mL of an ethyl acetate solution containing cyclododecane (33.6 mg, 0.2 mmol, 0.2 equiv) was added and the resulting green mixture was stirred at room temperature for 15 min, after which $Et_2Zn$ (1.5–3 mmol) was added dropwise. Finally, cyclic or acyclic enone (1 mmol, 1 equiv) was added at required temperature. The resulting brown solution was allowed to stir at the required temperature for 6–14 h and the reaction was quenched by the addition of 5 mL of a 1 N HCl solution. The product was extracted with 5 mL of $Et_2O$. The organic phase was washed with water and brine, dried over $MgSO_4$, filtrated, and concentrated under vacuo.

Conversions and enantiomeric purities of the products were obtained from GLC analysis (Chiraldex-GTA column).

### 4.6. Determination of the enantiomeric excesses

#### 4.6.1. 3-Ethylcyclohexanone

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 104 kPa, total He flow 9.2 mL/min; 90 °C (30 min)–15 °C/min–160 °C (10 min); $R_T(R)$ = 23.2 min; $R_T(S)$ = 25.1 min; $R_T$(2-cyclohexen-1-one) = 16.4 min; $R_T$(cyclododecane) = 26.7 min.

#### 4.6.2. 3-Ethylcycloheptanone

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 98.1 kPa, total He flow 9.1 mL/min; 90 °C (45 min)–1 °C/min–110 °C–15 °C/min–160 °C (10 min); $R_T(S)$ = 45.5 min; $R_T(R)$ = 46.8 min. $R_T$(2-cyclohepten-1-one) = 34.6 min; $R_T$(cyclododecane) = 27.0 min.

#### 4.6.3. 3-Isopropylcyclohexanon

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 99.6 kPa, total He flow 9.2 mL/min; 90 °C (40 min)–15 °C/min–160 °C (10 min); $R_T$ ($R$) = 36.5 min; $R_T(S)$ = 41.5 min. $R_T$(2-cyclohexen-1-one) = 15.8 min; $R_T$(cyclododecane) = 26.5 min.

#### 4.6.4. 3-Isopropylcyclopentanone

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 98.0 kPa, total He flow 9.7 mL/min; 70 °C (50 min)–1 °C/min–75 °C–15 °C/min–160 °C (10 min); $R_T(S)$ = 52.1 min; $R_T(R)$ = 54.5 min. $R_T$(2-cyclopenten-1-one) = 18.9 min; $R_T$(cyclododecane) = 58.2 min.

#### 4.6.5. 4-Ethyl-5-methylhexan-2-one

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 104.0 kPa, total He flow 9.9 mL/min; 80 °C (30 min)–10 °C/min–160 °C (5 min); $R_T(R)$ = 16.5 min; $R_T(S)$ = 18.1 min. $R_T$(5-methylhexan-2-one) = 11.6 min; $R_T$(cyclododecane) = 33.9 min.

#### 4.6.6. 4-Ethylnonan-2-one

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 104.0 kPa, total He flow 9.9 mL/min; 80 °C (60 min)–2 °C/min–100 °C–10 °C/min–160 °C (5 min); $R_T(S)$ = 50.0 min; $R_T(R)$ = 54.3 min. $R_T$(nonen-2-one) = 42.3 min; $R_T$(cyclododecane) = 40.2 min.

#### 4.6.7. 4-Phenylhexan-2-one

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 108.0 kPa, total He flow 9.7 mL/min; 100 °C (60 min)–2 °C/min–120 °C–10 °C/min–160 °C (5 min); $R_T(R)$ = 50.5 min; $R_T(S)$ = 53.3 min. $R_T$(phenylhexen-2-one) = 63.7 min; $R_T$(cyclododecane) = 16.8 min.

#### 4.6.8. 4-Isopropylnonan-2-one

Capillary column Chiraldex GTA, (0.12 μm, 30 m, 0.25 mm), pression 109.9 kPa, total He flow 10.5 mL/min; 80 °C (90 min)–10 °C/min–160 °C (10 min); $R_T$ (+) = 67.1 min; $R_T$ (−) = 69.9 min. $R_T$(nonen-2-one) = 40.9 min; $R_T$(cyclododecane) = 38.4 min.

## Acknowledgements

This work was supported by the CNRS, the Region Bretagne and the Ministère de la Recherche et de la Technologie (Grant to J.W. and D.R.). M.M. and C.C. thank Bretagne-Valorisation for his financial support related to the development of chiral ligands for asymmetric catalysis.

## References

1. (a) Perlmutter, P. *Conjugate Addition Reaction in Organic Synthesis*. In *Tetrahedron Organic Chemistry Series*; Pergamon Press: Oxford, 1992; Vol. 9; (b) Yamamoto, Y. *Methods Org. Chem.* (Houben-Weyl), 1995, *4* (stereoselective Synthesis), 2041–2057.
2. Selected reviews: (a) Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221–3236; (b) Krause, N.; Hoffman-Röder, A. *Synthesis* **2001**, 171–196; (c) Ferringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346–353.
3. Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829–2844.
4. For recent examples, see: (a) Mizutani, H.; Degrado, S. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 779–781; (b) Krauss, I. J.; Leighton, J. L. *Org. Lett.* **2003**, *5*, 3201–3203; (c) Clavier, H.; Coutable, L.; Guillemin, J. C.; Mauduit, M. *Tetrahedron: Asymmetry* **2005**, *16*, 921–924.
5. For examples, see: (a) Diégez, S. M.; Deeremberg, O.; Claver, C.; Van Leeuwen, P. W. N. M.; Kramer, P. *Tetrahedron: Asymmetry* **2000**, *11*, 3161–3166; (b) Fraser, P. K.; Woodward, S. *Chem. Eur. J.* **2003**, *9*, 776–783; (c) D'Augustin, M.; Palais, L.; Alexakis, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1376–1378.
6. For examples, see: (a) Lopez, F.; Harutyunyan, S. R.; Meetsma, A.; Minaard, A. J.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 2752–2756; (b) Lee, K.-S.; Brown, M. K.; Hird, A. W.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 7182–7184; (c) Martin, D.; Kehrli, S.; D'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A. *J. Am. Chem. Soc.* **2006**, *128*, 8416–8417.
7. Takaya, Y.; Ogasawara, M.; Hayashi, T. *J. Am. Chem. Soc.* **1998**, *120*, 5579–5580.
8. (a) Degrado, S. J.; Mizutani, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 755–756; (b) Degrado, S. J.; Mizutani, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 13362–13363; (c) Kevin Brown, M.; Degrado, S. J.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2005**, *44*, 5306–5310; (d) Kacprzynski, M. A.; Kazane, S. A.; May, T. L.; Hoveyda, A. H. *Org. Lett.* **2007**, *9*, 3187–3190.
9. Soeta, T.; Selim, K.; Kuriyama, M.; Tomioka, K. *Adv. Synth. Catal.* **2007**, *349*, 629–635.
10. Blaser, H.-U.; Pugin, B.; Spindler, F. *J. Mol. Catal. A: Chem.* **2005**, *231*, 1–20.
11. Selected recent papers: (a) Bernsmann, H.; van den Berg, M.; Hoen, R.; Minnaard, A. J.; Mehler, G.; Reetz, M. T.; de Vries, J. G.; Feringa, B. L. *J. Org. Chem.* **2005**, *70*, 943–951; (b) Palais, L.; Mikhel, I. S.; Bournaud, C.; Micouin, L.; Falciola, C. A.; Vuagnoux-d'Augustin, M.; Rosset, S.; Bernadinelli, G.; Alexakis, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7462–7465.
12. Bradar, D. B.; Gau, H.-M. *Tetahedron: Asymmetry* **2008**, *19*, 733–738.
13. Knizhnikov, V. A.; Azizbekyan, O. P.; Prishchepenko, V. M. *Russ. J. Gen. Chem.* **2003**, *73*, 1445–1447.
14. Alfonsi, K.; Colberg, J.; Dunn, P. J.; Fevig, T.; Jennings, S.; Johnson, T. A.; Kleine, H. P.; Knight, C.; Nagy, M. A.; Perry, D. A.; Stefaniak, M. *Green Chem.* **2008**, *10*, 31–36.
15. Alexakis, A.; Benhaim, C.; Rosset, S.; Humam, M. *J. Am. Chem. Soc.* **2002**, *124*, 5262–5263.
16. Hajra, A.; Yoshikai, N.; Nakamura, E. *Org. Lett.* **2006**, *8*, 4153–4155.
17. Lopez, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2004**, *126*, 12784–12785.
18. (a) Shibasaki, M.; Matsunaga, S. *Chem. Soc. Rev.* **2006**, *35*, 269–279; (b) Shibasaki, M.; Yoshikawa, N. *Chem. Rev.* **2002**, *102*, 2187–2209.