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Copper-catalyzed enantioselective conjugate addition of diethylzinc to acyclic enones with chiral sulfoxide–phosphine ligands

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ABSTRACT

The copper-catalyzed enantioselective conjugate addition of diethylzinc to acyclic enones was achieved with chiral sulfoxide–phosphine (SOP) ligands. This process showed good functional group tolerance and gave the 1, 4-adducts with excellent enantioselectivities (up to 96% ee).

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1. Introduction

The catalytic enantioselective conjugate addition of various organometallic reagents to α, β-unsaturated carbonyl compounds is one of the most widely used methods for asymmetric C–C bond formation in organic synthesis.[1] In the past decades the copper-catalyzed enantioselective addition of diethylzinc to enones has attracted great attention. A number of chiral auxiliaries and ligands have been reported and provided high enantioselectivities in this reaction.[2] Among those, phosphorus ligands have played a dominant role. The phosphates or phosphoramidites derived from BINOL,[3] TADDOL,[4] BIPOL[5] and SPINOL[6] were outstanding representations and have showed remarkable efficiency.[7] Nevertheless, in contrast to the excellent enantioselectivities (almost 100% ee) for diethylzinc addition to cyclic enones, highly enantioselective conjugate addition to acyclic enones are more challenging.[2–7]

In our group, we have developed a class of chiral sulfoxide–phosphine (SOP) ligands based on the stereogeometry and coordination properties of the *tert*-butylsulfinyl group, which can be synthesized concisely and showed excellent enantioselectivities and highly catalytic activities in a variety of asymmetric reactions.[8] However, the scope of developed reactions using such ligands was mainly limited in Pd-catalyzed asymmetric allylic alkylation and Rh-catalyzed conjugate addition of aryl boronic acids to cyclic enones.[9] Our group were focusing on exploring new reactions with this type ligands, and have found a series of Cu-catalyzed asymmetric reactions using the SOP ligands.[10] Herein, we reported the application of our chiral SOP ligands for the copper-catalyzed enantioselective conjugate addition of diethylzinc to acyclic enones.

2. Results and discussion

Initial investigation of the copper-catalyzed enantioselective conjugated addition was carried out between diethylzinc and chalcone (Table 1). Preliminary ligand screening was performed at different temperatures using $Cu(OTf)_2$ as the copper catalyst for its high performance in this reaction (Table 1, entries 1–6). As shown in entry 2, 99% conversion of substrate and 88% ee of 1, 4-adduct were obtained with ligand **2** after reacting in DCM at −30 °C for 24 h. Heightening or lowering the temperature decrease both the conversion and the enantioselectivity, and reaction almost cannot proceed at −78 °C. Other copper salts were inspected but didn't show better activity than $Cu(OTf)_2$, although both Cu(I) and Cu(II) salts produce good enantio-selectivities (Table 1, entry 7–10).

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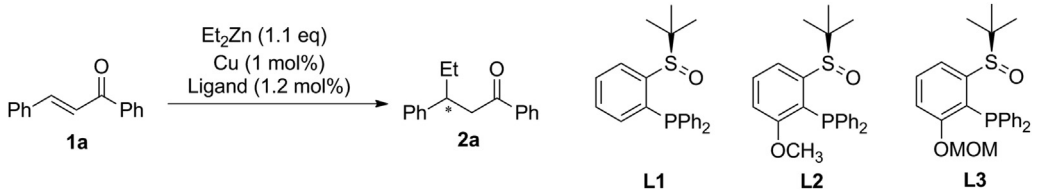
Table 1
Cu-catalyzed enantioselective conjugate addition of diethylzinc to chalcone[a]



Entry	Cu	Ligand	Solvent	T (oC)	Conv.[b] (%)	ee[c] (%)
1	$Cu(OTf)_2$	**L1**	DCM	−30	50	53
2	$Cu(OTf)_2$	**L2**	DCM	−30	99 (44)	88
3	$Cu(OTf)_2$	**L2**	DCM	0	51	62
4	$Cu(OTf)_2$	**L2**	DCM	−40	68	73
5	$Cu(OTf)_2$	**L2**	DCM	−78	Trace	–
6	$Cu(OTf)_2$	**L3**	DCM	−30	56	85
7	$Cu(OCOCF_3)_2 \cdot xH_2O$	**L2**	DCM	−30	90 (37)	84
8	$Cu(OTf)_2 \cdot C_6H_6$	**L2**	DCM	−30	99 (41)	88
9	CuTC	**L2**	DCM	−30	67 (30)	78
10	CuI	**L2**	DCM	−30	52 (20)	87
11	$Cu(OTf)_2$	**L2**	DCE	−30	99 (41)	93 (R)
12	$Cu(OTf)_2$	**L2**	Toluene	−30	56	69
13	$Cu(OTf)_2$	**L2**	EtOAc	−30	44	75
14	$Cu(OTf)_2$	**L2**	Et_2O	−30	99	85
15	$Cu(OTf)_2$	**L2**	MTBE	−30	95	85
16	$Cu(OTf)_2$	**L2**	DME	−30	31	58
17	$Cu(OTf)_2$	**L2**	THF	−30	35	7
18	$Cu(OTf)_2$	**L2**	Dioxane	−30	Trace	–

[a] Reaction conditions: **1a** (1 mmol), Et_2Zn (1.1 mmol, 1.0 M in hexane), copper catalyst (1 mol%), ligand (1.2 mol%) in 3 mL solvent stirring for 24 h.
[b] Isolated yield in parenthesis.
[c] Determined by HPLC analysis.

Solvent dependence was investigated subsequently (Table 1, entry 11–18). Comparing with polar solvents EtOAc, nonpolar solvent such as DCE has shown to be excellent solvent for high enantioselectivity. Acyclic ethers such as Et_2O and MTBE gave good enantioselectivities but cyclic ethers such as THF and dioxane gave poor results. Taking one with another, the catalyst system might be affected strongly by the coordination ability of the solvent.

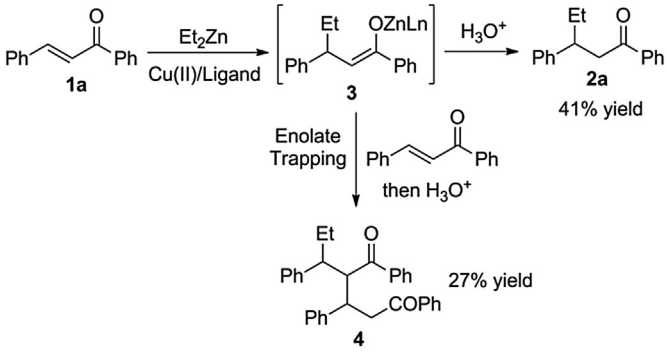
Using the conditions optimized above, the conjugate addition of Et_2Zn to various acyclic enones has been carried out to extend the range of substrates. The reactions of each substrate were examined in both DCM and DCE, and the better results were summarized in Table 2.[11] These two solvents were both proved to be favorable for this reaction since each of them was suitable for some substrates. Good functional group compatibility such as Me, OMe, F and Cl on each phenyl group of chalcone was demonstrated, affording the corresponding products with good to excellent enantioselectivities (Table 2, entry 1–5, 10–12). It was worth noting that the conjugate addition was also suitable for alkyl substrates such as benzylideneacetone derivatives (Table 2, entry 6–9). Benzylideneacetone seemed to be the most suitable substrate, the enantioselectivities of whose reaction in DCE was up to 96% (Table 2, entry 6).

We have noticed a confused but interesting fact in the substrates extension that the yields of these reactions were low in contrast with the high conversions. After investigation of the reaction mixture, we found that parts of the substrates proceeded intermolecular tandem conjugate/conjugate addition to form a dimer product. In the conjugate addition of Et_2Zn to enones, the intermediate Zn-enolates **3** were trapped by another enone molecule and activated another conjugate addition (Scheme 1). The dimer product **4** from chalcone was isolated in 27% yield and characterized.

Table 2
Cu-catalyzed enantioselective conjugate addition of diethylzinc to various acyclic enones[a]

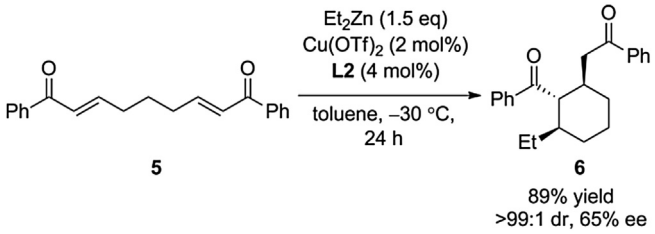
Entry	R_1	R_2	Solvent	Conv. (%)	Yield[b] (%)	ee[c] (%)
1	4-$CH_3OC_6H_4$	Ph (**1b**)	DCM	95	31 (**2b**)	92 (R)
2	4-$CH_3C_6H_4$	Ph (**1c**)	DCE	99	38 (**2c**)	84 (−)
3	2-$CH_3OC_6H_4$	Ph (**1d**)	DCE	99	80 (**2d**)	95 (+)
4	4-ClC_6H_4	Ph (**1e**)	DCM	58	18 (**2e**)	89 (R)
5	4-FC_6H_4	Ph (**1f**)	DCM	95	49 (**2f**)	93 (−)
6	Ph	Me (**1g**)	DCE	99	54 (**2g**)	96 (R)
7	Ph	Et (**1h**)	DCM	61	16 (**2h**)	92 (+)
8	4-$CH_3OC_6H_4$	Me (**1i**)	DCM	99	61 (**2i**)	95 (+)
9	4-ClC_6H_4	Me (**1j**)	DCM	99	59 (**2j**)	90 (+)
10	Ph	4-$MeOC_6H_4$ (**1k**)	DCE	80	10 (**2k**)	91 (+)
11	Ph	4-ClC_6H_4 (**1l**)	DCE	99	35 (**2l**)	78 (+)
12	Ph	4-BrC_6H_4 (**1m**)	DCE	99	35 (**2m**)	78 (+)

[a] Reaction conditions: **1** (1 mmol), Et_2Zn (1.1 mmol, 1.0 M in hexane), $Cu(OTf)_2$ (1 mol%), **L2** (1.2 mol%) in 3 mL solvent stirring for 24 h.
[b] Isolated yield.
[c] Determined by HPLC analysis.



Scheme 1. Intermolecular tandem conjugate addition/conjugate addition.

The property of this catalytic system inspired us to utilize it for construction of complex compounds with consecutive stereocenters through asymmetric tandem reactions. Catalytic asymmetric tandem transformations are an appealing strategy as it involves a multi-step transformation that enables a rapid increase in molecular complexity from readily available starting compounds.[12] In recent years, considerable efforts have been made to develop catalytic asymmetric tandem transformations initiated by conjugate additions.[13] We attempted the synthesis of cyclic compounds through intramolecular tandem conjugate addition/trapping cyclization reaction of compound **5**, which was only reported by Alexakis and co-workers.[14] As anticipated, high yield of cyclic product **6** was received with excellent diastereoselectivity and moderate enantioselectivity (Scheme 2).



Scheme 2. Asymmetric intramolecular tandem conjugate addition/trapping cyclization reaction.

3. Conclusions

In summary, we have demonstrated the Cu-catalyzed enantioselective conjugate addition of diethylzinc to acyclic enones using chiral sulfoxide–phosphine ligands. This process showed good functional group tolerance and gave the 1, 4-adducts with excellent enantioselectivities (up to 96% ee). A side-product resulted by tandem conjugate/conjugate addition was identified, and preliminary attempt to synthesize multi-chiral cyclic compounds was carried out. Further study of this reaction and its application are undertaking in our laboratory.

4. Experimental section

4.1. General experimental

All experiments were carried out under an argon atmosphere. All solvents were dried before use according to standard procedures. ^{1}H NMR and ^{13}C NMR spectra were acquired on a Bruker 400 spectrometer at 400 MHz and 100 MHz, respectively. Enantiomeric excess was determined by HPLC analysis on Chiralcel AD, OD or OJ column (Daicel Chemical Industries, LTD). Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Ligands **L1**–**3** were prepared by our previously reported method.[7] Compound **5** was prepared according to literature procedure.[14] All enones are known compounds.

4.2. General procedure for copper-catalyzed asymmetric conjugate addition

A mixture of $Cu(OTf)_2$ (3.6 mg, 0.01 mmol) and **L2** (4.8 mg, 0.012 mmol) in DCM or DCE (2 mL) was stirred at room temperature for 1 h under argon. The mixture was cooled to −30 °C and diethylzinc (1.1 mmol, 1.1 mL of 1.0 M solution in hexane) wad added dropwise. After stirring for 5 min at −30 °C the enone (1.0 mmol) in 1 mL solvent was added. The reaction was lasted at −30 °C for 24 h then quenched with saturated NH_4Cl aqueous solution. The mixture was extracted with diethyl ether. The combined organic layers were washed with $NaHCO_3$ and brine then dried over Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography. The enantiomeric excess of the product was determined by chiral HPLC.

4.3. Procedure for copper-catalyzed asymmetric tandem conjugate addition/trapping cyclization reaction

A mixture of $Cu(OTf)_2$ (7.2 mg, 0.02 mmol) and **L2** (15.9 mg, 0.04 mmol) in 2 mL CH_2Cl_2 were added to a Schlenk tube under argon. After stirring at room temperature for 1 h, the solvent was removed in vacuo and 2 mL toluene was added. After stirring for 5 min, the solution was cooled to −30 °C, and 1.5 mmol diethylzinc (1.0 M solution in hexane) was added dropwise. Then the enone (1.0 mmol) in 1 mL toluene was added. After 24 h, the reaction was quenched with saturated NH_4Cl aqueous solution. The reaction mixture was treated just as the methods mentioned above in the copper-catalyzed asymmetric conjugate addition. The enantiomeric excess of the cyclic product was determined by chiral HPLC.

4.4. Spectral characterization and analytical data of compounds 2, 4 and 6

*4.4.1. 1,3-Diphenyl-1-pentanone (**2a**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J=7.60 Hz 2H), 7.55–7.51 (m, 1H), 7.44–7.40 (m, 2H), 7.31–7.25 (m, 2H), 7.24–7.16 (m, 3H), 3.31–3.22 (m, 3H), 1.83–1.75 (m, 1H), 1.66–1.54 (m, 1H), 0.80 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 144.7, 137.3, 132.9, 128.5, 128.4, 128.1, 127.7, 126.3, 45.6, 43.0, 29.2, 12.1; HRMS-ESI (m/z): calcd for $C_{17}H_{18}O$ ($M+Na^+$): 260.1250, found 260.1246. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=5.74 min (S), 6.89 min (R).

*4.4.2. 3-(4-Methoxyphenyl)-1-phenyl-pentanone (**2b**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.88 (m, 2H),7.55–7.50 (m, 1H), 7.44–7.40 (m, 2H), 7.15–7.12 (m, 2H), 6.84–6.81 (m, 2H), 3.77 (s, 3H), 3.25–3.21 (m, 3H), 1.80–1.72 (m, 1H), 1.66–1.54 (m, 1H), 0.80 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 158.0, 137.3, 136.7, 128.9, 128.5, 128.4, 128.0, 113.8, 55.2, 45.9, 42.3, 29.4, 12.1; HRMS-ESI (m/z): calcd for $C_{18}H_{20}O_2$ ($M+Na^+$): 291.1356, found 291.1356. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=7.76 min (S), 10.96 min (R).

*4.4.3. 3-(4-Methylphenyl)-1-phenyl-pentanone (**2c**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91–7.89 (m, 2H),7.55–7.51 (m, 1H), 7.42–7.40 (m, 2H), 7.13–7.08 (m, 4H), 3.25–3.18 (m, 3H), 2.30 (s, 3H), 1.80–1.72 (m, 1H), 1.65–1.57 (m, 1H), 0.80 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 141.6, 137.3, 135.7, 132.9, 129.1, 128.5, 128.1, 127.5, 45.7, 42.6, 29.2, 21.0, 12.1; HRMS-ESI (m/z): calcd for $C_{18}H_{20}O$ ($M+Na^+$): 275.1406, found 275.1411. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=5.44 min, 7.05 min (major).

*4.4.4. 3-(2-Methoxyphenyl)-1-phenyl-pentanone (**2d**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.92 (m, 2H),7.54–7.49 (m, 1H), 7.44–7.39 (m, 2H), 7.19–7.14 (m, 2H), 6.92–6.88 (m, 1H), 6.85–6.82 (m, 1H), 3.77 (s, 3H), 3.67–3.60 (m, 1H), 3.33–3.27 (m, 1H), 3.23–3.16 (m, 1H), 1.79–1.68 (m, 2H), 0.80 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 157.5, 132.7, 128.4, 128.2, 128.1, 127.1, 120.6, 110.7, 55.3, 44.6, 37.1, 27.3, 12.1; HRMS-ESI (m/z): calcd for $C_{18}H_{20}O_2$ ($M+Na^+$): 291.1356, found 291.1352. The enantiomeric excess was

determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=6.03 min, 7.13 min (major).

*4.4.5. 3-(4-Chlorophenyl)-1-phenyl-pentanone (**2e**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J=7.4 Hz 2H), 7.56–7.51 (m, 1H), 7.45–7.40 (m, 2H), 7.26–7.23 (m, 2H), 7.17–7.14 (m, 2H), 3.26–3.20 (m, 3H),1.82–1.73 (m, 1H), 1.65–1.58 (m, 1H), 0.80 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 143.2, 137.2, 133.0, 131.9, 129.0, 128.6, 128.5, 128.0, 45.4, 42.4, 29.3, 12.0; HRMS-ESI (m/z): calcd for $C_{17}H_{17}ClO$ (M+Na^+): 295.0860, found 295.0854. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=5.94 min (S), 8.08 min (R).

*4.4.6. 3-(4-Fluorophenyl)-1-phenyl-pentanone (**2f**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.87 (m, 2H),7.56–7.51 (m, 1H), 7.45–7.41 (m, 2H), 7.20–7.15 (m, 2H), 6.99–6.93 (m, 2H), 3.28–3.20 (m, 3H),1.81–1.74 (m, 1H), 1.63–1.60 (m, 1H), 0.80 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 161.4 (J=242.3 Hz), 140.3 (J=3.2 Hz), 137.2, 133.0, 129.0 (J=7.7 Hz), 128.7, 128.0, 115.2 (J=20.9 Hz), 45.7, 42.3, 29.4, 12.0; HRMS-ESI (m/z): calcd for $C_{17}H_{17}FO$ (M+Na^+): 279.1156, found 279.1156. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=6.18 min, 7.79 min (major).

*4.4.7. 4-Phenyl-2-hexanone (**2g**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.28 (m, 3H), 7.23–7.19 (m, 2H), 3.09–3.02 (m, 1H), 2.75 (d, J=7.1 Hz, 2H), 2.04 (s, 3H), 1.74–1.55 (m, 2H), 0.80 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1, 144.3, 128.5, 127.6, 126.4, 50.6, 43.0, 30.7, 29.4, 12.0; HRMS-ESI (m/z): calcd for $C_{12}H_{16}O$ (M+Na^+): 199.1093, found 199.1094. The enantiomeric excess was determined by HPLC (Chiralcel OJ-H, hexane/2-propanol=95/5, 0.8 mL/min, 254 nm). T_R=10.75 min (S), 11.94 min (R).

*4.4.8. 5-Phenyl-3-heptanone (**2h**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.29 (m, 3H), 7.20–7.18 (m, 2H), 3.11–3.03 (m, 1H), 2.73–2.71 (m, 2H), 2.40–2.19 (m, 2H), 1.73–1.55 (m, 2H), 0.97 (t, J=7.3 Hz, 3H), 0.80 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.7, 144.5, 128.4, 127.6, 126.3, 49.4, 43.0, 36.7, 29.3, 12.0, 7.6; HRMS-ESI (m/z): calcd for $C_{13}H_{18}O$ (M+Na^+): 213.1250, found213.1251. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=5.75 min (major), 6.57 min.

*4.4.9. 4-(4-Methoxyphenyl)-2-hexanone (**2i**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12–7.10 (m, 2H), 6.86–6.84 (m, 2H), 3.80 (s, 3H), 3.03–2.96 (m, 1H), 2.72–2.70 (m, 2H), 2.03 (s, 3H), 1.69–1.63 (m, 1H), 1.58–1.50 (m, 1H), 0.80 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 158.0, 136.3, 128.4, 113.8, 55.2, 50.8, 42.3, 30.7, 29.5, 12.0; HRMS-ESI (m/z): calcd for $C_{13}H_{18}O_2$ (M+Na^+): 229.1199, found 229.1194. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=6.05 min (major), 6.60 min.

*4.4.10. 4-(4-Chlorophenyl)-2-hexanone (**2j**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.15–7.10 (m, 2H), 3.07–3.02 (m, 1H), 2.74–2.71 (m, 2H), 2.05 (s, 3H), 1.71–1.54 (m, 2H), 0.79 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 142.8, 131.9, 128.9, 128.6, 50.4, 42.2, 30.7, 29.3, 11.9; HRMS-ESI (m/z): calcd for $C_{12}H_{15}ClO$ (M+Na^+): 233.0704, found 233.0709. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=5.13 min (major), 5.50 min.

*4.4.11. 1-(4-Methoxyphenyl)-3-phenyl-1-pentanone (**2k**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.88 (m, 2H), 7.26–7.15 (m, 5H), 6.90–9.88 (m, 2H), 3.85 (s, 3H), 3.24–3.17 (m, 3H), 1.80–1.73 (m, 1H), 1.67–1.58 (m, 1H), 0.79 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 163.4, 144.8, 130.4, 130.3, 128.4, 127.7, 126.2, 113.7, 55.5, 45.3, 43.2, 29.2, 12.1; HRMS-ESI (m/z): calcd for $C_{18}H_{20}O_2$ (M+Na^+): 291.1356, found 291.1352. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=12.89 min, 20.21 min (major).

*4.4.12. 1-(4-Chlorophenyl)-3-phenyl-1-pentanone (**2l**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.80 (m, 2H), 7.40–7.37 (m, 2H), 7.30–7.25 (m, 2H), 7.22–7.15 (m, 3H), 3.27–3.17 (m, 3H), 1.81–1.73 (m, 1H), 1.68–1.60 (m, 1H), 0.80 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0, 144.4, 139.3, 135.6, 129.5, 128.8, 128.5, 127.6, 45.6, 43.1, 29.2, 12.1; HRMS-ESI (m/z): calcd for $C_{17}H_{17}ClO$ (M+Na^+): 295.0860, found 295.0850. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=7.03 min, 8.74 min (major).

*4.4.13. 1-(4-Bromophenyl)-3-phenyl-1-pentanone (**2m**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.73 (m, 2H), 7.57–7.54 (m, 2H), 7.30–7.25 (m, 2H), 7.22–7.15 (m, 3H), 3.26–3.17 (m, 3H), 1.81–1.74 (m, 1H), 1.68–1.60 (m, 1H), 0.81 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 144.4, 136.0, 131.8, 129.6, 128.5, 128.1, 127.6, 126.4, 45.6, 43.1, 29.2, 12.1; HRMS-ESI (m/z): calcd for $C_{17}H_{17}BrO$ (M+Na^+): 339.0355, found 339.0350. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=7.56 min, 9.38 min (major);

*4.4.14. 1,3,5-Triphenyl-2-(1-phenylpropyl)pentane-1,5-dione (**4**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76–7.73 (m, 2H), 7.65–7.62 (m, 2H), 7.47–7.35 (m, 1H), 7.35–7.26 (m, 10H), 7.09–7.07 (m, 3H), 6.92–6.90 (m, 2H), 4.54–4.49 (m, 1H), 3.81–3.79 (m, 1H), 3.32–3.24 (m, 1H), 3.14–3.12 (m, 1H), 3.08–3.00 (m, 1H), 1.69–1.65 (m, 1H), 1.56–1.52 (m, 1H), 0.61 (t, J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.5, 198.6, 142.2, 141.0, 139.8, 136.8, 132.8, 132.5, 129.0, 128.4, 128.33, 128.31, 127.9, 127.7, 126.5, 54.2, 48.5, 42.5, 41.6, 27.1, 11.9; HRMS-ESI (m/z): calcd for $C_{32}H_{30}O_2$ (M+Na^+): 469.2138, found 469.2139.

*4.4.15. 2-(2-Benzoyl-3-ethylcyclohexyl)-1-phenylethanone (**6**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05–8.01 (m, 2H), 7.78–7.77 (m, 2H), 7.57–7.26 (m, 6H), 3.19 (t, J=5.1 Hz, 1H), 2.89–2.85 (q, 1H), 2.48–2.44 (m, 2H), 1.79–1.74 (m, 1H), 1.73–1.62 (m, 3H), 1.27–1.22 (m, 4H), 1.05–0.99 (m, 2H), 0.77 (t, J=7.4 Hz, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 199.4, 139.4, 136.8, 133.3, 132.9, 128.8, 128.6, 128.2, 128.1, 44.2, 43.3, 38.8, 31.7, 30.5, 29.7, 27.7, 25.2, 11.2; HRMS-ESI (m/z): calcd for $C_{23}H_{26}O_2$ (M+Na^+): 357.1825, found 357.1815. The enantiomeric excess was determined by HPLC (Chiralpak AD-H, hexane/2-propanol=95/5, 1.0 mL/min, 254 nm). T_R=9.80 min (major), 10.53 min.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.12.062.

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