RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

Journal Name

RSCPublishing

ARTICLE

Cu(I)/TF-BiphamPhos-Catalyzed Asymmetric 1,3-Dipolar Cycloaddition of Azomethine Ylides with Dimethyl Itaconate and 2-Methyleneglutarate

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

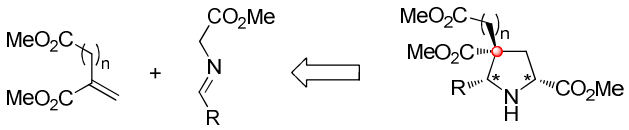
www.rsc.org/

Hai-Yan Tao,[a] Zhao-Lin He,[a] Yang Yang,[a] and Chun-Jiang Wang[a,b]

Catalytic asymmetric 1,3-dipolar cycloaddition of azomethine ylides with dimethyl itaconate and 2-methyleneglutarate was realized with Cu(I)/TF-BiphamPhos complex as the catalyst for the efficient construction of pyrrolidine derivatives bearing one unique all carbon-quaternary and two tertiary stereogenic centers. The current catalytic system exhibited excellent diastereoselectivity (>20:1), good enantioselectivity (88->99% ee) and broad substrate scope under mild conditions.

Introduction

Highly functionalized pyrrolidines bearing multiple stereogenic centers are one of the most important heterocyclic motifs, which are widely observed in many natural alkaloids and marketed pharmaceuticals.[1] Enantiomerically enriched pyrrolidine derivatives were also successfully employed as organocatalysts, chiral ligands and also useful building blocks in organic synthesis.[2] Among the developed methodologies for the optically active pyrrolidines syntheses, catalytic asymmetric 1,3-dipolar cycloaddition of azomethine ylides with electron-deficient olefins is one of the most powerful and atom-economical carbon-carbon bond-forming reaction[3] that provides an efficient approach and diversity-oriented synthesis (DOS)[4] for the construction of a variety of structurally and stereochemically diversified pyrrolidines from the readily-available starting materials. Since the first example on the catalytic asymmetric 1,3-dipolar cycloaddition of *in situ*-generated azomethine ylide reported in 2002,[5] much endeavours have been made to developing catalytic asymmetric protocols for 1,3-dipolar cycloaddition, in which various types of chiral metal complexes and chiral organocatalysts have been successfully employed as the efficient catalysts to afford stereochemically diversified pyrrolidine derivatives with moderate to high enantio-/diastereoselectivities in the last decade.[6] Although various electron-deficient alkenes have been utilized as the dipolarophiles in azomethine ylide-involved 1,3-dipolar cycloaddition, most of them are limited to maleates, fumarates, maleimides, acrylates, nitroalkenes, and vinyl phenyl sulfones.[3,6] Dimethyl itaconate or 2-methyleneglutarate, which were commonly used as substrates in asymmetric hydrogenation reactions,[7] have been seldom employed as dipolarophiles in the asymmetric 1,3-dipolar cycloaddition of azomethine ylides. To the best of our knowledge, only one racemic example has been reported involving itaconate as the dipolarophile so far.[8] In view of the simultaneous formation of one unique all carbon-quaternary[9] and two tertiary stereogenic centers in the pyrrolidine rings, it is a great challenge to control both diastereoselectivity and enantioselectivity in dimethyl itaconate and 2-methyleneglutarate-involved asymmetric 1,3-dipolar cycloaddition reaction (Scheme 1). In continuation of the interest in construction of biologically active and enantioenriched pyrrolidines,[10] we herein reported the first catalytic asymmetric 1,3-dipolar cycloaddition of azomethine ylides to dimethyl itaconate or 2-methyleneglutarate with excellent levels of diastereoselectivity and enantioselectivity. The current methodology could diversify the existing methodology for the facile access to the biologically active pyrrolidine derivatives.



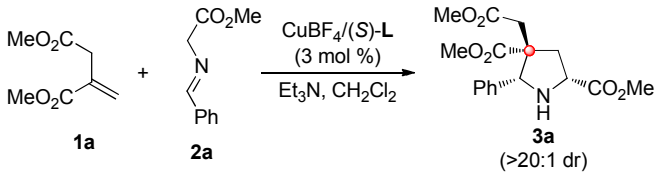
Scheme 1. Catalytic asymmetric 1,3-dipolar cycloaddition of azomethine ylides using dimethyl Itaconate as the dipolarophiles.

Results and Discussion

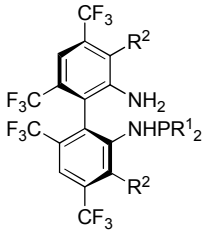
Initially, *N*-benzylidene glycine methyl ester **2a** was selected as the 1,3-dipole precursor and dimethyl itaconate **1** as the dipolarophile to investigate the stereoselective control in the presence of the combined metal salts and chiral ligand TF-BiphamPhos,[10a] and the representative results are listed in Table 1. The 1,3-dipolar cycloaddition reaction occurred smoothly and finished in 4 h with 3

[a]*College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, China. E-mail: cjwang@whu.edu.cn Fax: 86-27-68754067*
[b]*State Key Laboratory of Elemento-organic Chemistry, Nankai University Tianjin, 300071, China*
†Electronic supplementary information (ESI) available: Experimental section see DOI: 10.1039/c000000x/

Table 1. Catalytic asymmetric 1,3-dipolar cycloaddition of imino ester **2a** with dimethyl itaconate **1a**.[a]



1a **2a** **3a** (>20:1 dr)



L1: R^1 = Ph, R^2 = H
L2: R^1 = 3,5-bis(methyl)phenyl, R^2 = H
L3: R^1 = 3,5-bis(trifluoromethyl)phenyl, R^2 = H
L4: R^1 = Cy, R^2 = H
L5: R^1 = Ph, R^2 = Br

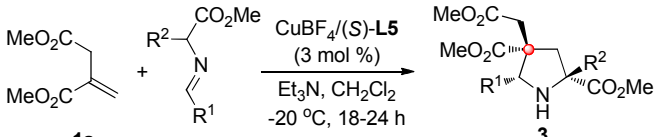
(*S*)-**TF-BiphamPhos**

entry	L	[M]	Solvent	T (°C)	Time (h)	yield[b] (%)	ee[c] (%)
1	**L1**	AgOAc	DCM	rt	12	91	40
2	**L1**	$Cu(CH_3CN)_4BF_4$	DCM	rt	8	90	73
3	**L2**	$Cu(CH_3CN)_4BF_4$	DCM	rt	8	79	60
4	**L3**	$Cu(CH_3CN)_4BF_4$	DCM	rt	8	81	74
5	**L4**	$Cu(CH_3CN)_4BF_4$	DCM	rt	8	52	65
6	**L5**	$Cu(CH_3CN)_4BF_4$	DCM	rt	8	92	81
7	**L5**	$Cu(CH_3CN)_4BF_4$	Et_2O	rt	12	79	73
8	**L5**	$Cu(CH_3CN)_4BF_4$	MeCN	rt	12	31	75
9	**L5**	$Cu(CH_3CN)_4BF_4$	EtOAc	rt	8	78	77
10	**L5**	$Cu(CH_3CN)_4BF_4$	MeOH	rt	12	90	65
11	**L5**	$Cu(CH_3CN)_4BF_4$	DCM	-10	12	88	83
12	**L5**	$Cu(CH_3CN)_4BF_4$	DCM	-20	20	81	90

[a] All reactions were carried out with 0.23 mmol of **1a** and 0.35 mmol of **2** in 2 mL solvent. [b] Isolated yield. [c] Dr was determined by the crude ^{1}H NMR and ee was determined by HPLC analysis.

mol % AgOAc/(*S*)-TF-BiphamPhos(**L1**) as the catalyst and 15 mol % Et_3N as base in dichloromethane at room temperature, the desired cycloadduct **3a** bearing a unique all carbon-quaternary and two tertiary stereogenic centers was obtained as a single isomer in good yield with exclusive diastereoselectivity (dr >20:1) and moderate enantioselectivity of 40% ee (Table 1, entry 1), which indicated that dimethyl itaconate could be applied as an effective dipolarophile in the azomethine ylide-involved 1,3-dipolar cycloaddition reaction for the synthesis of highly functionalized pyrrolidine derivatives. Encouraged by these promising results, we further pursue to improve the enantioselective control of this reaction. To our gratification, the enantioselectivity was greatly increased to 73% ee with maintained high diastereoselectivity for this cycloaddition by switching the metal precursor from AgOAc into $Cu(CH_3CN)_4BF_4$ (entry 2), which revealed that the corresponding active intermediate generated from chiral Cu(I)/TF-BiphamPhos coordinated by *in situ*-formed azomethine ylide has more favourable interactions with the dipolarophile itaconate and hence afforded higher enantioselectivity control than that from Ag(I)/TF-BiphamPhos complex. Next, $Cu(CH_3CN)_4BF_4$ was selected as the metal precursor for subsequent survey of other TF-BiphamPhos ligands with different substituents either on the phenyl ring of diaryl phosphine group or on the chiral backbone. It was found that the enantioselectivity in this 1,3-dipolar cycloaddition was greatly affected by both the electronic effect and steric effect of the chiral ligand: Deteriorative effect on the enantioselectivity was observed when the phenyl ring on the phosphorous atom of ligand (**L1**) was replaced by xylyl group (**L2**) or cyclohexyl group (**L4**) (entries 3 and 5). Similar enantioselective control were observed with chiral ligand bearing the strongly electron-withdrawing 3,5-bis(trifluoromethyl)-phenyl group (**L3**) (entry 4). Further ligand variant showed that TF-BiphamPhos (**L5**) was the most effective chiral ligand providing **3a** exclusively in 92% yield and 81% ee within 8 h (Table 1, entry 6). Next, the solvent effect on this annulation was also investigated, CH_2Cl_2 was revealed to be the best solvent in terms of the yield and enantioselectivity while polar solvents such as methanol and acetonitrile were less effective for this transformation (Table 1, entries 6-10). 90% ee with full conversion and exclusive diastereoselectivity was realized through reducing the reaction temperature to -20 °C with DCM as the solvent (Table 1, entry 12). Thus, the optimized reaction conditions were established as 3 mol% of $Cu(CH_3CN)_4BF_4$/**L5** and 15 mol % Et_3N in DCM at -20 °C.

Table 2. Substrate scope of Cu(I)/**L5**-catalyzed asymmetric 1,3-dipolar cycloaddition of various imino esters **2** with dimethyl itaconate **1a**.[a]



1a **2** **3** (>20:1 dr)

entry	R^1	R^2	3	yield (%)[b]	ee (%)[c]
1	Ph (**2a**)	H	**3a**	81	90
2	*p*-Cl-C_6H_4 (**2b**)	H	**3b**	85	91
3	*o*-Cl-C_6H_4 (**2c**)	H	**3c**	86	93
4	*m*-Cl-C_6H_4 (**2d**)	H	**3d**	90	88
5	*p*-Me-C_6H_4 (**2e**)	H	**3e**	95	>99
6	*o*-Me-C_6H_4 (**2f**)	H	**3f**	92	94
7	*m*-Me-C_6H_4 (**2g**)	H	**3g**	93	89
8	*p*-MeO-C_6H_4 (**2h**)	H	**3h**	81	92
9	*o*-MeO-C_6H_4 (**2i**)	H	**3i**	76	94
10	*m*-MeO-C_6H_4 (**2j**)	H	**3j**	88	90
11	Ph (**2k**)	Me	**3k**	82	93
12	Bu (**2l**)	H	-	-	-

[a] All reactions were carried out with 0.23 mmol of **1a** and 0.35 mmol of **2** in 2 mL CH_2Cl_2. $CuBF_4$ = $Cu(CH_3CN)_4BF_4$. [b] Isolated yield. [c] Dr was determined by the crude ^{1}H NMR and ee was determined by HPLC analysis.

Under the optimized reaction conditions, we investigated the substrate scope of this 1,3-dipolar cycloaddition of dimethyl itaconate **1a** with respect to azomethine ylide. As shown in Table 2, a series of representative imino esters derived from various aromatic aldehydes and glycinate reacted smoothly with dimethyl itaconate **1a** leading to the corresponding adducts (**3a-3j**) in good yields (76-95%), excellent diastereoselectivity (dr >20:1) and high enantio-

selectivities (88->99%) at -20 °C within 18-24 h. It appears that the electronic property of the substituents on the aryl rings has little effect on the stereoselectivities. Imino esters bearing electron-neutral group (Table 2, entry 1), electron-deficient group (entries 2-4), and electron-rich groups (entries 5-10) on the aryl rings all worked well in this cycloaddition. On the contrary, the substituent pattern of the aromatic rings has some effect on the enantioselectivities. A little lower enantioselectivities was observed for *meta*-chloro and *meta*-methyl-substituted imino esters **2d** and **2g** (entries 4 and 7). Remarkably, comparable excellent diastereoselectivity and enantioselectivity were still obtained for the sterically hindered *ortho*-chloro, *ortho*-methyl, *ortho*-methoxyl-substituted imino esters **2c**, **2f** and **2i** (entries 3, 6 and 9). However, no cycloaddition occurred when the less reactive alkyl substituted imino ester was tested under the optimal reaction conditions (entry 12). Notably, α-methyl substituted imino ester **3k** derived from alanine was also tolerated in this transformation, affording the desired pyrrolidines bearing one all-carbon quaternary and one nitrogen-substituted quaternary stereogenic centers in good yield with the maintained exclusive diastereoselectivity (>20:1) and excellent enantioselectivity (93% ee) (entry 11). The absolute configuration of the cycloadduct **3c** was determined to be (2*R*,4*S*,5*S*) by X-ray analysis† (Figure 1), and the relative and absolute configuration of all other cycloadducts was tentatively assigned by analogy.

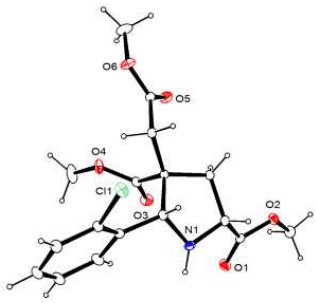


Figure 1. ORTEP representation of the cycloadduct (2*R*,4*S*,5*S*)-**3c** at 30% probability for the drawing of thermal ellipsoids.

To further investigate the generality of the dipolarophile for this 1,3-dipolar cycloaddition reaction, dimethyl 2-methyleneglutarate was also tested under the optimal reaction conditions. As shown in Figure 2, dimethyl 2-methyleneglutarate **1b** has also proven to be excellent dipolarophile in this annulation producing the corresponding cycloadducts **3l** and **3m** in high yields with high diastereoselectivities and excellent enantioselectivities.

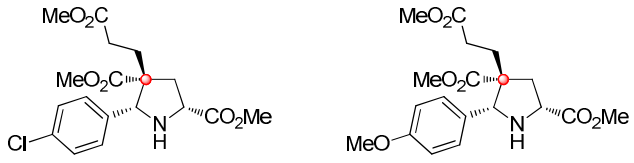


Figure 2. The results of 1,3-dipolar cycloaddition of azomethine ylides with dimethyl 2-methyleneglutarate as the dipolarophile.

The stereochemical results of this annulation can be explained through the proposed transition state in Figure 3. Azomethine ylide is coordinated to the chiral copper (I) metallic center in such way to form tetracoordinated active spiecies,[6k,11] subsequently followed by the annulation with dimethyl itaconate from the *Si* face (C=N) of the ylide giving rise to the cycloadduct **3a** in *endo*-configuration. The carbonyl group connected to unsaturated C=C bond in dimethyl itaconate could coordinate more preferentially with the Cu(I) center than another one, which may benefit for stabilizing the negatively charged oxygen atom. It cannot eliminate the possible hydrogen-bonding interaction between the carbonyl group in the dipolarophile and the NH_2 group in the ligand TF-BiphamPhos.[12]

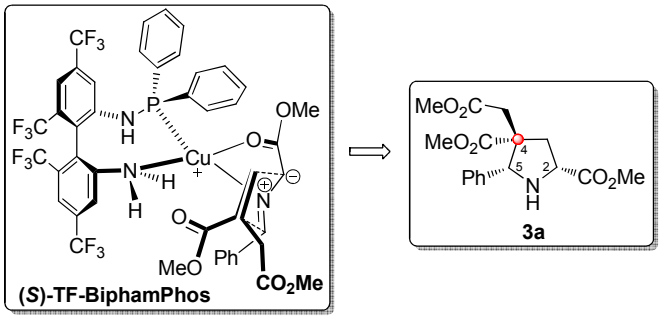


Figure 3. Proposed transition state.

Conclusions

In conclusion, we reported a Cu(I)/TF-BiphamPhos-catalyzed asymmetric 1,3-dipolar cycloaddition reaction of azomethine ylides with dimethyl itaconate and 2-methyleneglutarate to provide a series of highly substituted pyrrolidines bearing one unique all-carbon quaternary and two tertiary stereogenic centers for the first time. Excellent stereoselective control and broad substrate scope were uniformly observed for various azomethine ylides. The easy availability of the substrates and the bioactive importance of the enantioenriched pyrrolidine derivatives make the present methodology particularly interesting in organic synthesis. Further studies on the mechanistic details and its application are ongoing in this laboratory.

Experimental

General

All reactions were carried out using standard Schlenk techniques unless specified other otherwise. The degassed dry solvents are used throughout each experiment. ^{1}H NMR spectra were recorded on a VARIAN Mercury 300 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The data are reported as (s = single, d = double, t = triple, q = quartet, m = multiple or unresolved, brs = broad single, coupling constant(s) in Hz, integration). ^{13}C NMR spectra were recorded on a VARIAN Mercury 75 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with silica gel-coated plates. Diastereomeric ratios were determined from crude ^{1}H NMR. Enantiomeric excesses were determined by HPLC, using a chiralpak IA, a chiralpak AS-H, chiralpak AD-H, or chiralcel OD-H column with hexane and i-PrOH as solvents. Dimethyl 2-methyleneglutarate[13] and imino esters,[10a] were prepared according to the literature procedure. Chiral ligands **L1-L5** were prepared according to the literature procedure reported by us.[10a]

Synthetic details

General Procedure for Asymmetric 1,3-Dipolar Cycloaddition of Azomethine Ylides with Dimethyl Itaconate Catalyzed by $Cu(CH_3CN)_4BF_4$/(*S*)-TF-BiphamPhos (L5) Complex.

Under argon atmosphere, (*S*)-TF-BiphamPhos **L5** (6.1 mg, 0.0076 mmol) and $Cu(CH_3CN)_4BF_4$ (2.2 mg, 0.0069 mmol) were dissolved in 2 mL of DCM. After stirring at room temperature for about 0.5 h, the reaction mixture was dropped to -20 °C. Then, imino ester substrate (0.35 mmol), Et_3N (0.03 mmol) and dimethyl itaconate (0.23 mmol) were added sequentially. Once starting material was consumed (monitored by TLC), the mixture was filtered through celite and the filtrate was concentrated to dryness. The product was purified by column chromatography to give the corresponding cycloadduct, which was then directly analysed by HPLC to determine the enantiomeric excess

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-5-phenylpyrrolidine-2,4-dicarboxylate (3a)

The title compound was prepared according to the general procedure as described above in 81% yield (62 mg) as white solid. m.p. 147-148 °C; $[\alpha]^{25}_D$ = +16.2 (*c* 1.09, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.33-7.23 (m, 5H), 4.09 (s, 1H), 4.05 (dd, J_1 = 6.3 Hz, J_2 = 15.9 Hz, 1H), 3.85 (s, 3H), 3.65 (s, 3H), 3.25 (s, 3H), 3.11 (d, *J* = 16.8 Hz, 1H), 3.06-3.01 (m, 1H), 2.58 (br, 1H), 2.51 (d, *J* = 16.8 Hz, 1H), 2.28 (dd, J_1 = 9.6 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 173.9, 172.8, 171.4, 137.1, 128.2, 126.5, 72.4, 58.7, 56.0, 52.1, 51.6, 51.4, 40.2, 39.6; IR (KBr) ν 2954, 2923, 2844, 2396, 1736, 1460, 1437, 1359, 1117, 1082, 1005, 926, 889, 669 cm^{-1}. HRMS calcd. for $C_{17}H_{21}NO_6$+H^+: 336.1447, found 336.1442. The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak IA, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm); t_r = 13.96 and 18.29 min.

(2*R*,4*S*,5*R*)-dimethyl 5-(4-chlorophenyl)-4-(2-methoxy-2-oxoethyl)pyrrolidine-2,4-dicarboxylate (3b)

The title compound was prepared according to the general procedure as described above in 85% yield (72 mg) as white solid. m.p. 167-168 °C; $[\alpha]^{25}_D$ = +31.4 (*c* 1.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 4.07(s, 1H), 4.01 (dd, J_1 = 6.3 Hz, J_2 = 9.3 Hz, 1H), 3.84 (s, 3H), 3.66 (s, 3H), 3.29 (s, 3H), 3.09 (d, *J* = 16.8 Hz, 1H), 3.03 (dd, J_1 = 6.3 Hz, J_2 = 13.8 Hz, 1H), 2.51 (d, *J* = 17.1 Hz, 1H), 2.27 (dd, J_1 = 9.3 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 173.8, 172.5, 171.2, 136.1, 133.7, 128.3, 128.0, 71.3, 58.4, 55.9, 52.1, 51.6, 51.5, 40.1, 39.0; IR (KBr) ν 2952, 2399, 1736, 1490, 1438, 1354, 1094, 1010, 669 cm^{-1}. HRMS calcd. for $C_{17}H_{20}ClNO_6$ +H^+: 370.1057, found 370.1062. The product was analyzed by HPLC to determine the enantiomeric excess: 91% ee (Chiralpak AS-H, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ = 220 nm); t_r = 7.63 and 11.66 min.

(2*R*,4*S*,5*S*)-dimethyl 5-(2-chlorophenyl)-4-(2-methoxy-2-oxoethyl)pyrrolidine-2,4-dicarboxylate (3c)

The title compound was prepared according to the general procedure as described above in 86% yield (73 mg) as white solid. m.p. 160-161 °C; $[\alpha]^{25}_D$ = +24.7 (*c* 1.28, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.47-7.45 (m, 1H), 7.37-7.35 (m, 1H), 7.26-7.20 (m, 3H), 4.79 (s, 1H), 4.03 (m, 1H), 3.84 (s, 3H), 3.65 (s, 3H), 3.32 (d, *J* = 17.7 Hz, 1H), 3.26 (s, 3H), 3.11 (dd, J_1 = 6.9 Hz, J_2 = 13.8 Hz, 1H), 2.63 (d, *J* = 17.4 Hz, 1H), 2.26 (dd, J_1 = 9.0 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 173.8, 172.7, 171.6, 135.6, 133.6, 129.5, 129.0, 127.9, 126.7, 66.4, 58.5, 56.7, 52.1, 51.6, 51.5, 40.7, 39.5; IR (KBr) ν 2954, 2923, 2849, 1739, 1437, 1361, 1120, 1080, 1037, 1000, 668 cm^{-1}. HRMS calcd. for $C_{17}H_{20}ClNO_6$+H^+: 370.1057, found 370.1060.The product was analyzed by HPLC to determine the enantiomeric excess: 93% ee (Chiralpak AS-H, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ = 220 nm); t_r = 6.48 and 13.44 min.

(2*R*,4*S*,5*R*)-dimethyl 5-(3-chlorophenyl)-4-(2-methoxy-2-oxoethyl)pyrrolidine-2,4-dicarboxylate (3d)

The title compound was prepared according to the general procedure as described above in 90% yield (76 mg) as white solid. m.p. 163-164 °C; $[\alpha]^{25}_D$ = +30.4 (*c* 1.60, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.26 (m, 3H), 7.16 (m, 1H), 4.05-3.99 (m, 2H), 3.85 (s, 3H), 3.66 (s, 3H), 3.31 (s, 3H), 3.10 (d, *J* = 17.1 Hz, 1H), 3.04 (dd, J_1 = 6.3 Hz, J_2 = 13.8 Hz, 1H), 2.51 (d, *J* = 16.8 Hz, 1H), 2.26 (dd, J_1 = 9.6 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 173.8, 172.5, 171.2, 139.7, 134.1, 129.5, 128.3, 126.9, 124.9, 71.5, 58.5, 56.0, 52.2, 51.7, 51.5, 40.2, 39.0; IR (KBr) ν 2954, 2928, 2853, 2399, 1738, 1598, 1575, 1437, 1360, 1118, 1081, 1002, 872, 668 cm^{-1}. HRMS calcd. for $C_{17}H_{20}ClNO_6$ +H^+: 370.1057, found 370.1058. The product was analyzed by HPLC to determine the enantiomeric excess: 88% ee (Chiralpak IA, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm); t_r = 18.79 and 28.93 min.

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-5-(p-tolyl)-pyrrolidine-2,4- dicarboxylate (3e)

The title compound was prepared according to the general procedure as described above in 95% yield (76 mg) as white solid. m.p. 155-156 °C; $[\alpha]^{25}_D$ = +32.2 (*c* 1.39, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.12 (m, 4H), 4.02-3.98 (m, 2H), 3.84 (s, 3H), 3.64 (s, 3H), 3.29 (s, 3H), 3.09 (d, *J* = 17.1 Hz, 1H), 3.03 (dd, J_1 = 6.0 Hz, J_2 = 14.1 Hz, 1H), 2.47 (d, *J* = 16.8 Hz, 1H), 2.32 (s, 3H), 2.27-2.22 (m, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 174.1, 173.0, 171.5, 137.9, 133.7, 129.0, 126.4, 72.4, 58.7, 55.9, 52.2, 51.7, 51.5, 40.2, 39.8, 21.0; IR (KBr) ν 2994, 2953, 2854, 1737, 1606, 1515, 1436, 1359, 1323, 1205, 1117, 1079, 1020, 897, 811 cm^{-1}. HRMS calcd. for $C_{18}H_{23}NO_6$+H^+: 350.1604, found 350.1611. The product was analyzed by HPLC to determine the enantiomeric excess: >99% ee (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm); t_r = 15.04 and 23.32 min.

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-5-(o-tolyl)-pyrrolidine-2,4- dicarboxylate (3f)

The title compound was prepared according to the general procedure as described above in 92% yield (74 mg) as white solid. m.p. 136-137 °C; $[\alpha]^{25}_D$ = +1.8 (*c* 1.29, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.37-7.15 (m, 4H), 4.48 (s, 2H), 4.05-3.99 (m, 1H), 3.84 (s, 3H), 3.65 (s, 3H), 3.27 (s, 3H), 3.13 (d, *J* = 16.5 Hz 1H), 3.07 (dd, J_1 = 7.2 Hz, J_2 = 14.1 Hz, 1H), 2.56 (d, *J* = 16.5 Hz, 1H), 2.30 (s, 3H), 2.26 (dd, J_1 = 9.0 Hz, J_2 = 13.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 174.0, 173.0, 171.3, 136.0, 135.8, 130.6, 127.7, 126.0, 125.7, 67.0, 58.8, 56.7, 51.7, 51.5, 40.7, 39.7, 20.0; IR (KBr) ν 2954, 2928, 1738, 1458, 1437, 1357, 1319, 1118, 1077, 1005, 668 cm^{-1}. HRMS calcd. for $C_{18}H_{23}NO_6$+H^+: 350.1604, found 350.1608. The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (Chiralpak AD-H, *i*-

propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm); t_r = 6.31 and 10.75 min.

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-5-(m-tolyl)-pyrrolidine-2,4- dicarboxylate (3g)

The title compound was prepared according to the general procedure as described above in 93% yield (75 mg) as white solid. m.p. 132-133 °C; $[\alpha]^{25}_D$ = +10.2 (*c* 1.29, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.24-7.18 (m, 1H), 7.11-7.03 (m, 3H), 4.04-3.99 (m, 2H), 3.85 (s, 3H), 3.65 (s, 3H), 3.28 (s, 3H), 3.10 (d, *J* = 17.1 Hz, 1H), 3.04 (dd, J_1 = 5.7 Hz, J_2 = 13.8 Hz, 1H); 2.48 (d, *J* = 16.8 Hz, 1H), 2.34 (s, 3H), 2.26 (dd, J_1 = 9.9 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 173.9, 173.0, 171.5, 137.9, 136.6, 129.0, 128.2, 127.2, 123.7, 72.5, 58.7, 56.0, 52.2, 51.7, 51.4, 40.2, 39.8, 21.3; IR (KBr) ν 2952, 2923, 2852, 1735, 1435, 1358, 1201, 1176, 1122, 1078, 1003, 879, 795, 781, 699 cm^{-1}. HRMS calcd. for $C_{18}H_{23}NO_6$+H^+: 350.1604, found 350.1610. The product was analyzed by HPLC to determine the enantiomeric excess: 89% ee (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm); t_r = 14.35 and 31.06 min.

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-5-(4-methoxyphenyl) pyrrolidine -2,4-dicarboxylate (3h)

The title compound was prepared according to the general procedure as described above in 81% yield (68 mg) as white solid. m.p. 148-149 °C; $[\alpha]^{25}_D$ = +25.9 (*c* 1.19, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.16 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.03 (s, 1H), 3.99 (dd, J_1 = 12.3 Hz, J_2 = 18.6 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.65 (s, 3H), 3.30 (s, 3H), 3.08 (d, *J* = 17.1 Hz, 1H), 3.02 (dd, J_1 = 6.3 Hz, J_2 = 14.1 Hz, 1H) , 2.47 (d, *J* = 17.1 Hz, 1H), 2.26 (dd, J_1 = 9.6 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 174.0, 173.0, 171.5, 159.4, 129.0, 127.7, 113.6, 72.0, 58.6, 55.9, 55.1, 52.2, 51.6, 51.5, 40.2, 39.6; IR (KBr) ν 2954, 2928, 1736, 1612, 1515, 1438, 1112, 1035, 669 cm^{-1}. HRMS calcd. for $C_{18}H_{23}NO_7$+H^+: 366.1553, found 366.1551. The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (Chiralpak AS-H, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ = 220 nm); t_r = 6.49 and 13.04 min.

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-5-(2-methoxyphenyl) pyrrolidine -2,4-dicarboxylate (3i)

The title compound was prepared according to the general procedure as described above in 76% yield (64 mg) as white solid. m.p. 142-143 °C;$[\alpha]^{25}_D$ = +4.4 (*c* 1.10, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.26-7.21 (m, 2H), 6.95-6.85 (m, 2H), 4.59 (s, 1H), 4.00 (dd, J_1 = 6.0 Hz, J_2 = 9.6 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.64 (s, 3H), 3.27 (s, 3H), 3.20 (d, *J* = 17.7 Hz, 1H), 3.04 (dd, J_1 = 6.6 Hz, J_2 = 14.1 Hz, 1H), 2.53 (d, *J* = 17.4 Hz, 1H), 2.24 (dd, J_1 = 9.9 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 173.9, 173.4, 172.0, 156.9, 128.9, 126.7, 124.8, 120.3, 110.4, 65.3, 58.8, 56.1, 55.2, 52.1, 51.6, 51.5, 40.5, 40.4; IR (KBr) ν 2999, 2952, 2923, 2852, 1736, 1601, 1579, 1493, 1437, 1358, 1324, 1246, 1204, 1176, 1115, 1079, 1026, 900, 759 cm^{-1}. HRMS calcd. for $C_{18}H_{23}NO_7$+H^+: 366.1553, found 366.1560. The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm); t_r = 10.74 and 24.50 min.

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-5-(3-methoxyphenyl) pyrrolidine-2,4-dicarboxylate (3j)

The title compound was prepared according to the general procedure as described above in 88% yield (74 mg) as white solid. m.p. 137-138 °C; $[\alpha]^{25}_D$ = +17.9 (*c* 1.13, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.24-7.22 (m, 1H), 6.84-6.81 (m, 3H), 4.04-3.99 (m, 2H), 3.84 (s, 3H), 3.80 (s, 3H), 3.66 (s, 3H), 3.30 (s, 3H), 3.13 (d, *J* = 17.1 Hz, 1H), 3.04 (dd, J_1 = 6.0 Hz, J_2 = 13.8 Hz, 1H), 2.49 (d, *J* = 17.1 Hz, 1H), 2.27 (dd, J_1 = 9.6 Hz, J_2 = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 174.0, 172.8, 171.5, 159.5, 138.8, 129.3, 118.8, 113.4, 112.6, 72.4, 58.8, 56.1, 55.1, 52.2, 51.7, 51.5, 40.3, 39.6; IR (KBr) ν 2954, 2925, 2844, 1737, 1602, 1492, 1456, 1437, 1360, 1112, 1077, 1049, 998, 699, 666 cm^{-1}. HRMS calcd. for $C_{18}H_{23}NO_7$+H^+: 366.1553, found 366.1558. The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralcel OD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm); t_r = 15.82 and 28.07 min.

(2*R*,4*S*,5*R*)-dimethyl 4-(2-methoxy-2-oxoethyl)-2-methyl-5-phenylpyrrolidine-2,4-dicarboxylate (3k)

The title compound was prepared according to the general procedure as described above in 82% yield (66 mg) as white solid. m.p. 124-125 °C; $[\alpha]^{25}_D$ = +25.0 (*c* 1.83, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.33-7.19 (m, 5H), 4.15 (s, 1H), 3.86 (s, 3H), 3.64 (s, 3H), 3.42 (d, *J* = 14.1 Hz, 1H), 3.28 (s, 3H), 3.07 (d, *J* = 17.1 Hz, 1H), 2.41 (d, *J* = 17.1 Hz, 1H), 1.85 (d, *J* = 14.1 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 177.1, 173.0, 171.5, 136.3, 128.4, 128.3, 126.5, 71.6, 65.0, 57.7, 52.5, 51.7, 51.4, 48.4, 40.5, 29.0; IR (KBr) ν 2950, 2397, 1735, 1487, 1359, 1084, 1008, 673 cm^{-1}. HRMS calcd. for $C_{18}H_{23}NO_6$+H^+: 350.1604, found 350.1605. The product was analyzed by HPLC to determine the enantiomeric excess: 93% ee (Chiralcel AD-H, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm); t_r = 8.67 and 9.82 min.

(2*R*,4*R*,5*R*)-dimethyl 5-(4-chlorophenyl)-4-(3-methoxy-3-oxopropyl)pyrrolidine-2,4-dicarboxylate (3l)

The title compound was prepared according to the general procedure as described above in 85% yield (75 mg) as white solid. m.p. 155-156 °C; $[\alpha]^{25}_D$ = +28.1 (*c* 1.05, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.29 (d, *J* = 8.4 Hz), 7.23 (d, *J* = 8.4 Hz), 4.10 (s, 1H), 4.03 (dd, J_1 = 6.0 Hz, J_2 = 9.0 Hz, 1H), 3.84 (s, 3H), 3.68 (s, 3H), 3.27 (s, 3H), 2.72 (dd, J_1 = 6.0 Hz, J_2 = 13.2 Hz, 1H), 2.36-2.26 (m, 3H), 2.15 (dd, J_1 = 9.6 Hz, J_2 = 13.5 Hz, 1H), 1.86-1.80 (m, 1H);^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 174.0, 173.1, 172.9, 136.7, 133.6, 128.2, 128.1, 72.7, 58.4, 52.2, 51.7, 51.5, 37.5, 31.0, 30.8; IR (KBr) ν 2997, 2953, 2918, 2844, 1732, 1489, 1435, 1377, 1304, 1203, 1176, 1117, 1089, 1013, 986, 834, 694 cm^{-1}. HRMS calcd. for $C_{18}H_{22}ClNO_6$+H^+: 384.1214, found 384.1219. The product was analyzed by HPLC to determine the enantiomeric excess: 93% ee (Chiralpak AS-H, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ = 220 nm); t_r = 6.93 and 10.29 min.

(2*R*,4*R*,5*R*)-dimethyl 4-(3-methoxy-3-oxopropyl)-5-(4-methoxyphenyl)pyrrolidine-2,4-dicarboxylate (3m)

The title compound was prepared according to the general procedure as described above in 81% yield (71 mg) as white solid. m.p. 140-141 °C; $[\alpha]^{25}_D$ = +25.0 (*c* 1.83, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 7.18 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 4.07 (s, 1H), 4.02 (dd, J_1 = 6.3 Hz, J_2 = 9.9 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.67 (s, 3H), 3.28 (s, 3H), 2.70 (dd, J_1 = 5.7 Hz, J_2 = 13.2 Hz, 1H), 2.36-2.25 (m, 3H), 2.14 (dd, J_1 = 9.3 Hz, J_2 = 12.9 Hz, 1H), 1.82-1.79 (m, 1H); ^{13}C

NMR ($CDCl_3$, TMS, 75 MHz) δ 174.1, 173.3, 173.2, 159.2, 129.7, 127.7, 113.5, 73.3, 58.5, 58.3, 55.1, 52.2, 51.6, 51.4, 38.0, 31.1, 31.0; IR (KBr) ν 2997, 2953, 2847, 2360, 2342, 1736, 1698, 1685, 1600, 1578, 1260, 1161, 1027, 835, 669 cm^{-1}. HRMS calcd. for $C_{19}H_{25}NO_7+H^+$: 380.1709, found 380.1706. The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AS-H, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ = 220 nm); t_r = 8.68 and 13.41 min.

Acknowledgements

We gratefully acknowledge financial support from the 973 Program (2011CB808600), NSFC (21172176) and HPNSF (ZRZ0273).

Notes and references

‡ Crystal data for (2*R*,4*S*,5*S*)-**3c**: $C_{17}H_{20}ClNO_6$, M_r = 369.79, T = 296 K, Orthorhombic, space group $P2_12_12_1$, a = 9.8397(12), b = 10.1420(13), c = 17.897(2) Å, V = 1786.1(4) $Å^3$, Z = 4, 11885 reflections measured, 3273 unique (R_{int} = 0.0332) which were used in all calculations. The final wR_2 = 0.0870 (all data), Flack χ = 0.03(6). CCDC 985571

1 (*a*) S. G. Pyne, A. S. Davis, N. J. Gates, J. Nicole, J. P. Hartley, K. B. Lindsay, T. Machan, M. Tang, *Synlett* 2004, 2670; (*b*) L. M. Harwood, R. J. Vickers, In *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; A. Padwa, W. Pearson, Eds.; Wiley & Sons: New York, 2002.

2 (*a*) *Privileged Chiral Ligands and Catalysts*; Q.-L. Zhou, Eds.; Wiley-VCH, Weinheim 2011; (*b*) A. Berkessel, H. Gröger, *Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis*, Wiley-VCH, Weinheim 2004.

3 For recent reviews about 1,3-dipolar cycloaddition reactions of azomethine ylides, see: (*a*) J. Yu, F. Shi and L.-Z. Gong, *Acc. Chem. Res.*, 2011, **44**, 1156; (*b*) J. Adrio and J. C. Carretero, *Chem. Commun*., 2011, **47**, 6784; (*c*) B. Engels and M. Christl, *Angew. Chem., Int. Ed.*, 2009, **48**, 7968; (*d*) L. M. Stanley and M. P. Sibi, *Chem. Rev.*, 2008, **108**, 2887; (*e*) M. Alvarez-Corral, M. Munoz-Dorado and I. Rodrıguez-Garcıa, *Chem. Rev.*, 2008, **108**, 3174; (*f*) M. Bonin, A. Chauveau and L. Micouin, *Synlett*, 2006, 2349; (*g*) C. Nájera and J. M. Sansano, *Angew. Chem., Int. Ed.,* 2005, **44**, 6272.

4 (*a*) S. L. Schreiber, *Science* 2000, **287**, 1964. (*b*) C. Chen, X. Li and S. L. Schreiber, *J. Am. Chem. Soc.* 2003, **125**, 10174.

5 (*a*) J. M. Longmire, B. Wang and X. Zhang, *J. Am. Chem. Soc.*, 2002, **124**, 13400; (*b*) A. S. Gothelf, K. V. Gothelf, R. G. Hazell and K. A. Jørgensen, *Angew. Chem., Int. Ed*., 2002, **41**, 4236.

6. For recent examples, see: (*a*) Atsuko Awata and Takayoshi Arai, *Chem. Eur. J.*, 2012, **18**, 8278; (*b*) L. Wang, X.-M. Shi, W.-P. Dong, L.-P. Zhu, R. Wang, *Chem. Commun*., 2013, **49**, 3458; (*c*) L. He, X.-H. Chen, D.-N. Wang, S.-W. Luo, W.-Q. Zhang, J. Yu, L. Ren and L.-Z. Gong, *J. Am. Chem. Soc.*, 2011, **133**, 13504; (*d*) X.-H. Chen, W.-Q. Zhang and L.-Z. Gong, *J. Am. Chem. Soc.*, 2008, **130**, 5652; (*e*) W. Zeng, G.-Y. Chen, Y.-G. Zhou and Y.-X. Li, *J. Am. Chem. Soc.*, 2007, **129**, 750; (*f*) W. Zeng and Y.-G. Zhou, *Org. Lett.*, 2005, **7**, 5055; (*g*) J.-W. Shi, M.-X. Zhao, Z.-Y. Lei and M. Shi, *J. Org. Chem.*, 2008, **73**, 305;(*h*) T. Arai, A. Mishiro, N. Yokoyama, K. Suzuli and H. Sato, *J. Am. Chem. Soc.*, 2010, **132**, 5338; (*i*) C. Nájera, M. D. G. Retamosa and J. Sansano, *Angew. Chem., Int. Ed.*, 2008, **47**, 6055; (*j*) C. Chen, X. Li and S. L. Schreiber, *J. Am. Chem. Soc.*, 2003, **125**, 10174; (*k*) X.-X. Yan, Q. Peng, Y. Zhang, K. Zhang, W. Hong, X.-L. Hou and Y.-D. Wu, *Angew. Chem., Int. Ed.*, 2006, **45**, 1979. (*l*) S. Cabrera, R. Gómez Arrayás and J. C. Carretero, *J. Am. Chem. Soc.*, 2005, **127**, 16394; (*m*) S. Saito, T. Tsubogo and S. Kobayashi, *J. Am. Chem. Soc.*, 2007, **129**, 5364; (*n*) Y. Yamashita, T. Imaizumi and S. Kobayashi, *Angew. Chem., Int. Ed.*, 2011, **50**, 4893; (*o*) H. Y. Kim, J.-Y. Li, S. Kim and K. Oh, *J. Am. Chem. Soc.*, 2011, **133**, 20750; (*p*) J. Hernández-Toribio, S. Padilla, J. Adrio and J. C. Carretero, *Angew. Chem., Int. Ed.*, 2012, **51**, 8854. (*p*) R. Narayan, J. O. Bauer, C. Strohmann, A. P. Antonchick and H. Waldmann, *Angew. Chem. Int. Ed.,* 2013, **52**, 12892. (*q*) S. Watanabe, A. Tada, Y. Tokoro and S.-i. Fukuzawa, *Tetrahedron Lett.*, 2014, **55**, 1306.

7 (*a*) W. Tang, X. Zhang, *Chem. Rev*. 2003, **103**, 3029; (b) H. U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal*. 2003, **345**, 103; (c)

8 Y. S. Or, C. Wang, X. Peng, L. Ying, Y.-L. Qiu, 2010, US 20100074863.

9 (*a*) Quaternary Stereocenters: *Challenges and Solution for Organic Synthesis*; J. Christoffers and A. Baro, Eds.; WILEY-VCH, Weinheim, 2005; (*b*) B. M. Trost and C. Jiang, *Synthesis*, 2006, 369.

10 (*a*) C.-J. Wang, G. Liang, Z.-Y. Xue and F. Gao, *J. Am. Chem. Soc.* 2008, **130**, 17250; (*b*) C.-J. Wang, Z.-Y. Xue, G. Liang and Z. Lu, *Chem. Commun.,* 2009, 2905; (*c*) G. Liang, M.-C. Tong and C.-J. Wang, *Adv. Synth. Catal.*, 2009, **351**, 3101; (*d*) Z.-Y. Xue, T.-L Liu, Z. Lu, H. Huang, H.-Y. Tao and C.-J. Wang, *Chem. Commun.*, 2010, **46**, 1727; (*e*) G. Liang, M.-C. Tong, H.-Y. Tao and C.-J. Wang, *Adv. Synth. Catal.*, 2010, **352**, 1851; (*f*) T.-L. Liu, Z.-Y. Xue, H.-Y. Tao and C.-J. Wang, *Org. Biomol. Chem.*, 2011, **9**, 1980; (*g*) Z.-Y. Xue, X. Fang and C.-J. Wang, *Org. Biomol. Chem.*, 2011**, 9**, 3622; (*h*) T.-L. Liu, Z.-L. He, H.-Y. Tao and C.-J. Wang, *Chem. Eur. J.*, 2012, **18**, 8042; (*i*) T.-L. Liu, Z.-L. He, H.-Y. Tao, Y.-P. Cai and C.-J. Wang, *Chem. Commun*., 2011, **47**, 2616; (*j*) Q.-H. Li, M.-C. Tong, J. Li, H.-Y. Tao and C.-J. Wang, *Chem. Commun.*, 2011, **47**, 11110; (*k*) T.-L. Liu, Z.-L. He and C.-J. Wang, *Chem. Commun.*, 2011**, 47**, 9600; (*l*) H.-L. Teng, H. Huang, H.-Y. Tao and C.-J. Wang, *Chem. Commun.*, 2011, **47**, 5494; (*m*) H.-L. Teng, F.-L. Luo, H.-Y. Tao and C.-J. Wang, *Org. Lett.*, 2011, **13**, 5600; (*n*) T.-L. Liu, Z.-L. He, Q.-H. Li, H.-Y. Tao and C.-J. Wang, *Adv. Synth. Catal.,* 2011, **353**, 1713; (*o*) M.-C. Tong, J. Li, H.-Y. Tao, Y.-X. Li and C.-J. Wang, *Chem. Eur. J.*, 2011, **17**, 12922; (*p*) D. Yan, Q. Li and C.-J. Wang, *Chin. J. Chem.*, 2012, **30**, 2714; (*q*) Q.-H. Li, Z.-Y. Xue, H.-Y. Tao and C.-J. Wang, *Tetrahedron Lett.*, 2012, **53**, 3650; (*r*) T.-L. Liu, Z.-L. He, H.-Y. Tao and C.-J. Wang, *Chem. Eur. J.*, 2012, **18**, 8042; (*s*) H.-L. Teng, H. Huang and C.-J. Wang, *Chem. Eur. J.*, 2012, **18**, 16214; (*t*) K. Liu, H.-L. Teng, L. Yao, H.-Y. Tao and C.-J. Wang, *Org. Lett.* 2013, **15**, 2250; (*u*) Z.-L. He, H.-L. Teng and C.-J. Wang, *Angew. Chem.*, *Int. Ed.*, 2013, **52**, 2934.

11 (*a*) H. Y. Kim, H.-J. Shih, W. E. Knabe, K. Oh, *Angew. Chem., Int. Ed*. 2009, **48**, 7420; (*b*) C. Nájera, M. D. G. Retamosa, J. M. Sansano, A. Cózar, F. P. Cossío, *Tetrahedron: Asymmetry* 2008, **19,** 2913.

12 For review on N-H effect in asymmetric synthesis, see: (*a*) B. Zhao, Z. Han, K. L. Ding, *Angew. Chem., Int. Ed*. 2013, **53**, 4744; (*b*) Z.-Y. Xue, Q.-H. Li, H.-Y. Tao, C.-J. Wang, *J. Am. Chem. Soc.* 2011, **133**, 11757; (*c*) M.-C. Tong, J. Li, H.-Y. Tao, Y.-X. Li, C.-J. Wang, *Chem.-Eur. J.* 2011, **17**, 12922; (*d*) M. Wang, C.-J. Wang, Z. Lin, *Organometallic* 2012, **31**, 7870. (*e*) P. Fackler, C. Berthold, F. Voss, T. Bach, *J. Am. Chem. Soc*. 2010, **132**, 15911.

13 Z.-C. Duan, X.-P. Hu, J. Deng, S.-B. Yu, D.-Y. Wang, Z. Zheng *Tetrahedron: Asymmetry* 2009**, 20**, 588.

