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Enantioselective 1,4-conjugate addition of diethylzinc to (*E*)-alkenyl aryl ketones catalysed by Cu/DiPPAM complex

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ABSTRACT

We report here the use of the DiPPAM-**L1** ligand for copper-catalysed asymmetric conjugate addition (ACA) of diethylzinc to various (*E*)-alkenyl aryl ketones where the aryl ring is either a phenyl group substituted by nitro, chloro or methoxy groups or not substituted, or a naphthyl group. When the conjugate addition was performed in the greener AcOEt solvent with 1 or 2 mol % of $Cu(OTf)_2$/DiPPAM complex, moderate to good yields (45–83%) and high enantioselectivities (up to 98%) were reached.

1. Introduction

Among chiral ligands, the Schiff-base family is probably the most useful and accessible chiral scaffold used to promote enantioselective inductions in many metal-catalysed transformations.[1] Indeed, their simple access (in one or few steps) from a wide range of chiral amines and/or chiral aldehydes and ketones makes them really attractive for the chemists. Historically, the first enantioselective induction promoted by a chiral organometallic complex was originally proposed by Nozaki et al. in 1966 and involved the chiral Schiff-base copper complex **1** for the cyclopropanation of styrene[2] (Fig. 1). Since these pioneering works, Schiff-base ligands have been intensively studied through many structural modifications enabling to promote excellent enantioselections in various organometallic reactions.[1] Among all these modifications, the introduction of a peptidic moiety, originally disclosed by Inoue's group in 1992,[3] allowed to access to a really efficient class of chiral ligands. Important breakthroughs were achieved in this direction notably by Hoveyda's group with their well-known small-peptide ligands,[4] which allowed remarkable enantioselectivities in many C–C bond-forming reactions, including notably the copper-catalysed Asymmetric Conjugate Addition (ACA).[5] Recently, our group has developed a new chiral ligand **L1**, called DiPPAM (or DiPhenylPhosphinoAzoMethinylate salts), structurally related to Hoveyda's ligands. Advantageously, it is synthesized in a single quantitative step of direct condensation of *o*-diphenylphosphinobenzaldehyde and the carboxylate sodium salt of L-*tert*-leucine. It shows excellent stability in storage, probably owing to the carboxylate function.[6] DiPPAM-**L1** proved its efficiency in both 1,4-Cu/ACA[7] and Palladium-catalysed Tsuji-Trost[8] reactions.

Very recently, excellent regio- and enantioselectivities (up to 99%) were observed in the more challenging copper-catalysed 1,6-addition of diorganozinc reagents to cyclic dienones.[9] We decided to extend the scope of DiPPAM-**L1** in 1,4-ACA through its evaluation in the Cu-catalysed addition of diethylzinc to (*E*)-alkenyl aryl ketones **2** substituted by nitro, chloro or methoxy groups, that could afford interesting new chiral building-blocks,[10] and we report here our results.

2. Results and discussion

We evaluated first the influence of the copper source (Cu(I) versus Cu(II)) and also the effect of the solvent media (THF vs AcOEt) on the enantioselection of the addition of diethylzinc to standard acyclic enones **3** and **5** (Table 1). Although no significant difference in reactivity occurred when copper(I) triflate was used in both solvents, we were delighted to observe a higher enantioselection (96%) for the adduct **4** when the addition was performed in the greener AcOEt solvent[11] (entries 1 and 2). When copper(II)

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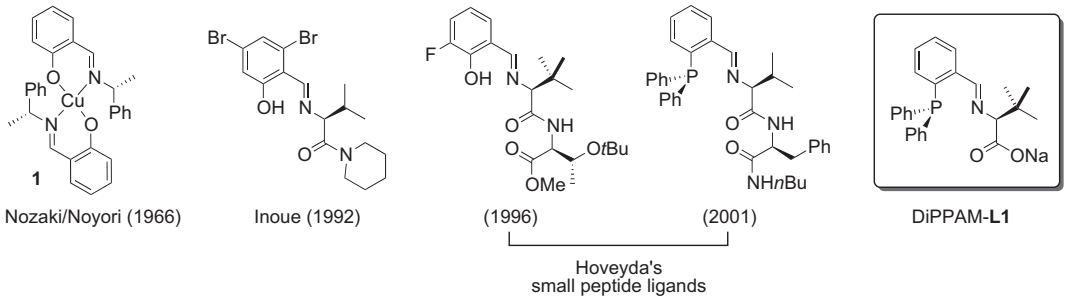
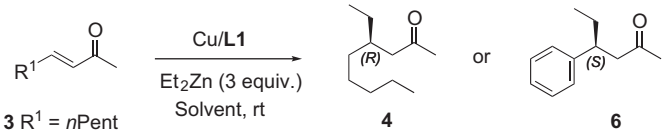


Fig. 1. Selected chiral Schiff-base ligands.

Table 1
Influence of the copper source and solvent for ACA of Et_2Zn to (*E*)-alkenyl methyl ketones **3** and **5** involving DiPPAM-**L1**



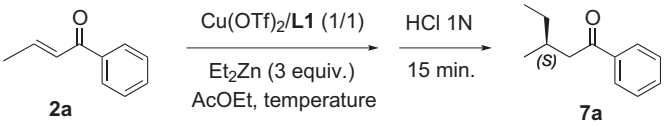
Entry	Substrate	Cu/**L1** (ratio,[a] mol %)	Solvent	Time (h)	Conv.[b] (%)	ee[c] (%)
1	**3**	$(CuOTf)_2$-Tol/**L1** (2/1, 1)	THF	4	97	80
2		$(CuOTf)_2$-Tol/**L1** (2/1, 1)	AcOEt	4	>99	96
3		$Cu(OTf)_2$/**L1** (1/1, 2)	THF	20	>99	82
4		*$Cu(OTf)_2$/**L1** (1/1, 2)*	*AcOEt*	*1*	*>99*	*97*
5	**5**	$(CuOTf)_2$-Tol/**L1** (2/1, 1)	THF	14	57	83
6		$(CuOTf)_2$-Tol/**L1** (2/1, 2)	AcOEt	6	>99	98
7		*$Cu(OTf)_2$/**L1** (1/1, 2)*	*AcOEt*	*1*	*>99 (71)*[d]	*99*

The italic values represents the best result in term of enantioselectivity.
[a] Ratio between metal Copper and **L1**.
[b] Determined by ^1H NMR.
[c] Determined by chiral GC (average of two experiments).
[d] Isolated yield after purification by SiO_2 chromatography.

triflate was used in AcOEt, both reactivity and enantioselectivity were improved, the adduct **4** being obtained in complete conversion after only 1 h (vs 20 h in THF) and 97% ee (entries 3 and 4). Concerning the acyclic enone **5**, AcOEt proved also to be superior in term of ee (98% vs 83% in THF), while copper(II) salts allowed us to reduce the reaction time to 1 h (vs 6 h with Cu-(I) triflate). The adduct **6** could be isolated in 71% yield when the reaction was run in AcOEt in the presence of $Cu(OTf)_2$/DiPPAM-**L1**. Therefore, these conditions appeared to us as the most efficient for the 1,4-addition of acyclic enone substrates.

These two crucial parameters being studied, we started the evaluation of (*E*)-alkenyl aryl ketones **2**. Different reaction conditions (temperature, catalyst loading and reaction time) were tested using (*E*)-1-phenylbuten-2-en-1-one **2a** as model substrate. As depicted in Table 2, the adduct **7a** was isolated in 61% of yield and an excellent enantioselectivity of 96% when the reaction was run at 0 °C in presence of 2 mol % of copper/DiPPAM-**L1** (entry 2). The decrease of the temperature of the media down to −18 °C led to reduce the rate of the addition without any improvement of the selectivity (89% ee, entry 3). When catalyst loading was diminished to 1 mol %, the catalytic system remained active even at −18 or 0 °C (total conversion after 4 h, entries 4 and 5) but the adduct **7a** was obtained with lower enantiomeric excesses (83.5 and 86%, respectively). Finally, in order to improve the isolated yield of **7a**, we tried to modify the work-up procedure either by increasing the time of the acidic hydrolysis (30 vs 15 min) or by replacing aqueous HCl with solid NH_4Cl. Curiously, although better-isolated yields were reached as expected, the enantioselectivity was slightly diminished down to 93 and 90%, respectively (entries 6 and 7). It is

Table 2
Optimisation of reaction conditions for ACA of Et_2Zn to (*E*)-1-phenylbuten-2-en-1-one **2a** catalysed by $Cu(OTf)_2$/DiPPAM-**L1**



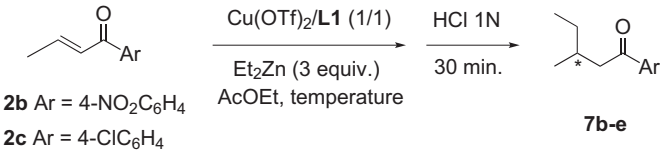
Entry	$Cu(OTf)_2$/**L1** (mol %)	Temp (°C)	Time (h)	conv.[a]/yield[c] (%)	ee[b] (%)
1	2	20	0.45	>99/51	83
2	*2*	*0*	*1*	*>99/61*	*96*
3	2	−18	2	>99	89
4	1	0	3.5	>99/41	83.5
5	1	−18	4	>99/73	86
6[d]	2	0	1	>99/68	93
7[e]	2	0	1	>99/67	90

The italic values represents the best result in term of enantioselectivity.
[a] Determined by ^1H NMR.
[b] Determined by chiral GC (average of two experiments).
[c] Isolated yield after purification by SiO_2 chromatography.
[d] HCl 1 N 30 min.
[e] NH_4Cl solid 1 h.

worth highlighting that the selectivity for adduct **7a** obtained here (96%) is close to the best reported result in the literature so far (95% ee),[12] attesting the attractive capacity of the Cu/DiPPAM complex to produce highly enantioenriched 1,4-adducts.

After having validated the suitability of our catalytic system towards the model substrate **2a**, we were interested in extending the scope to other (*E*)-alkenyl aryl ketones **2b**–**e** bearing different substituents on the aryl moiety, in order to evaluate their influence on the selectivity of the addition. Such structure–reactivity relationship had never been examined previously. We started with the addition of diethylzinc to the aryl ketone **2b** where the aromatic group is substituted by a 4-NO_2 function (Table 3). As expected, the electronic withdrawing effect of the nitro improved the reactivity of the enone leading to a completion of the addition within 1 h even at −18 °C in presence of 1 mol % of Cu/DiPPAM-**L1** complex. In these conditions, the corresponding adduct **7b** was isolated in 57% of yield and an enantioselectivity ranged between 83 and 86% (entries 1 and 2). Both reaction time and chiral induction were significantly improved by using 2 mol % of catalyst at −18 °C, affording the desired 1,4-adduct in 65% yield and 95% ee (entry 3). It must be noticed that the isolated yield could be improved by employing 4 mol % of chiral complex (79%, entry 4). We suspect that a premature degradation of the catalytic species could occur during this addition. Excellent results were obtained with the aryl ketones **2c** bearing a chlorine atom in *para* position (entries 5 and 6). Within 1 h at −18 °C in presence of 2 mol % of catalyst, the corresponding 1,4-adduct **7c** was isolated in 78% yield with an enantio-induction of 98%. In the case of 4-methoxy substituted aryl ketones **2d**, the electron-donating effect of the methoxy group decreased the rate of the addition of the organozinc, as 6 h of reaction were required to

Table 3
ACA of Et_2Zn to various substituted (*E*)-alkenyl aryl ketones **2b**-**2e** catalysed by $Cu(OTf)_2$/DiPPAM-**L1**



2b Ar = 4-$NO_2C_6H_4$
2c Ar = 4-ClC_6H_4
2d Ar = 4-$MeOC_6H_4$
2e Ar = 2-Naptyl

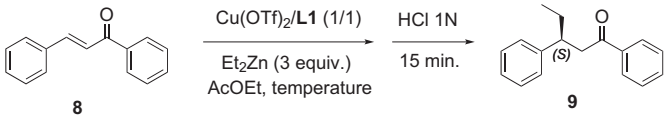
Entry	2	$Cu(OTf)_2$/**L1** (mol %)	Temp (°C)	Time (h)	conv.[a]/yield[c] (%)	ee[b] (%)
1[d]	**2b**	1	0	0.45	>99/56	83
2[d]		1	−18	1	>99/57	86
3		2	−18	0.15	>99/65	95
4		*4*	*−18*	*0.1*	*>99/79*	*96*
5[d]	**2c**	2	0	0.45	>99/83	88
6		*2*	*−18*	*1*	*>99/78*	*98*
7[d]	**2d**	*2*	*−18*	*6*	*>99/63*	*>97*
8	**2e**	1	0	3.5	>99/83	89
9		1	−18	18	>99/44	94
10		2	0	1	>99/66	96
11		*2*	*−18*	*2.5*	*>99/73*	*96*

The italic values represents the best result in term of enantioselectivity.
[a] Determined by ^1H NMR.
[b] Determined by chiral GC for **2b** and **2c** and by chiral HPLC for **2d** and **2e** (average of two experiments).
[c] Isolated yield after purification by SiO_2 chromatography.
[d] HCl 1 N 15 min.

reach a full conversion at −18 °C (entry 7). However, the desired adduct was isolated in 63% of yield and an enantiomeric excess of >97%. The last substrate of this series was (*E*)-1-(2-naphthyl)buten-2-en-1-one **2e**. As showed in the entries 8 and 9, at 1 mol % of catalyst loading, a decrease of temperature led to an improvement of the ee (94 vs 89%) along with a significant drop of the isolated yield (44 vs 83%). Nevertheless, at higher catalyst loading (2 mol %), the reaction time, the yield and the selectivity could be improved (2 h 30 min, 76% and 96% ee, entry 11).

We then decided to extend further the scope by evaluating the well-known chalcone **8**, which has been intensively studied with many chiral ligands. Although some of them were able to promote the addition of diethylzinc with excellent enantioselectivities (up to >98%),[12,13] our Cu/DiPPAM-**L1** catalyst met some difficulties to achieve this simple addition both in terms of reactivity and chiral induction (Table 4). Indeed, the best result (77% ee, 45% yield, entry 2) was observed when the reaction was run 4 h at 0 °C with 2 mol % of catalyst. Either lengthening the reaction time, or decreasing temperature to −18 °C or increasing the catalyst loading to 4 mol % did not allow us to improve the results (entries 1, 3 and 4). We were

Table 4
ACA of Et_2Zn to chalcone **8** catalysed by $Cu(OTf)_2$/DiPPAM-**L1**



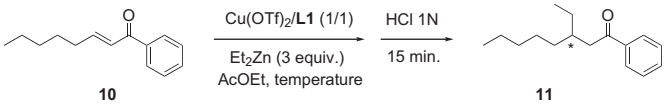
Entry	$Cu(OTf)_2$/**L1** (mol %)	Temp (°C)	Time (h)	conv.[a]/yield[c] (%)	ee[b] (%)
1	2	20	5	>99/42	73
2	*2*	*0*	*4*	*90/45*	*76.5*
3	2	−18	20	95/29	77
4	4	−18	20	>99/36	74

The italic values represents the best result in term of enantioselectivity.
[a] Determined by ^1H NMR.
[b] Determined by chiral HPLC (average of two experiments).
[c] Isolated yield after purification by SiO_2 chromatography.

astonished by this lack of selectivity as excellent ee's (95–99%) were reached with enones **2a** and **4** bearing a phenyl group at the 1- or 4-position, respectively (Tables 1 and 2). This last result shows clearly that it is really difficult to predict the enantioselective induction of any chiral ligand in asymmetric catalysis even for the same class of substrates. Some theoretical calculations need to be achieved to rationalize the selectivity of our Cu/DiPPAM-**L1** catalytic system in ACA of acyclic enones.

Finally, we decided to complete the screening of (*E*)-alkenyl aryl ketones by the substrate **10** bearing an aliphatic pentyl chain instead of the methyl one (Table 5). We observed a significant decrease of the addition rate in comparison with the crotyl aryl ketone **2a** under the same conditions (−18 °C and 2 mol % of copper complex; 18 h vs 2 h). However, adduct **11** was isolated in very good yield and ee (65 and 94%, respectively). This last result is really close to the best enantioselectivity reported in the literature for **11** (97% ee).[13]

Table 5
ACA of Et_2Zn to (*E*)-alkenyl aryl ketone **10** catalysed by $Cu(OTf)_2$/DiPPAM-**L1**



Entry	$Cu(OTf)_2$/**L1** (mol %)	Temp (°C)	Time (h)	conv.[a]/yield[c] (%)	ee[b] (%)
1	2	−18	18	>99/65	94

[a] Determined by ^1H NMR.
[b] Determined by chiral HPLC (average of two experiments).
[c] Isolated yield after purification by SiO_2 chromatography.

3. Conclusion

In summary, we have successfully extended the application of our Cu/DiPPAM-**L1** catalytic system to the 1,4-addition of diethylzinc to various (*E*)-alkenyl aryl ketones, as moderate to good yields and excellent ee values up to 98% were obtained. The evaluation of the Cu/DiPPAM-**L1** catalytic system to the more challenging 1,6-ACA on (*E*,*E*)-dienyl aryl ketones is currently underway in our group and the results will be published in the future.

4. Experimental

4.1. General information

^1H (400 MHz), ^{13}C (100 MHz), NMR spectra were recorded on a Bruker ARX400 spectrometer with complete proton decoupling for nucleus other than ^1H. Chemical shifts are reported in parts per million with the solvent resonance as the internal standard ($CDCl_3$, ^1H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm). Data are reported as follows: chemical shift [δ in ppm, multiplicity (s=singlet, d=doublet, t=triplet, m=multiplet), coupling constants (Hz), integration and attribution]. Optical rotations were recorded using a polarimeter Perkin–Elmer 341. High resolution mass spectroscopy analyses were performed at the Centre Régional de Mesures Physiques de l'Ouest (CRMPO), Université de Rennes 1.

All non-aqueous reactions were performed under an argon atmosphere using oven-dried glassware. Et_2Zn 1 M solution in hexanes was purchased from Aldrich®. Ethyl acetate was distilled from calcium hydride under argon. Tetrahydrofuran was desiccated on drying column under nitrogen. Copper complexes and solvents were obtained from commercial sources and used without further purification. All (*E*,*E*)-dienyl aryl ketones were synthesized via a Wittig reaction according the literature procedures.[17]

4.2. General procedure for the Cu-catalysed ACA of enone with Et_2Zn

A flame-dried Schlenk tube was charged with copper source (1–4 mol %) and ligand (1–4 mol %). Next, 3 mL of ethyl acetate was added and the resulting green mixture was stirred at room temperature for 15 min, after which Et_2Zn (3 mmol) was added dropwise. Finally, acyclic enone (1 mmol, 1 equiv) was added at required temperature. The resulting brown solution was allowed to stir at the required temperature for 0.1–20 h and the reaction was quenched by the addition of 5–8 mL of a 1 N HCl solution. The product was extracted with AcOEt. The organic phase was washed with a saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$, filtrated and concentrated under vacuo. The product was purified by silica gel column chromatography (pentane/Et_2O).

4.3. Analytical data

*4.3.1. Compound **4**: 4-ethylnonan-2-one.* The ee was determined by chiral GC: Capillary column Chiraldex GTA (0.12 μm, 30 m, 0.25 mm), pression 104 kPa, total He flow 9.9 mL/min; 80 °C (60 min)–2 °C/min–100 °C–10 °C/min–160 °C (5 min); t_R (R)=44.4 min, t_R (*S*)=47.6 min. $[\alpha]_{D^{20}}$ +2.4 (*c* 2.3, $CHCl_3$, ee=97%) {lit. $[\alpha]_{D^{20}}$ +2.7 (*c* 2.3, $CHCl_3$, ee=90%, (*R*) enantiomer)[16]}.

*4.3.2. Compound **6**: 4-phenylhexan-2-one.* The ee was determined by chiral GC: Capillary column Chiraldex GTA (0.12 μm, 30 m, 0.25 mm), pression 108 kPa, total He flow 9.7 mL/min; 90 °C (85 min)–2 °C/min–120 °C–10 °C/min–160 °C (5 min); t_R (*R*)=83.5 min, t_R (*S*)=86.9 min. $[\alpha]_{D^{20}}$ +30.6 (*c* 1, EtOH, ee=99%) {lit. $[\alpha]_{D^{20}}$ +27 (*c* 1.32, EtOH, ee=81%, (*S*) enantiomer)[16]}.

*4.3.3. Compound **7a**: 1-phenyl-3-methyl pentan-1-one.* Colourless oil. ^{1}H NMR ($CDCl_3$): δ 7.97–7.93 (m, 2H, H_{ar}), 7.58–7.52 (m, 1H, H_{ar}), 7.48–7.43 (m, 2H, H_{ar}), 2.95 (dd, *J*=15.6, 5.6 Hz, 1H, CH_2CO), 2.74 (dd, *J*=15.6, 7.8 Hz, 1H, CH_2CO), 2.15–2.03 (m, 1H, CH), 1.49–1.38 (m, 1H, CH_2CH_3), 1.33–1.22 (m, 1H, CH_2CH_3), 0.95 (d, *J*=6.4 Hz, 3H, CH_3CH), 0.93 (t, *J*=7.6 Hz, 3H, CH_3CH_2); ^{13}C NMR: δ 200.5 (CO), 137.4 (C_{ar}), 132.8 (CH_{ar}), 128.5 (2 CH_{ar}), 128.1 (2 CH_{ar}), 45.6 (CH_2CO), 31.4 (CH), 29.7 (CH_2CH_3), 19.5 (CH_3CH), 11.4 (CH_3CH_2). The ee was determined by chiral GC: Capillary column Chiraldex GTA (0.12 μm, 30 m, 0.25 mm), pression 105 kPa, total He flow 50 mL/min; 70 °C (30 min)–0.2 °C/min–100 °C–10 °C/min–160 °C (3 min); t_R (1)=151.4 min, t_R (2)=153.4 min. $[\alpha]_{D^{20}}$ +17 (*c* 1.5, Et_2O, ee=96%, (*S*) enantiomer) {lit. $[\alpha]_{D^{20}}$ −15 (*c* 1.5, Et_2O, ee=93%, (*R*) enantiomer)[15]}.

*4.3.4. Compound **7b**: 1-(4-nitrophenyl)-3-methylpentan-1-one.* Yellow oil. ^{1}H NMR ($CDCl_3$): δ 8.32–8.28 (m, 2H, H_{ar}), 8.11–8.07 (m, 2H, H_{ar}), 2.99 (dd, *J*=16.4, 5.6 Hz, 1H, CH_2CO), 2.79 (dd, *J*=16.1, 7.9 Hz, 1H, CH_2CO), 2.15–2.02 (m, 1H, $CHCH_3$), 1.49–1.38 (m, 1H, CH_2CH_3), 1.35–1.23 (m, 1H, CH_2CH_3), 0.96 (d, *J*=6.4 Hz, 3H, CH_3CH), 0.93 (t, *J*=7.5 Hz, 3H, CH_3CH_2); ^{13}C NMR: δ 198.7 (CO), 150.1 (C_{ar}), 141.7 (C_{ar}), 129.0 (2 CH_{ar}), 123.7 (2 CH_{ar}), 46.0 (CH_2CO), 31.1 ($CHCH_3$), 29.5 (CH_2CH_3), 19.4 (CH_3CH), 11.3 (CH_3CH_2). The ee was determined by chiral GC: Capillary column Chiraldex GTA (0.12 μm, 30 m, 0.25 mm), pression 100 kPa, total He flow 50 mL/min; 90 °C (40 min)–0.2 °C/min–150 °C–10 °C/min–160 °C (3 min); t_R (1)=324.5 min, t_R (2)=326.1 min. $[\alpha]_{D^{20}}$ +19.6 (*c* 1.5, Et_2O, ee=95%). HRMS: $[M+Na]^+$ ($C_{12}H_{15}NO_3Na$) calcd 244.09496; found 244.0948 (1 ppm).

*4.3.5. Compound **7c**: 1-(4-chlorophenyl)-3-methylpentan-1-one.* - White solid. ^{1}H NMR ($CDCl_3$): δ 7.91–7.87 (m, 2H, H_{ar}), 7.45–7.41 (m, 2H, H_{ar}), 2.91 (dd, *J*=15.6, 5.7 Hz, 1H, CH_2CO), 2.71 (dd, *J*=15.6, 8.0 Hz, 1H, CH_2CO), 2.13–2.01 (m, 1H, $CHCH_3$), 1.47–1.37 (m, 1H, CH_2CH_3), 1.33–1.22 (m, 1H, CH_2CH_3), 0.95 (d, *J*=6.4 Hz, 3H, CH_3CH), 0.92 (t, *J*=6.8 Hz, 3H, CH_3CH_2); ^{13}C NMR: δ 199.2 (CO), 139.2 (C_{ar}), 135.7 (C_{ar}), 129.5 (2 CH_{ar}), 128.8 (2 CH_{ar}), 45.5 (CH_2CO), 31.4 ($CHCH_3$), 29.7 (CH_2CH_3), 19.5 (CH_3CH), 11.4 (CH_3CH_2). The ee was determined by chiral GC: Capillary column Chiraldex GTA (0.12 μm, 30 m, 0.25 mm), pression 105 kPa, total He flow 50 mL/min; 85 °C (140 min)–0.2 °C/min–120 °C–10 °C/min–160 °C (8 min); t_R (1)=261.8 min, t_R (2)=263.5 min. $[\alpha]_{D^{20}}$ +9.1 (*c* 1.5, Et_2O, ee=98%). HRMS: $[M+Na]^+$ ($C_{12}H_{15}O_3ClNa$) calcd 233.07091; found 233.0708 (0 ppm).

*4.3.6. Compound **7d**: 1-(4-methoxyphenyl)-3-methylpentan-1-one.*- Yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.96–7.92 (m, 2H, H_{ar}), 6.95–6.91 (m, 2H, H_{ar}), 3.87 (s, 3H, OCH_3), 2.89 (dd, *J*=15.4, 5.7 Hz, 1H, CH_2CO), 2.68 (dd, *J*=15.4, 8 Hz, 1H, CH_2CO), 2.13–2.01 (m, 1H, $CHCH_3$), 1.48–1.37 (m, 1H, CH_2CH_3), 1.32–1.21 (m, 1H, CH_2CH_3), 0.94 (d, *J*=6.8 Hz, 3H, CH_3CH), 0.92 (t, *J*=7.2 Hz, 3H, CH_3CH_2); ^{13}C NMR: δ 199.2 (CO), 163.3 (C_{ar}), 130.6 (C_{ar}), 130.4 (2 CH_{ar}), 113.6 (2 CH_{ar}), 55.4 (OCH_3), 45.3 (CH_2CO), 31.6 ($CHCH_3$), 29.7 (CH_2CH_3), 19.5 (CH_3CH), 11.4 (CH_3CH_2). The ee was determined by chiral HPLC: two OD-H columns; *n*-hexane/*i*-PrOH: 99.9/0.1; flow: 0.5 mL min^{-1}; 254 nm; t_R (1): 220.63 min, t_R (2) 234.7 min. $[\alpha]_{D^{20}}$ +16.7 (*c* 1.5, Et_2O, ee >97%). HRMS: $[M+Na]^+$ ($C_{13}H_{18}O_2Na$) calcd 229.12045; found 229.1204 (0 ppm).

*4.3.7. Compound **7e**: 1-(2-naphthyl)-3-methylpentan-1-one.* Yellow oil. ^{1}H NMR ($CDCl_3$): δ 8.46 (s, 1H, CH_{ar}), 8.05–7.87 (m, 4H, CH_{ar}), 7.62–7.53 (m, 2H, CH_{ar}), 3.08 (dd, *J*=15.6, 5.7 Hz, 1H, CH_2CO), 2.88 (dd, *J*=15.6, 7.9 Hz, 1H, CH_2CO), 2.22–2.10 (m, 1H, $CHCH_3$), 1.54–1.43 (m, 1H, CH_2CH_3), 1.38–1.27 (m, 1H, CH_2CH_3), 1.00 (d, *J*=6.8 Hz, 3H, CH_3CH), 0.96 (t, *J*=7.6 Hz, 3H, CH_3CH_2); ^{13}C NMR: δ 200.5 (CO), 135.5 (C_{ar}), 134.8 (C_{ar}), 132.5 (C_{ar}), 129.6 (CH_{ar}), 129.5 (CH_{ar}), 128.4 (CH_{ar}), 128.3 (CH_{ar}), 127.7 (CH_{ar}), 126.7 (CH_{ar}), 124.0 (CH_{ar}), 45.6 (CH_2CO), 31.6 ($CHCH_3$), 29.7 (CH_2CH_3), 19.6 (CH_3CH), 11.5 (CH_3CH_2). The ee was determined by chiral HPLC: OD-H column; *n*-hexane/*i*-PrOH: 99.9/0.1; 0.8 mL min^{-1}; 254 nm; t_R (1)=84.4 min, t_R (2)=93.7 min. $[\alpha]_{D^{20}}$ +22.1 (*c* 1.5, Et_2O, ee=94%). HRMS: $[M+Na]^+$ ($C_{16}H_{18}ONa$) calcd 249.12554; found 249.1256 (0 ppm).

*4.3.8. Compound **9**: 1,3-diphenylpentan-2-one.* The ee was determined by chiral HPLC: OD-H column; *n*-hexane/*i*-PrOH: 99.75/0.25; flow: 1 mL min^{-1}; 254 nm; t_R (*S*): 25.1 min, t_R (*R*): 30.5 min. $[\alpha]_{D^{20}}$ +4.1 (*c* 1.52, EtOH, ee=77%, *S* enantiomer) {lit. $[\alpha]_{D^{20}}$ +7.3 (*c* 1.52, EtOH, ee=86%, (*S*) enantiomer)[14]}. $[\alpha]_{D^{20}}$ +1.14 (*c* 1.93, $CHCl_3$, ee=77%, *S* enantiomer) {lit. $[\alpha]_{D^{20}}$ +1.83 (*c* 1.93, $CHCl_3$, ee=98%, (*S*) enantiomer)[13]}.

*4.3.9. Compound **11**: 3-ethyl-1-phenyloctan-1-one.* The ee was determined by chiral HPLC: OD-H column; *n*-hexane/*i*-PrOH: 99.95/0.05; flow: 1 mL min^{-1}; 254 nm; t_R (1): 23.0 min, t_R (2) 24.4 min. $[\alpha]_{D^{20}}$ +2.3 (*c* 1.6, EtOH, ee=94%) {lit. $[\alpha]_{D^{20}}$ +1.7 (*c* 1.6, EtOH, ee=62%)[16]}.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.05.011.

References and notes

1. For selected examples dealing with chiral Schiff base ligands in asymmetric reactions, see (a) Jiang, J.-J.; Huang, J.; Wang, D.; Yuan, Z.-L.; Zhao, M.-X.; Wang, F.-J.; Shi, M. *Chirality* **2011**, *23*, 272–276; (b) Tanaka, T.; Sano, Y.; Hayashi, M. *Chem.—Asian. J.* **2008**, *3*, 1465–1471; (c) Radosevich, A. T.; Musich, C.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 1090–1091; (d) Ohta, C.; Shimizu, H.; Kondo, A.; Katsuki, T. *Synlett* **2002**, 161–163; (e) Legros, J.; Bolm, C. *Chem.—Eur. J.* **2005**, *11*, 1086–1092; (f) Braun, M.; Kotter, W. *Angew. Chem., Int. Ed.* **2004**, *43*, 514–517; (g) Bolm, C. *Coord. Chem. Rev.* **2003**, *237*, 245–256; (h) Fan, Q.; Lin, L.; Liu, J.; Huang, Y.; Feng, X.; Zhang, G. *Org. Lett.* **2004**, *6*, 2185–2188; (i) Wang, W.; Gou, S.; Liu, X.; Feng, X. *Synlett* **2007**, 2875–2878; (j) Zhou, X.; Liu, X.; Yang, X.; Shang, D.; Xin, J.; Feng, X. *Angew. Chem., Int. Ed.* **2008**, *47*, 392–394.
2. ee (6%) was reached with 1 mol% of chiral Cu-Schiff based complex **1**, see (a) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, *7*, 5239–5244; (b) Nozaki, H.; Takaya, H.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655–3669.
3. Nitta, H.; Yu, D.; Kudo, M.; Mori, A.; Inoue, S. *J. Am. Chem. Soc.* **1992**, *114*, 7969–7975.
4. (a) Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **1996**, *35*, 1668–1671; (b) Degrado, S. J.; Mizutani, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 755–756; (c) For a review on small-peptide ligands dealing with their applications in catalysis, see: Hoveyda, A. H.; Hird, A. W.; Kacprzynski, M. A. *Chem. Commun.* **2004**, 1779–1785.
5. For reviews on asymmetric conjugate additions, see (a) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354–362; (b) Krause, N.; Hoffmann-Röder, A. *Synthesis* **2001**, 171–196; (c) Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221–3236; (d) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829–2844; (e) Alexakis, A.; Backvall, J. E.; Krause, N.; Pamies, O.; Dieguez, M. *Chem. Rev.* **2008**, *108*, 2796–2823; (f) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824–2852.
6. Wencel, J.; Rix, D.; Crévisy, C.; Mauduit, M. PCT Int Appl WO2009050284, 2009.
7. Wencel, J.; Rix, D.; Jennequin, T.; Labat, S.; Crévisy, C.; Mauduit, M. *Tetrahedron: Asymmetry* **2008**, *19*, 1804–1809.
8. Wencel, J.; Laurent, I.; Toupet, L.; Crévisy, C.; Mauduit, M. *Organometallics* **2010**, *29*, 1530–1533.
9. Wencel-Delord, J.; Alexakis, A.; Crévisy, C.; Mauduit, M. *Org. Lett.* **2010**, *12*, 4335–4337.
10. ACA involving acyclic enones are really useful in synthesis of natural products, for examples see (a) Clift, M. D.; Thomson, R. J. *J. Am. Chem. Soc.* **2009**, *131*, 14579–14583; (b) Kehrli, S.; Martin, D.; Rix, D.; Mauduit, M.; Alexakis, A. *Chem.—Eur. J.* **2010**, *16*, 9890–9904.
11. AcOEt may be considered as a grener solvant: 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.
12. Uchida, T.; Katsuki, T. *Tetrahedron Lett.* **2009**, *50*, 4741–4743.
13. Endo, K.; Ogawa, M.; Shibata, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 2410–2413.
14. Shintani, R.; Fu, G. C. *Org. Lett.* **2002**, *4*, 3699–3702.
15. Nishimura, T.; Katoh, T.; Takatsu, K.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 14158–14159.
16. López, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2004**, *126*, 12784–12785.
17. (a) Therkelsen, F. D.; Hansen, A.-L. L.; Pedersen, E. B.; Nielsen, C. *Org. Biomol. Chem.* **2003**, *1*, 2908–2918; (b) Marquez-lopez, E.; Herrera, R. P.; Marks, T.; Jacobs, W. C.; Konning, D.; Figueire, R. M.; Christmann, M. *Org. Lett.* **2009**, *11*, 4116–4119.