Tetrahedron: *Asymmetry* xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

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

Asymmetric Michael addition of malonates to unsaturated ketones catalyzed by rare earth metal complexes bearing phenoxy functionalized chiral diphenylprolinolate ligands

Qinqin Qian, Wenguo Zhu, Chengrong Lu, Bei Zhao *, Yingming Yao *

College of Chemistry, Chemical Engineering and Materials Science, Dushu Lake Campus, Soochow University, Suzhou 215123, PR China

ARTICLE INFO

Article history:
Received 22 April 2016
Revised 14 July 2016
Accepted 20 July 2016
Available online xxxx

ABSTRACT

A simple, efficient catalytic asymmetric Michael addition of malonates to unsaturated ketones has been successfully developed. This process was promoted by rare earth metal complexes **1**–**4** bearing a chiral phenoxy functionalized prolinol ligand at room temperature [$L^1RE(L^1H)$ (H_2L^1 = (*S*)-2,4-di-*tert*-butyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol, RE = Yb **1**, Y **2**, Sc **3** and $L^2Sc(L^2H)$ **4** (H_2L^2 = (*S*)-2,4-di-dimethylbenzyl-6-((2-(hydroxydiphenylmethyl)-pyrrolidin-1-yl)methyl)phenol)]. Complex **3** was the best catalyst in the transformation and the products were obtained in up to 99% yield and with 90% ee. In addition, the molecular structures of the catalysts were well characterized, including X-ray determination of complex **3**.

1. Introduction

Optically active 1,5-dicarbonyl compounds are key intermediates in organic synthesis,[1] which can be simply synthesized by asymmetric Michael addition of 1,3-dicarbonyl compounds to α, β-unsaturated carbonyl compounds.[2] Malonates are relatively popular Michael donors in Michael additions because of their high contents of enolates, which are stabilized by two electron-withdrawing ester groups under mild conditions. Over the past two decades, various chiral catalysts, such as organocatalysts,[3–7] including chiral ammonium salts[4,6] and amino acid salts,[5] and metal complexes,[8–13] have been developed to realize the asymmetric Michael addition. In the 1990s, Shibasaki et al. reported a type of multifunctional heterobimetallic chiral catalyst, which was successfully applied in the synthesis of chiral 1,5-dicarbonyl compounds via the addition of malonate with cyclohexenone.[9] However, in the first example, the enantioselectivities of the corresponding adducts were not satisfactory when the chalcone derivatives were used as the Michael acceptors. 1,5-Dicarbonyl compounds were obtained with excellent ee values by Maruoka,[6] Wang,[7] Kobayashi[10] and Feng[11] using chalcones as substrates. Until now, except for some simple ketones, α,β-unsaturated cyclohexenones and chalcones,[3a,c,4a,6,7,8a,c,h,10,11] 2-enoylpyridine *N*-oxides,[12] β,γ-unsaturated α-ketoesters[8b] and unsaturated 1,4-diketone compounds[13] have been used as the Michael acceptors. To the best of our knowledge, only a few rare earth metal compounds have been applied to catalyze the asymmetric Michael addition of malonates and suitable Michael acceptors.[8b,9,11] Feng's discovery in 2009 is noteworthy: they employed a catalyst combination derived from 5 mol % scandium triflate and 6 mol % *N*,*N*′-dioxides to catalyze the conjugate addition of malonates to chalcones and yielded the corresponding dicarbonyl products with excellent selectivities (96–99% ee).[11] This is the only successful case in which the transformation is catalyzed by rare earth metal catalysts with excellent yield and excellent enantioselectivity until now. Hence, more attention was paid to develop new and high efficient chiral rare earth metal catalysts continuously.

Our group previously developed a set of heterobimetallic rare earth metal–lithium complexes bearing a chiral phenoxy-functionalized diphenylprolinolate ligand and successfully introduced them in the asymmetric epoxidation of α,β-unsaturated ketones.[14] Recently, we addressed the further issue of asymmetric epoxidation of α,β-unsaturated ketones catalyzed by rare-earth amides $[(Me_3Si)_2N]_3RE(\mu\text{-}Cl)Li(THF)_3$ with a series of phenoxy-functionalized chiral prolinols.[15] The ytterbium complex [$L^1Yb(L^1H)$] (H_2L^1 = (*S*)-2,4-di-*tert*-butyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol) was also proved to have an effect on the epoxidation reaction. All of the results indicated that the rare earth metal complexes supported by chiral phenoxy-functionalized prolinolate ligand are high efficient system in some homogenous asymmetric catalytic reactions. We

* Corresponding authors. Tel./fax: +86 512 65880305 (B.Z.).
E-mail addresses: zhaobei@suda.edu.cn (B. Zhao), yaoym@suda.edu.cn (Y. Yao).

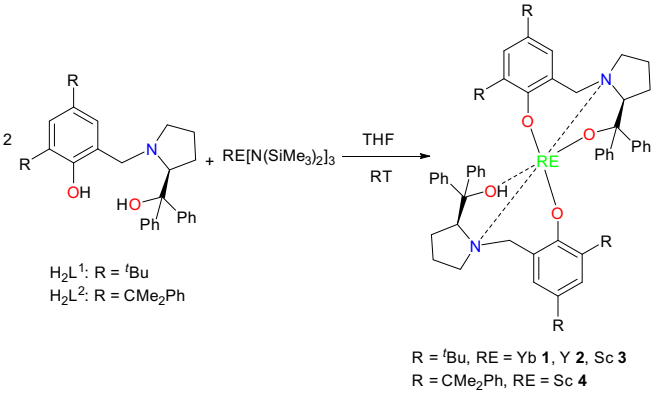
http://dx.doi.org/10.1016/j.tetasy.2016.07.014
0957-4166/

believe that these rare earth metal complexes have potential in enantioselective Michael additions of malonates to chalcones and their derivatives.

2. Results and discussion

2.1. Synthesis and characterization of rare earth metal complexes 1–4

In order to investigate the effects of the central metal and the ligand of the catalyst on the reaction, four rare earth metal complexes **1**–**4** stabilized by chiral phenoxy functionalized prolinolate ligands were synthesized according to the literature[15] and well characterized. As depicted in Scheme 1, treatment of RE[N(SiMe$_3$)$_2$]$_3$ with 2 equiv of proligand (*S*)-2,4-di-substituted-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol in THF for 3 h, after work-up, gave colorless crystals of complexes **1**–**4**, which were recrystallized in toluene. Crystals of complex **3** were suitable for X-ray diffraction and the definite solid-state structure of it is depicted in Figure 1. The scandium complex has a centrosymmetric structure with two chiral ligands in the unit cell, just the same as that of the known complex **1**.[15] One hydrogen atom of the hydroxyl group in one of the chiral prolinolates remained to meet the requirement of the common trivalence of the central Sc atom. The structure of complex **3** was also confirmed by ^{1}H NMR analysis, in which the signal at 9.38 assigned to the proton of the free hydroxyl group was observed. Unsatisfactory results from X-ray diffraction were obtained and only the skeletons of the molecular structures of **2** and **4** could be determined. Fortunately, NMR spectra of complexes **2** and **4** and the elemental analysis results of them are informative. It can be deduced that the molar ratio of the chiral prolinolates to the metal center is 2:1. Therefore, it is presumed that the solid structures of complexes **1**–**4** are isostructural, considering of the atomic radius of Yb (**1**), Y (**2**), and Sc (**3** and **4**).



Scheme 1. Synthesis of complexes **1**–**4**.

2.2. Catalytic asymmetric Michael addition of malonates to unsaturated ketones

Inspired by our previous studies,[14,15] we started with the model asymmetric Michael addition of chalcone **5a** with diethyl malonate **6a** to investigate the effects of various rare earth metal complexes. The known complex **1** was first tested in the reaction at -20 °C in toluene for 24 h. The yield of the product was 51%, however, the ee value was only 17% (Table 1, entry 1). When the reaction was conducted at room temperature, both the yield and ee value of the product were almost doubled after 18 h (Table 1, entry 2). If the catalyst ytterbium amide [(Me$_3$Si)$_2$N]$_3$Yb and the

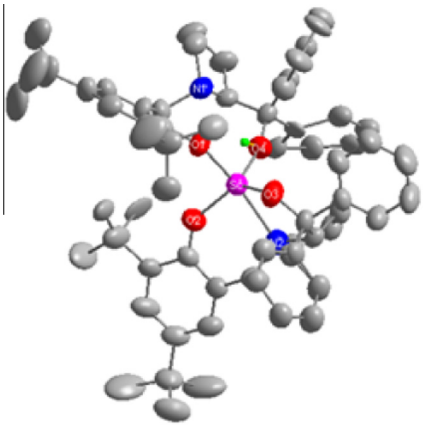
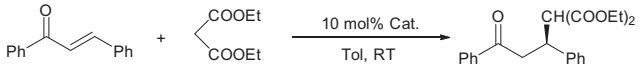


Figure 1. Molecular structure of **3** showing 20% probability ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Sc(1)–O(1) 2.013(3), Sc(1)–O(2) 1.974(4), Sc(1)–O(3) 1.947(4), Sc(1)–O(4) 1.955(3), Sc(1)–N(2) 2.404(4), O(3)–Sc(1)–O(4) 113.01(16), O(3)–Sc(1)–O(2) 127.50(16), O(4)–Sc(1)–O(2) 115.45(16), O(3)–Sc(1)–O(1) 98.59(14), O(4)–Sc(1)–O(1) 96.29(14), O(2)–Sc(1)–O(1) 95.10(15), O(3)–Sc(1)–N(2) 73.35(15), O(4)–Sc(1)–N(2) 97.68(15), O(2)–Sc(1)–N(2) 81.36(16), O(1)–Sc(1)–N(2) 165.76(15).

Table 1
Screening of various rare earth metal catalysts[a]



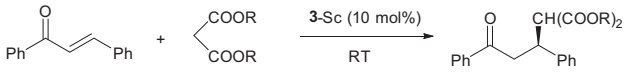
Entry	Cat.	Time (h)	*T* (°C)	Yield (%)[b]	ee (%)[c]
1	**1**-Yb	24	−20	51	17
2	**1**-Yb	18	25	90	35
3	Yb[N(SiMe$_3$)$_2$]$_3$ + 2H$_2$L^1	18	25	99	5
4	[Yb(L^1)$_2$][{(THF)$_3$Li}$_2$(μ-Cl)]	18	25	91	34
5	[(Me$_3$Si)$_2$N]$_3$Yb(μ-Cl)Li(THF)$_3$ + 1.5H$_2$L^1	18	25	88	27
6	**2**-Y	18	25	90	33
7	**3**-Sc	21	25	82	45
8	**4**-Sc	21	25	50	49
9[d]	**3**-Sc	21	25	76	40

[a] Reactions were performed with **5a** (0.3 mmol) and the catalyst (10 mol %) in Tol. (2 mL) under argon for 30 min, then **6a** (0.36 mmol) was added.
[b] Isolated yield.
[c] Determined by HPLC analysis.
[d] 5 mol % catalyst **3** was used.

phenoxy-functionalized chiral prolinol H$_2$L^1 were added separately in a 1:2 molar ratio, the ee value decreased dramatically (Table 1, entry 3). The effects of two known catalysts, a heterobimetallic Yb–Li complex [Yb(L^1)$_2$][{(THF)$_3$Li}$_2$(μ-Cl)][14] and the combination of [(Me$_3$Si)$_2$N]$_3$Yb(μ-Cl)Li(THF)$_3$ with H$_2$L^1 in a 1:1.5 molar ratio[15] were also tested and the outcomes were comparable with those of complex **1** (Table 1, entries 4 and 5). It was found that the metal centers of the complexes had an influence on the asymmetric addition. Y-based complex **2** almost had the same effect on the reaction as that of complex **1**, while Sc-based complex **3** gave us higher enantioselectivity on the addition (Table 1, entries 2, 6 and 7). Since the substituent group at the aromatic ring in the chiral ligand had significant effect on the enantioselectivity of the asymmetric reaction,[15] the steric effect of the chiral ligand was also investigated. As a result, the enantioselectivity of the current reaction was slightly increased in the presence of Sc-based complex **4** with the bulky ligand H$_2$L^2 (cumenyl group instead of *tert*-butyl group), although the yield of the Michael adduct was observed to decrease

under the same conditions (Table 1, entry 8). If the catalytic amount of complex **3** was reduced by half, both the yield and the ee value decreased (Table 1, entry 9). After screening of the catalysts in hand, Sc-based complex **3** was found to be ideal in the following experiments. Using the complex **3** as the catalyst, the reaction conditions, including solvent, reaction time and the amount of malonate were screened. Among the various solvents used, a high yield of the Michael adduct (82%) was obtained in toluene, but the enantioselectivity was still poor (Table 2, entry 1). In dichloromethane (DCM), the enantioselectivity of the product was at its best (up to 77% ee), but the yield was medium and unsatisfactory (Table 2, entry 2). Coordinated solvents, such as THF, diethyl ether and 1,4-dioxane, and aprotic solvent DMSO gave poor results (Table 2, entries 3–6). 1.2 equiv of diethyl malonate proved to be optimal (Table 2, entries 7–9). When the reaction time was prolonged to 50 h and the dosage of DCM was lowered to 1 mL, **7a** was obtained in 95% yield, while the ee value was maintained (Table 2, entry 10). An ester group effect of malonates was studied for the enantioselective Michael addition as well (Table 2, entries 10–12). Diisopropyl malonate turned out to be an outstanding Michael donor and product **7c** was obtained in 97% yield and with 85% ee (Table 2, entry 12). When 3 Å MS was introduced, the ee value of **7c** was continuously improved to 90% (Table 2, entry 13).

Table 2
Optimal conditions of the Michael reaction of malonates and chalcone[a]



5a 6a-c 7a-c

Entry	R	Time (h)	Solvent	Yield (%)[b]	ee (%)[c]
1	Et	21	TOL	82	45
2	Et	21	DCM	69	77
3	Et	21	DMSO	Trace	—
4	Et	21	THF	15	53
5	Et	21	Et_2O	79	49
6	Et	21	1,4-Dioxane	Trace	—
7	Et	48	DCM	78	77
8[d]	Et	48	DCM	70	43
9[e]	Et	48	DCM	68	74
10[f]	Et	50	DCM	95	78
11[f]	Me	50	DCM	85	70
12[f]	^{i}Pr	50	DCM	97	85
13[f,g]	^{i}Pr	50	DCM	95	90
14[f]	^{t}Bu	50	DCM	93	83

[a] Reactions were performed with **5a** (0.3 mmol) and the catalyst **3** (10 mol %) in solvent (2 mL) under argon for 30 min, then **6a** (0.36 mmol, 1.2 equiv) was added.
[b] Isolated yield.
[c] Determined by HPLC analysis.
[d] 1.0 equiv of malonate was used.
[e] 1.5 equiv of malonate was added.
[f] 1 mL DCM was used.
[g] 3 Å MS (60 mg) was used.

The optimal reaction conditions were established as follows; the molar ratio of diisopropyl malonate and chalcone was 1.2:1, and 10 mol % Sc-based complex **3** as the catalyst, 1 mL DCM, 50 h, at room temperature, in the presence of 3 Å MS.

The substrate scope of the Michael addition catalyzed by complex **3** was investigated, and the results are summarized in Table 3. It can be seen that most of chalcones, except for the substrates bearing very strong electron-withdrawing groups, CF_3 and NO_2, at the *para*-position of either phenyl ring, underwent the reactions smoothly to produce the desired products in high to excellent yields and with high enantioselectivities (Table 3, **7d**–**7n**). Similarly, α,β-unsaturated ketones bearing electron-rich heteroaromatic rings were also suitable Michael acceptors for the conjugate reaction and afforded products **7o** and **7p** in excellent yields with high enantioselectivities, while 2-enoylpyridine *N*-oxide with an electron-deficient heteroaromatic ring directly attached to the carbonyl group retarded the addition (Table 3, **7q**). Unfortunately, the current catalytic system is not suitable for the trisubstituted α,β-unsaturated ketones (Table 3, **7r**–**7t**). Furthermore, the enantiomeric purity of the products improved significantly after recrystallization (Table 3, **7i**, **7k**, and **7p**).

3. Conclusions

In conclusion, four rare earth metal complexes **1**–**4** stabilized by chiral phenoxy functionalized prolinolate ligands have been synthesized and well characterized. All of the complexes, together with three known chiral catalysts, were found to be efficient catalysts in the Michael addition of malonates with α,β-unsaturated ketones. In particular, complex **3** with the central metal Sc gave excellent results in the conjugate Michael addition of malonates. Moreover, enantio-enriched 1,5-ketoesters were obtained in good yield and with moderate to good enantiomeric excesses from chalcone derivatives (77–90% ee). Further studies of the promising applications of the current catalyst system are underway.

4. Experimental

4.1. General

All reagents are commercially available, reagent grade, and used as received unless otherwise noted. Experiments involving air and water sensitive components were performed in a glovebox or using the standard Schlenk techniques. Solvents were distilled before use from calcium hydride or sodium/benzophenone. ^{1}H and ^{13}C spectra were obtained on a Bruker AVANCEIII 400 MHz spectrometer using tetramethylsilane (TMS) as an internal reference. HRMS data were obtained on a Micromass GCT instrument. Enantiomeric excesses (ee) were determined by HPLC analysis (Shimadzu LC-20A) using the Daicel column IA and column ID. Suitable single crystals of complex **3** were sealed in a thin-walled glass capillary for determining the single-crystal structure. Intensity data were collected with a Rigaku Mercury CCD area detector in ω scan mode using Mo-Kα radiation (λ = 0.71075 Å). The diffracted intensities were corrected for Lorentz polarization effects and empirical absorption corrections.

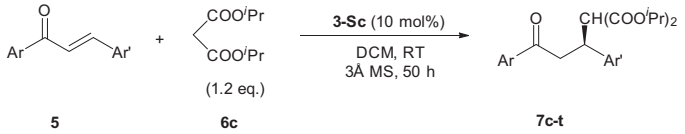
4.2. Synthesis of $L^1Yb(L^1H)$ 1

According to our previous work,[1] to a THF solution of $Yb[N(TMS)_2]_3$ (2 mmol), a THF solution of H_2L^1 (4 mmol) (H_2L^1 = (*S*)-2,4-di-*tert*-butyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol) was added and the mixture was stirred at room temperature for 12 h. The solvent was evaporated and the mixture was crystallized in toluene. The colorless crystals were obtained at room temperature after 1 or 2 days (1.38 g, yield 62% based on ytterbium). Anal. Calcd for $C_{64}H_{79}N_2O_4Yb$: C, 69.04; H, 7.15; N, 2.52; Yb, 15.54. Found: C, 69.32; H, 7.23; N, 2.69; Yb, 15.65.

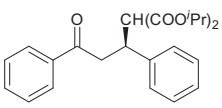
4.3. Synthesis of $L^1Y(L^1H)$ 2

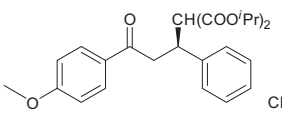
The synthesis of complex **2** was carried out in the same way as that described for complex **1**, but $Y[N(TMS)_2]_3$ (2 mmol) was used instead of $Yb[N(TMS)_2]_3$. After work-up, colorless crystals were obtained from Tol-hexane solution (1.09 g, yield 53% based on yttrium). Anal. Calcd for $C_{64}H_{79}N_2O_4Y$: C, 74.69; H, 7.74; N, 2.72; Y, 8.64. Found: C, 74.81; H, 8.03; N, 2.98; Y, 8.88. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): 7.78 (m, 3H, ArH), 7.72 (m, 2H, ArH),

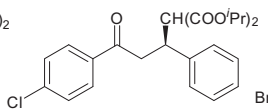
Table 3
Scope of α,β-unsaturated ketones

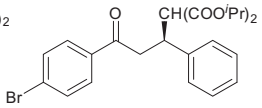


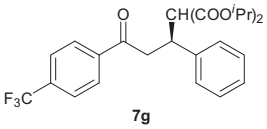
5 6c 7c-t

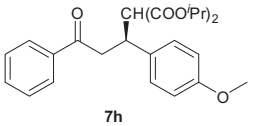

7c
yield: 95%
ee: 90%

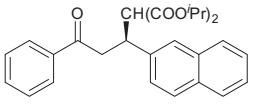

7d
yield: 92%
ee: 83%

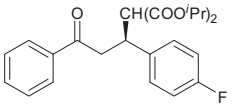

7e
yield: 99%
ee: 89%

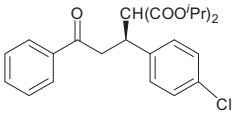

7f
yield: 99%
ee: 87%

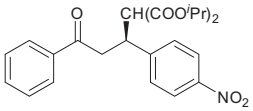

7g
yield: 90%
ee: 64%

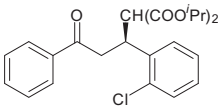

7h
yield: 82%
ee: 88%

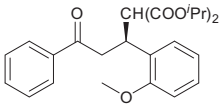

7i
yield: 90% (78%)[a]
ee: 88% (96%)[a]

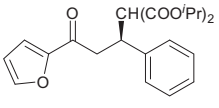

7j
yield: 95%
ee: 86%

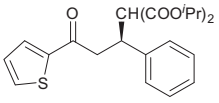

7k
yield: 97%(86%)[a]
ee: 84%(91%)[a]

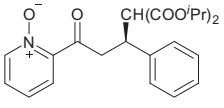

7l
yield: 99%
ee: 77%

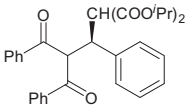

7m
yield: 86%
ee: 81%

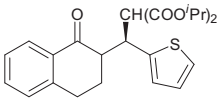

7n
yield: 80%
ee: 86%

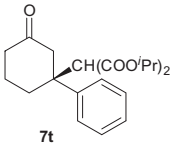

7o
yield: 97%
ee: 89%


7p
yield: 95%(83%)[a]
ee: 82%(91%)[a]


7q
yield: 65%
ee: 40%


7r
yield: 30%
ee: 26%


7s
trace


7t
trace

[a]Data in parentheses were obtained after recrystallization

7.52 (m, 3H, ArH), 7.28 (m, 1H, ArH), 7.22 (m, 9H, ArH), 7.12 (m, 4H, ArH), 6.85 (m, 1H, ArH), 6.77 (m, 1H, ArH), 4.26 (m, 4H, NCH_2Ar), 3.71 (m, 2H, NCH), 3.14 (m, 2H, NCH_2), 2.81 (m, 2H, NCH_2), 2.64 (m, 2H, CH_2), 2.01 (m, 2H, CH_2), 1.82 (m, 4H, CH_2), 1.44 (m, 9H, C$(CH_3)_3$), 1.36 (m, 15H, C$(CH_3)_3$), 1.28 (m, 12H, C$(CH_3)_3$). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.6 (Ph), 160.6 (Ph), 153.5 (Ph), 148.4 (Ph), 147.8 (Ph), 146.2 (Ph), 145.9 (Ph), 140.3 (Ph), 136.7 (Ph), 136.0 (Ph), 135.1 (Ph), 128.8 (Ph), 128.6 (Ph), 128.4 (Ph), 128.1 (Ph), 127.8 (Ph), 127.2 (Ph), 126.9 (Ph), 126.5 (Ph), 126.1 (Ph), 125.9 (Ph), 125.6 (Ph), 124.5 (Ph), 123.8 (Ph), 123.4 (Ph), 122.8 (Ph), 122.3 (Ph), 82.4 ($OCPh_2$), 81.6 ($OCPh_2$), 79.9 (NCH_2Ar), 77.4 (NCH_2Ar), 76.3 (NCH), 72.8 (NCH), 68.1 (NCH_2), 67.2 (NCH_2), 66.0 ($C(CH_3)_3$), 62.0 ($C(CH_3)_3$), 61.8 ($C(CH_3)_3$), 55.3 ($C(CH_3)_3$), 53.5 (CH_2), 51.1 (CH_2), 35.1 (CH_2), 34.0 (CH_2), 32.0 ($C(CH_3)_3$), 31.8 (C$(CH_3)_3$), 30.5 ($C(CH_3)_3$), 30.2 ($C(CH_3)_3$), 30.1 ($C(CH_3)_3$), 29.6 (C$(CH_3)_3$), 29.5 ($C(CH_3)_3$), 28.7 ($C(CH_3)_3$), 25.7 ($C(CH_3)_3$), 24.4 (C$(CH_3)_3$), 20.6 ($C(CH_3)_3$), 15.4 ($C(CH_3)_3$).

4.4. Synthesis of $L^1Sc(L^1H)$ 3

The synthesis of complex **3** was carried out in the same way as that described for complex **1**, but $Sc[N(TMS)_2]_3$ (2 mmol) was used instead of $Yb[N(TMS)_2]_3$. After work-up, colorless crystals were obtained from toluene. (1.62 g, yield 82% based on scandium). Anal. Calcd for $C_{64}H_{79}N_2O_4Sc$: C, 78.02; H, 8.08; N, 2.84; Sc, 4.56. Found: C, 78.44; H, 8.17; N, 2.97; Sc, 4.84. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 9.38 (s, 1H, OH), 7.94 (m, 5H, ArH), 7.52 (m, 5H, ArH), 7.17 (m, 11H, ArH), 6.82 (m, 3H, ArH), 5.41 (s, 1H, NCH_2Ar), 4.64 (s, 1H, NCH_2Ar), 4.89 (m, 4H, NCH_2Ar, NCH), 2.85 (m, 4H, NCH_2), 2.06 (m, 3H, CH_2), 1.74 (s, 9H, C$(CH)_3$), 1.42 (m, 3H, CH_2), 1.21 (m, 27H, C$(CH)_3$). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.8 (Ph), 160.2 (Ph), 153.5 (Ph), 152.5 (Ph), 146.2 (Ph), 145.9 (Ph), 145.2 (Ph), 142.7 (Ph), 140.3 (Ph), 138.9 (Ph), 137.2 (Ph), 136.8 (Ph), 135.9 (Ph), 135.1 (Ph), 134.4 (Ph), 128.6 (Ph), 128.4 (Ph), 128.3 (Ph), 128.3 (Ph), 127.9 (Ph), 127.8 (Ph), 127.6 (Ph), 126.1

(Ph), 125.9 (Ph), 124.1 (Ph), 119.1 (Ph), 83.3 ($OCPh_2$), 82.4 ($OCPh_2$), 82.2(NCH_2Ar), 79.9 (NCH_2Ar), 79.7 (NCH), 77.4 (NCH), 72.8 (NCH_2), 65.0 (NCH_2), 62.5 ($C(CH_3)_3$), 62.0 ($C(CH_3)_3$), 55.3($C(CH_3)_3$), 53.0 ($C(CH_3)_3CH_2$), 51.0 (CH_2), 35.5 (CH_2), 35.0 (CH_2), 34.2 (CH_2), 34.0 ($C(CH_3)_3$), 32.0 ($C(CH_3)_3$), 31.8 ($C(CH_3)_3$), 30.4 ($C(CH_3)_3$), 29.6 ($C(CH_3)_3$), 25.8 ($C(CH_3)_3$), 24.4 ($C(CH_3)_3$), 23.0 ($C(CH_3)_3$), 19.3 ($C(CH_3)_3$).

4.5. Synthesis of $L^2Sc(L^2H)$ 4

The synthesis of complex **4** was carried out in the same way as that described for complex **3**, but H_2L^2 (2.144 g, 3.6 mmol) ((*S*)-2,4-di-cumenyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol) was used instead of H_2L^1. After work-up, yellow solid was obtained from Tol-*n*-hexane solvent at 0 °C (1.50 g, yield 61% based on scandium). Anal. Calcd for $C_{84}H_{87}N_2O_4Sc$: C, 81.79; H, 7.11; N, 2.27; Sc, 3.64. Found: C, 81.83; H, 7.43; N, 2.52; Sc, 3.75. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.86 (s, 1H, OH), 7.99 (m, 2H, ArH), 7.62 (m, 3H, ArH), 7.47 (m, 6H, ArH), 7.03 (m, 28H, ArH), 6.89 (m, 2H, ArH), 6.73 (m, 1H, ArH), 6.63 (m, 6H, ArH), 6.45 (m, 6H, ArH), 3.89 (m, 1H, NCH_2Ar), 3.73 (m, 3H, NCH_2Ar), 3.29 (m, 1H, NCH), 3.00 (m, 1H, NCH), 2.62 (m, 3H, NCH_2), 2.55 (m, 3H, NCH_2, CH_2), 1.94 (m, 2H, CH_2), 1.78 (m, 2H, CH_2), 1.64 (m, 18H, $C(CH)_3$), 1.36 (m, 6H, $C(CH)_3$), 1.13 (m, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.6 (Ph), 160.6 (Ph), 152.7 (Ph), 152.3 (Ph), 152.2 (Ph), 152.1 (Ph), 151.9 (Ph), 151.6 (Ph), 151.4 (Ph), 150.7 (Ph), 146.4 (Ph), 145.9 (Ph), 145.2 (Ph), 142.7 (Ph), 140.1 (Ph), 137.9 (Ph), 136.2 (Ph), 135.4 (Ph), 134.5 (Ph), 131.6 (Ph), 128.1 (Ph), 128.0 (Ph), 127.9 (Ph), 127.8 (Ph), 127.7 (Ph), 127.6 (Ph), 126.9 (Ph), 126.9 (Ph), 126.8 (Ph), 126.1 (Ph), 119.8 (Ph), 83.4 ($OCPh_2$), 81.9 ($OCPh_2$), 79.3 ($NCH_2(Ar)$), 78.8 ($NCH_2(Ar)$), 72.1 (NCH), 64.1 (NCH), 61.8 (NCH_2), 59.9 (NCH_2), 55.0 ($C(CH_3)_2Ph$), 52.5 ($CC(CH_3)_2Ph$), 50.6 ($C(CH_3)_2Ph$), 43.4 ($C(CH_3)_2Ph$), 42.6 (CH_2), 42.5 (CH_2), 42.3 (CH_2), 42.1 (CH_2), 34.7 ($C(CH_3)_2Ph$), 31.3 ($C(CH_3)_2Ph$), 28.5 ($C(CH_3)_2Ph$), 26.7 ($C(CH_3)_2Ph$), 25.5 ($C(CH_3)_2Ph$), 24.2 ($C(CH_3)_2Ph$), 23.2 ($C(CH_3)_2Ph$), 19.2 ($C(CH_3)_2Ph$).

4.6. General procedure for the asymmetric Michael addition of malonates to α,β-unsaturated ketones

The procedures for the asymmetric Michael addition of α,β-unsaturated ketones catalyzed by complexes **1**–**4** are similar, and a typical procedure is given as follows. A 10 mL Schlenk flask was charged with a mixture of chalcone (0.3 mmol), catalyst (0.03 mmol), molecular sieve 3 Å (60 mg, 30 mg/mmol of starting material), and 1 mL DCM. After stirring for approximately 30 min. at room temperature, the malonate (0.36 mmol) was added in one portion. The reaction system was maintained at 25 °C for 50 h, then quenched by adding water, and the reaction mixture was purified by flash chromatography (petroleum ether : ethyl acetate = 20 : 1) on silica gel to afford the desired product. The enantiomeric excess of the product was determined by chiral stationary-phase HPLC analysis.

4.7. Characterization of the products

4.7.1. Diisopropyl 2-(3-oxo-1,3-diphenylpropyl)malonate 7c

A white powder; yield 95%, ee 90%; $[\alpha]_D^{20}$ = +18.9 (*c* 0.925, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (m, 2H, Ar), 7.52 (m, 1H, Ar), 7.41 (m, 2H, Ar), 7.24 (m, 4H, Ar), 7.15 (m, 1H, Ar), 5.08 (m, 1H, OCH), 4.79 (m, 1H, OCH), 4.15 (td, J_1 = 9.7 Hz, J_2 = 4.2 Hz, 1H, CH), 3.78 (d, J = 9.9 Hz, 1H, CH), 3.55 (dd, J_1 = 16.5 Hz, J_2 = 3.8 Hz, 1H, CH_2), 3.43 (dd, J_1 = 16.9 Hz, J_2 = 9.6 Hz, 1H, CH_2), 1.25 (d, J = 6.3 Hz, 6H, CH_3), 1.05 (d, J = 6.2 Hz, 3H, CH_3), 0.96 (d, J = 6.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.77, 168.09, 167.39, 140.60, 137.01, 133.10, 128.66, 128.51, 128.45, 128.24, 127.19, 69.38, 68.98, 58.01, 43.08, 40.89, 21.81, 21.68, 21.47, 21.42; HPLC: Daicel column ID, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, 18.5 min (major), 21.6 min (minor). HRMS (ESI) calcd for $C_{24}H_{28}O_5$ [M+H$^+$]: 397.2015, found: 397.2021.

4.7.2. Diisopropyl 2-(3-(4-methoxyphenyl)-3-oxo-1-phenylpropyl)malonate 7d

A white powder; yield 92%, ee 83%; $[\alpha]_D^{20}$ = +17.8 (*c* 0.449, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (m, 2H, Ar), 7.29 (m, 4H, Ar), 7.19 (m, 1H, Ar), 6.92 (m, 2H, Ar), 5.14 (m, 1H, OCH), 4.85 (m, 1H, OCH), 4.02 (td, J_1 = 9.8 Hz, J_2 = 4.2 Hz, 1H, CH), 4.89 (s, 3H, OCH_3), 3.83 (d, J = 10.0 Hz, 1H, CH), 3.54 (dd, J_1 = 16.2 Hz, J_2 = 4.2 Hz, 1H, CH_2), 3.41 (dd, J_1 = 16.1 Hz, J_2 = 9.7 Hz, 1H, CH_2), 1.29 (dd, J_1 = 6.2 Hz, J_2 = 1.2 Hz, 6H, CH_3), 1.09 (d, J = 6.6 Hz, 3H, CH_3), 1.00 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.68, 167.51, 166.80, 162.88, 140.02, 129.92, 129.51, 127.89, 127.79, 126.53, 113.17, 68.73, 68.32, 57.46, 54.95, 42.16, 40.53, 21.19, 21.06, 20.85, 20.80; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 14.22 min, t_r (minor) = 25.42 min. HRMS (ESI) calcd for $C_{25}H_{30}O_6$ [M+H$^+$]: 427.2115, found: 427.2121.

4.7.3. Diisopropyl 2-(1-phenyl-3-oxo-3-(4-chlorophenyl)propyl)malonate 7e

A white powder; yield 99%, ee 89%; $[\alpha]_D^{20}$ = +14.5 (*c* 0.932, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (m, 2H, Ar), 7.40 (m, 2H, Ar), 7.23 (m, 4H, Ar), 7.17 (m, 1H, Ar), 5.07 (m, 1H, OCH), 4.78 (m, 1H, OCH), 4.11 (td, J_1 = 9.8 Hz, J_2 = 4.0 Hz, 1H, CH), 3.75 (d, J = 9.9 Hz, 1H, CH), 3.50 (dd, J_1 = 16.3 Hz, J_2 = 4.0 Hz, 1H, CH_2), 3.37 (dd, J_1 = 16.6 Hz, J_2 = 9.7 Hz, 1H, CH_2), 1.23 (d, J = 6.2 Hz, 6H, CH_3), 1.03 (d, J = 6.2 Hz, 3H, CH_3), 0.96 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.69, 168.08, 167.30, 140.27, 139.54, 135.21, 129.70, 128.98, 128.51, 128.42, 127.32, 69.47, 69.04, 57.88, 43.12, 40.96, 21.80, 21.66, 21.45, 21.41; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 10.55 min, t_r (minor) = 19.08 min. HRMS (ESI) calcd for $C_{24}H_{27}ClO_5$ [M+H$^+$]: 431.1619, found: 431.1629.

4.7.4. Diisopropyl 2-(1-phenyl-3-oxo-3-(4-bromophenyl)propyl) malonate 7f

A white powder; yield 99%, ee 87%; $[\alpha]_D^{20}$ = +10.4 (*c* 0.869, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (m, 2H, Ar), 7.57 (m, 2H, Ar), 7.24 (m, 4H, Ar), 7.17 (m, 1H, Ar), 5.07 (m, 1H, OCH), 4.80 (m, 1H, OCH), 4.13 (td, J_1 = 9.7 Hz, J_2 = 4.0 Hz, 1H, CH), 3.78 (d, J = 9.9 Hz, 1H, CH), 3.55 (dd, J_1 = 16.3 Hz, J_2 = 4.1 Hz, 1H, CH_2), 3.41 (dd, J_1 = 16.3 Hz, J_2 = 9.7 Hz, 1H, CH_2), 1.26 (d, J = 6.2 Hz, 6H, CH_3), 1.06 (d, J = 6.2 Hz, 3H, CH_3), 0.98 (d, J = 6.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.87, 168.07, 167.29, 140.32, 135.68, 131.97, 129.81, 128.51, 128.43, 128.28, 127.31, 69.44, 69.03, 57.89, 43.09, 40.97, 21.80, 21.66, 21.45, 21.41; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 11.10 min, t_r (minor) = 20.29 min. HRMS (ESI) calcd for $C_{24}H_{27}BrO_5$ [M+H$^+$]: 475.1115, found: 475.1110.

4.7.5. Diisopropyl 2-(1-phenyl-3-oxo-3-(4-trifluoromethylphenyl)propyl)malonate 7g

A colorless liquid; yield 90%, ee 64%; $[\alpha]_D^{20}$ = +8.8 (*c* 0.963, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (m, 2H, Ar), 7.69 (m, 2H, Ar), 7.23 (m, 4H, Ar), 7.17 (m, 1H, Ar), 5.11 (m, 1H, OCH), 4.81 (m, 1H, OCH), 4.16 (td, J_1 = 9.8 Hz, J_2 = 4.0 Hz, 1H, CH), 3.81 (d, J = 9.9 Hz, 1H, CH), 3.64 (dd, J_1 = 16.4 Hz, J_2 = 4.0 Hz, 1H, CH_2), 3.48 (dd, J_1 = 16.4 Hz, J_2 = 9.7 Hz, 1H, CH_2), 1.26 (d, J = 6.3 Hz, 6H, CH_3), 1.06 (d, J = 6.2 Hz, 3H, CH_3), 0.98 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.92, 168.01, 167.20, 140.20, 139.57, 134.40, 134.07, 133.74, 128.94, 128.53, 128.49, 128.37, 128.07, 127.74, 127.31, 125.67, 125.65, 125.03, 122.32, 119.61, 69.42,

68.99, 57.76, 43.38, 40.86, 21.70, 21.56, 21.36, 21.31; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 9.31 min, t_r (minor) = 14.04 min. HRMS (ESI) calcd for $C_{25}H_{27}F_3O_5$ [M+H$^+$]: 465.1883, found: 465.1881.

4.7.6. Diisopropyl 2-(1-(4-methoxyphenyl)-3-oxo-3-phenylpropyl)malonate 7h

A white powder; yield 82%, ee 88%; $[\alpha]_D^{20}$ = +23.8 (*c* 0.126, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (m, 2H, Ar), 7.52 (m, 1H, Ar), 7.42 (m, 2H, Ar), 7.17 (m, 2H, Ar), 6.77 (m, 2H, Ar), 5.07 (m, 1H, OCH), 4.80 (m, 1H, OCH), 4.10 (td, J_1 = 9.9 Hz, J_2 = 4.0 Hz, 1H, CH), 3.73 (m, 4H, OCH_3, CH), 3.53 (dd, J_1 = 16.4 Hz, J_2 = 4.1 Hz, 1H, CH_2), 3.40 (dd, J_1 = 16.3 Hz, J_2 = 9.8 Hz, 1H, CH_2), 1.25 (dd, J_1 = 6.4 Hz, J_2 = 2.8 Hz, 6H, CH_3), 1.06 (d, J = 6.2 Hz, 3H, CH_3), 0.98 (d, J = 6.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.35, 167.53, 166.82, 158.00, 136.41, 132.46, 131.91, 128.90, 128.04, 127.64, 113.20, 68.72, 68.32, 57.60, 54.67, 42.67, 39.62, 21.21, 21.07, 20.91, 20.86; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 13.28 min, t_r (minor) = 28.83 min. HRMS (ESI) calcd for $C_{25}H_{30}O_6$ [M+H$^+$]: 427.2115, found: 427.2122.

4.7.7. Diisopropyl 2-(1-naphthyl-3-oxo-3-phenylpropyl)malonate 7i

A white powder; yield 90%, ee 88%; $[\alpha]_D^{20}$ = +23.6 (*c* 0.742, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (m, 2H, Ar), 7.72 (m, 4H, Ar), 7.51 (m, 1H, Ar), 7.42 (m, 5H, Ar), 5.08 (m, 1H, OCH), 4.74 (m, 1H, OCH), 4.34 (td, J_1 = 9.4 Hz, J_2 = 4.5 Hz, 1H, CH), 3.88 (d, J = 9.5 Hz, 1H, CH), 3.58 (m, 2H, CH_2), 1.24 (dd, J_1 = 6.2 Hz, J_2 = 2.2 Hz, 6H, CH_3), 1.00 (d, J = 6.3 Hz, 3H, CH_3), 0.89 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.69, 168.10, 167.38, 138.20, 136.98, 133.38, 133.14, 132.70, 128.67, 128.25, 128.17, 127.93, 127.67, 127.41, 126.57, 126.04, 125.78, 69.45, 69.03, 58.04, 43.03, 40.91, 21.82, 21.70, 21.49, 21.39; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 12.53 min, t_r (minor) = 21.67 min. HRMS (ESI) calcd for $C_{28}H_{30}O_5$ [M+H$^+$]: 447.2166, found: 447.2167.

4.7.8. Diisopropyl 2-(1-(4-fluorophenyl)-3-oxo-3-phenylpropyl) malonate 7j

A white powder; yield 95%, ee 86%; $[\alpha]_D^{20}$ = +22.0 (*c* 0.726, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (m, 2H, Ar), 7.55 (m, 1H, Ar), 7.44 (m, 2H, Ar), 7.23 (m, 2H, Ar), 6.91 (m, 2H, Ar), 5.07 (m, 1H, OCH), 4.82 (m, 1H, OCH), 4.16 (td, J_1 = 9.9 Hz, J_2 = 4.0 Hz, 1H, CH), 3.74 (d, J = 9.9 Hz, 1H, CH), 3.54 (dd, J_1 = 16.7 Hz, J_2 = 4.0 Hz, 1H, CH_2), 3.39 (dd, J_1 = 16.6 Hz, J_2 = 9.8 Hz, 1H, CH_2), 1.25 (dd, J_1 = 6.2 Hz, J_2 = 3.4 Hz, 6H, CH_3), 1.07 (d, J = 6.3 Hz, 3H, CH_3), 0.99 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.65, 167.93, 167.29, 136.89, 133.25, 130.16, 130.09, 128.73, 128.22, 115.40, 115.19, 69.50, 69.12, 57.99, 43.10, 40.20, 21.82, 21.68, 21.51, 21.47; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 9.61 min, t_r (minor) = 20.00 min. HRMS (ESI) calcd for $C_{24}H_{27}FO_5$ [M+H$^+$]: 415.1915, found: 415.1919.

4.7.9. Diisopropyl 2-(1-(4-chlorophenyl)-3-oxo-3-phenylpropyl) malonate 7k

A white powder; yield 97%, ee 84%; $[\alpha]_D^{20}$ = +17.1 (*c* 0.703, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (m, 2H, Ar), 7.54 (m, 1H, Ar), 7.43 (m, 2H, Ar), 7.21 (m, 4H, Ar), 5.07 (m, 1H, OCH), 4.81 (m, 1H, OCH), 4.13 (td, J_1 = 9.8 Hz, J_2 = 4.0 Hz, 1H, CH), 3.73 (d, J = 9.8 Hz, 1H, CH), 3.54 (dd, J_1 = 16.7 Hz, J_2 = 4.0 Hz, 1H, CH_2), 3.41 (dd, J_1 = 16.7 Hz, J_2 = 9.8 Hz, 1H, CH_2), 1.24 (dd, J_1 = 6.2 Hz, J_2 = 3.2 Hz, 6H, CH_3), 1.08 (d, J = 6.2 Hz, 3H, CH_3), 0.99 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.46, 167.84, 167.20, 139.19, 136.81, 133.27, 132.93, 129.94, 128.72, 128.59, 128.19, 69.53, 69.17, 57.74, 42.83, 40.20, 21.79, 21.65, 21.49, 21.45; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 10.77 min, t_r (minor) = 22.61 min. HRMS (ESI) calcd for $C_{24}H_{27}ClO_5$ [M+H$^+$]: 431.1619, found: 431.1626.

4.7.10. Diisopropyl 2-(1-(4-nitrophenyl)-3-oxo-3-phenylpropyl) malonate 7l

A white powder; yield 99%, ee 77%; $[\alpha]_D^{20}$ = +23.6 (*c* 0.826, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (m, 2H, Ar), 7.88 (m, 2H, Ar), 7.55 (m, 1H, Ar), 7.47 (m, 4H, Ar), 5.08 (m, 1H, OCH), 4.84 (m, 1H, OCH), 4.27 (td, J_1 = 9.7 Hz, J_2 = 4.0 Hz, 1H, CH), 3.80 (d, J = 9.7 Hz, 1H, CH), 3.61 (dd, J_1 = 17.1 Hz, J_2 = 4.0 Hz, 1H, CH_2), 3.48 (dd, J_1 = 17.1 Hz, J_2 = 9.8 Hz, 1H, CH_2), 1.25 (dd, J_1 = 6.2 Hz, J_2 = 2.5 Hz, 6H, CH_3), 1.07 (d, J = 6.2 Hz, 3H, CH_3), 1.01 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.94, 167.50, 166.94, 148.64, 147.07, 136.53, 133.56, 129.63, 128.84, 128.15, 123.66, 69.84, 69.52, 57.23, 42.44, 40.41, 21.80, 21.65, 21.51; HPLC: Daicel column IC, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 16.18 min, t_r (minor) = 17.43 min. HRMS (ESI) calcd for $C_{24}H_{27}NO_7$ [M+H$^+$]: 442.1860, found: 442.1862.

4.7.11. Diisopropyl 2-(1-(2-chlorophenyl)-3-oxo-3-phenylpropyl)malonate 7m

A colorless liquid; yield 86%, ee 81%; $[\alpha]_D^{20}$ = +29.1 (*c* 0.808, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (m, 2H, Ar), 7.52 (m, 1H, Ar), 7.41 (m, 2H, Ar), 7.32 (m, 2H, Ar), 7.12 (m, 2H, Ar), 5.06 (m, 1H, OCH), 4.85 (m, 1H, OCH), 4.63 (m, 1H, CH), 4.06 (d, J = 9.2 Hz, 1H, CH), 3.63 (m, 2H, CH_2), 1.24 (d, J = 6.2 Hz, 3H, CH_3), 1.18 (d, J = 6.3 Hz, 3H, CH_3), 1.06 (m, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.56, 167.90, 167.31, 137.92, 136.81, 134.22, 133.09, 130.04, 129.71, 128.58, 128.25, 128.16, 126.77, 69.28, 69.09, 55.68, 40.85, 37.53, 21.66, 21.58, 21.40, 21.33; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 7.68 min, t_r (minor) = 10.16 min. HRMS (ESI) calcd for $C_{24}H_{27}ClO_5$ [M+H$^+$]: 431.1619, found: 431.1622.

4.7.12. Diisopropyl 2-(1-(2-methoxyphenyl)-3-oxo-3-phenylpropyl)malonate 7n

A colorless liquid; yield 80%, ee 86%; $[\alpha]_D^{20}$ = +18.3 (*c* 0.601, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (m, 2H, Ar), 7.50 (m, 1H, Ar), 7.40 (m, 2H, Ar), 7.13 (m, 2H, Ar), 6.78 (m, 2H, Ar), 5.07 (m, 1H, OCH), 4.75 (m, 1H, OCH), 4.28 (td, J_1 = 10.1 Hz, J_2 = 3.8 Hz, 1H, CH), 4.13 (d, J = 10.4 Hz, 1H, CH), 3.80 (s, 3H, OCH_3), 3.63 (dd, J_1 = 16.1 Hz, J_2 = 9.8 Hz, 1H, CH_2), 3.45 (dd, J_1 = 16.1 Hz, J_2 = 3.8 Hz, 1H, CH_2), 1.24 (d, J = 6.2 Hz, 6H, CH_3), 1.02 (d, J = 6.2 Hz, 3H, CH_3), 0.95 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.50, 168.55, 167.78, 157.68, 137.24, 132.82, 131.19, 128.52, 128.42, 128.25, 127.78, 120.42, 110.91, 69.08, 68.61, 55.53, 55.33, 41.11, 38.44, 21.81, 21.67, 21.47, 21.38; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 7.55 min, t_r (minor) = 8.68 min. HRMS (ESI) calcd for $C_{25}H_{30}O_6$ [M+H$^+$]: 427.2115, found: 427.2114.

4.7.13. Diisopropyl 2-(3-(furan-2-yl)-3-oxo-1-phenylpropyl) malonate 7o

A white powder; yield 97%, ee 89%; $[\alpha]_D^{20}$ = +27.4 (*c* 0.821, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (m, 1H, Ar), 7.25 (m, 4H, Ar), 7.14 (m, 2H, Ar), 6.47 (m, 1H, Ar), 5.07 (m, 1H, OCH), 4.78 (m, 1H, OCH), 4.13 (td, J_1 = 9.8 Hz, J_2 = 4.2 Hz, 1H, CH), 3.78 (d, J = 10.0 Hz, 1H, CH), 3.78 (d, J = 7.0 Hz, 2H, CH_2), 1.25 (d, J_1 = 6.3 Hz, J_2 = 2.4 Hz, 6H, CH_3), 1.04 (d, J = 6.2 Hz, 3H, CH_3), 0.97 (d, J = 6.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.76, 167.96, 167.30, 152.76, 146.36, 140.36, 128.50, 128.45, 127.24, 117.31, 112.30, 69.40, 68.98, 57.92, 42.89, 40.79, 21.80, 21.67, 21.45, 21.42; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 9.54 min, t_r (minor) = 13.87 min. HRMS (ESI) calcd for $C_{22}H_{26}O_6$ [M+H$^+$]: 387.1802, found: 387.1812.

4.7.14. Diisopropyl 2-(3-(thiophen-2-yl)-3-oxo-1-phenylpropyl) malonate 7p

A white powder; yield 95%, ee 82%; $[\alpha]_D^{20}$ = +14.4 (*c* 0.766, $CHCl_3$); ^1H NMR (4 00 MHz, $CDCl_3$): δ 7.73 (m, 1H, Ar), 7.57 (m, 1H, Ar), 7.25 (m, 4H, Ar), 7.17 (m, 1H, Ar), 7.08 (m, 1H, Ar), 5.07 (m, 1H, OCH), 4.78 (m, 1H, OCH), 4.12 (m, 1H, CH), 4.13 (d, J = 10.1 Hz, 1H, CH), 3.46 (dd, J_1 = 15.8 Hz, J_2 = 4.2 Hz, 1H, CH_2), 3.34 (dd, J_1 = 15.8 Hz, J_2 = 9.7 Hz, 1H, CH_2), 1.25 (d, J_1 = 6.3 Hz, J_2 = 1.8 Hz, 6H, CH_3), 1.04 (d, J = 6.3 Hz, 3H, CH_3), 0.97 (d, J = 6.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.66, 168.03, 167.30, 144.32, 140.21, 13376, 132.23, 128.48, 128.46, 128.19, 127.29, 69.46, 69.02, 57.81, 43.79, 41.29, 21.80, 21.67, 21.45, 21.41; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 9.90 min, t_r (minor) = 14.78 min. HRMS (ESI) calcd for $C_{22}H_{26}O_5S$ [M+H$^+$]: 403.1574, found: 403.1572.

4.7.15. 2-(5-Isopropoxy-4-(isopropoxycarbonyl)-5-oxo-3-phenylpentanoyl)pyridine 1-oxide 7q

A yellow powder; yield 65%, ee 40%; $[\alpha]_D^{20}$ = +13.2 (*c* 0.088, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (m, 1H, Ar), 724 (m, 8H, Ar), 5.07 (m, 1H, OCH), 4.74 (m, 1H, OCH), 4.09 (td, J_1 = 10.3 Hz, J_2 = 4.2 Hz, 1H; CH), 3.86 (dd, J_1 = 17.2 Hz, J_2 = 10.0 Hz, 1H, CH_2), 3.67 (d, J = 10.7 Hz, 1H, CH), 3.64 (dd, J_1 = 17.2 Hz, J_2 = 4.2 Hz, 1H, CH_2), 1.26 (dd, J_1 = 9.0 Hz, J_2 = 6.3 Hz, 6H, CH_3), 1.02 (d, J = 6.2 Hz, 3H, CH_3), 0.91 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.54, 167.70, 167.20, 146.76, 140.53, 140.36, 128.65, 128.33, 127.78, 127.14, 126.83, 125.40, 69.37, 68.83, 58.03, 47.37, 40.96, 21.79, 21.62, 21.42, 21.33; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 11.32 min, t_r (minor)v12.85 min. HRMS (ESI) calcd for $C_{23}H_{27}NO_6$ [M+H$^+$]: 414.1911, found: 414.1920.

4.7.16. Diisopropyl 2-(2-benzoyl-3-oxo-1,3-diphenylpropyl) malonate 7r

A white powder; yield 30%, ee 24%; $[\alpha]_D^{20}$ = +11.2 (*c* 0.102, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (m, 2H, Ar), 7.73 (m, 2H, Ar), 7.51 (m, 1H, Ar), 7.41 (m, 3H, Ar), 7.35 (m, 2H, Ar), 7.28 (m, 2H, Ar), 7.05 (m, 3H, Ar), 6.42 (d, J = 16.1 Hz, 1H, CH), 4.84 (m, 2H, OCH), 4.59 (t, J = 8.6 Hz, 1H, CH), 4.24 (d, J = 8.4 Hz, 1H, CH), 1.11 (d, J = 6.3 Hz, 3H, CH_3), 1.02 (dd, J_1 = 6.2 Hz, J_2 = 4.4 Hz, 6H; CH_3), 0.95 (d, J = 6.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.11, 194.83, 168.20, 168.01, 137.45, 137.13, 136.71, 133.65, 133.20, 130.36, 128.98, 128.95, 128.63, 128.59, 128.05, 127.38, 69.41, 69.09, 59.39, 55.23, 45.67, 21.53, 21.50, 21.41, 21.36; HPLC: Daicel column IA, 90% hexanes, 10% ^{i}PrOH, 1.0 mL/min, t_r (major) = 8.63 min, t_r (minor) = 10.93 min. HRMS (ESI) calcd for $C_{31}H_{32}O_6$ [M+H$^+$]: 501.2272, found: 501.2266.

Acknowledgments

We gratefully acknowledge financial supports from the National Natural Science Foundation of China (Grants 21372172, and 21572151), PAPD, and the Qing Lan Project.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetasy.2016.07.014.

References

1. (a) Miyazaki, T.; Maekawa, H.; Yonemura, K.; Yamamoto, Y.; Yamanaka, Y.; Nishiguchi, I. *Tetrahedron* **2011**, *67*, 1598; (b) Somaiah, S.; Sashikanth, S.; Raju, V.; Reddy, K. V. *Tetrahedron: Asymmetry* **2011**, *22*, 1; (c) Fang, H.; Wu, X.; Nie, L.; Dai, X.; Chen, J.; Cao, W.; Zhao, G. *Org. Lett.* **2010**, *12*, 5366; (d) Sun, Y.; Fan, R. *Chem. Commun.* **2010**, 6834; (e) Figueiredo, R. M.; Christmann, M. *Eur. J. Org. Chem.* **2007**, 2575.
2. (a) Halland, N.; Aburel, P. S.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 1272; (b) Wu, F.; Li, H.; Hong, R.; Deng, L. *Angew. Chem., Int. Ed.* **2006**, *45*, 947; (c) Wu, F.; Hong, R.; Khan, J.; Liu, X.; Deng, L. *Angew. Chem., Int. Ed.* **2006**, *45*, 4301; (d) Brandau, S.; Landa, A.; Franzn, J.; Marigo, M.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4305; (e) Marigo, M.; Bertelsen, S.; Landa, A.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 5475; (f) Carlone, A.; Marigo, M.; North, C.; Landa, A.; Jørgensen, K. A. *Chem. Commun.* **2006**, 4928; (g) Rigby, C. L.; Dixon, D. J. *Chem. Commun.* **2008**, 3798; (h) Palomo, C.; Oiarbide, M.; Lopez, R. *Chem. Soc. Rev.* **2009**, *38*, 632; (i) Tarí, S.; Chinchilla, R.; Nájera, C. *Tetrahedron: Asymmetry* **2009**, *20*, 2651; (j) Tarí, S.; Chinchilla, R.; Nájera, C. *Tetrahedron: Asymmetry* **2010**, *21*, 2872; (k) Sternativo, S.; Calandriello, A.; Costantino, F.; Testaferri, L.; Tiecco, M.; Marini, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 9382; (l) Duque, M. M.; Basle, O.; Isambert, N.; Gaudel-Siri, A.; Genisson, Y.; Plaquevent, J. C.; Rodriguez, J.; Constantieux, T. *Org. Lett.* **2011**, *13*, 3296; (m) Kang, Y. K.; Lee, H. J.; Moon, H. W.; Kim, D. Y. *RSC Adv.* **2013**, *3*, 1332; (n) Liu, S.; Tong, M.; Yu, Y.; Xie, H.; Li, H.; Wang, W. *Chem. Commun.* **2015**, 11221.
3. (a) Halland, N.; Aburel, P. S.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 661; (b) Knudsen, K. R.; Mitchell, C. E. T.; Ley, S. V. *Chem. Commun.* **2006**, 66; (c) Mao, Z.; Jia, Y.; Li, W.; Wang, R. *J. Org. Chem.* **2010**, *75*, 7428; (d) Fleischer, I.; Pfaltz, A. *Chem. Eur. J.* **2010**, *16*, 95; (e) Dudzinski, K.; Pakulska, A. M.; Kwiatkowski, P. *Org. Lett.* **2012**, *14*, 4222; (f) Maltsev, O. V.; Kucherenko, A. S.; Zlotin, S. G. *Eur. J. Org. Chem.* **2009**, 5134; (g) Li, P.; Wen, S.; Yu, F.; Liu, Q.; Li, W.; Wang, Y.; Liang, X.; Ye, J. *Org. Lett.* **2009**, *11*, 753; (h) Company_o, X.; Hejnov_a, M.; Kamlar, M.; Vesely, J.; Moyano, A.; Rios, R. *Tetrahedron Lett.* **2009**, *50*, 5021; (i) Riguet, E. *Tetrahedron Lett.* **2009**, *50*, 4283; (j) Ma, A.; Zhu, S.; Ma, D. *Tetrahedron Lett.* **2008**, *49*, 3075; (k) Waschkowski, V.; Knudsen, K. R.; Mitchell, C. E. T.; Ley, S. V. *Chem. Eur. J.* **2008**, *14*, 6155; (l) Andres, J. M.; Manzano, R.; Pedrosa, R. *Chem. Eur. J.* **2008**, *14*, 5116; (m) Yang, Y. Q.; Zhao, G. *Chem. Eur. J.* **2008**, *14*, 10888; (n) Palomo, C.; Landa, A.; Mielgo, A.; Oiarbide, M.; Puente, A.; Vera, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 8431; (o) Hirashima, S.; Sakai, T.; Nakashima, K.; Watanabe, N.; Koseki, Y.; Mukai, K.; Kanada, Y.; Tada, N.; Itoh, A.; Miura, T. *Tetrahedron Lett.* **2014**, *55*, 4334.
4. (a) Kim, D. Y.; Huh, S. C.; Kim, S. M. *Tetrahedron Lett.* **2001**, *42*, 6299; (b) Dere, R. T.; Pal, R. R.; Patil, P. S.; Salunkhe, M. M. *Tetrahedron Lett.* **2003**, *44*, 5351; (c) Wang, Z.; Wang, Q.; Zhang, Y.; Bao, W. *Tetrahedron Lett.* **2005**, *46*, 4657.
5. (a) Yoshida, M.; Narita, M.; Hara, S. *J. Org. Chem.* **2011**, *76*, 8513; (b) Yoshida, M.; Nagasawa, Y.; Kubara, A.; Hara, S.; Yamanaka, M. *Tetrahedron* **2013**, *69*, 10003.
6. Ooi, T.; Ohara, D.; Fukumoto, K.; Maruoka, K. *Org. Lett.* **2005**, *7*, 3195.
7. Wang, J.; Li, H.; Zu, L.; Jiang, W.; Xie, H.; Duan, W.; Wang, W. *J. Am. Chem. Soc.* **2006**, *128*, 12652.
8. (a) Chen, C.; Zhu, S. F.; Wu, X. Y.; Zhou, Q. L. *Tetrahedron: Asymmetry* **2006**, *17*, 2761; (b) Zhou, L.; Lin, L.; Wang, W.; Ji, J.; Liu, X.; Feng, X. *Chem. Commun.* **2010**, 3601; (c) Annamalai, V.; DiMauro, E. F.; Carroll, P. J.; Kozlowski, M. C. *J. Org. Chem.* **2003**, *68*, 1973; (d) Xu, Y.; Ohori, K.; Ohshima, T.; Shibasaki, M. *Tetrahedron* **2002**, *58*, 2585; (e) Kumaraswamy, G.; Sastry, M. N. V.; Jena, N. *Tetrahedron Lett.* **2001**, *42*, 8515; (f) End, N.; Macko, L.; Zehnder, M.; Pfaltz, A. *Chem. Eur. J.* **1998**, *4*, 818; (g) Nakajima, M.; Yamaguchi, Y.; Hashimoto, S. *Chem. Commun.* **2001**, 1596; (h) Naka, H.; Kanase, N.; Ueno, M.; Kondo, Y. *Chem. Eur. J.* **2008**, *14*, 5267; (i) Conquiere, D.; Feringa, B. L.; Roelfes, G. *Angew. Chem., Int. Ed.* **2007**, *46*, 9308; (j) Park, S. Y.; Morimoto, H.; Matsunaga, S.; Shibasaki, M. *Tetrahedron Lett.* **2007**, *48*, 2815; (k) Kantam, M. L.; Ranganath, K. V. S.; Mahendar, K.; Chakrapani, L.; Choudary, B. M. *Tetrahedron Lett.* **2007**, *48*, 7646; (l) Takita, R.; Ohshima, T.; Shibasaki, M. *Tetrahedron Lett.* **2002**, *43*, 4661; (m) Robinson, J. R.; Fan, X.; Yadav, J.; Carroll, P. J.; Wooten, A. J.; Pericàs, M. A.; Schelter, E. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2014**, *136*, 8034.
9. (a) Sasai, H.; Arai, T.; Satow, Y.; Houk, K. N.; Shibasaki, M. *J. Am. Chem. Soc.* **1995**, *117*, 6194; (b) Kim, Y. S.; Matsunaga, S.; Das, J.; Sekine, A.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 6506.
10. Agostinho, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2008**, *130*, 2430.
11. Chen, D.; Chen, Z.; Xiao, X.; Yang, Z.; Lin, L.; Liu, X.; Feng, X. *Chem. Eur. J.* **2009**, *15*, 6807.
12. Ray, S. K.; Singh, P. K.; Singh, V. K. *Org. Lett.* **2011**, *13*, 5812.
13. Lippur, K.; Kaabel, S.; Järving, I.; Rissanen, K.; Kanger, T. *J. Org. Chem.* **2015**, *76*, 8513.
14. Qian, Q.; Tan, Y.; Zhao, B.; Feng, T.; Shen, Q.; Yao, Y. *Org. Lett.* **2014**, *16*, 4516.
15. Zeng, C.; Yuan, D.; Zhao, B.; Yao, Y. *Org. Lett.* **2015**, *17*, 2242.