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Asymmetric α-alkylation of cyclic β-keto esters and β-keto amides by phase-transfer catalysis†

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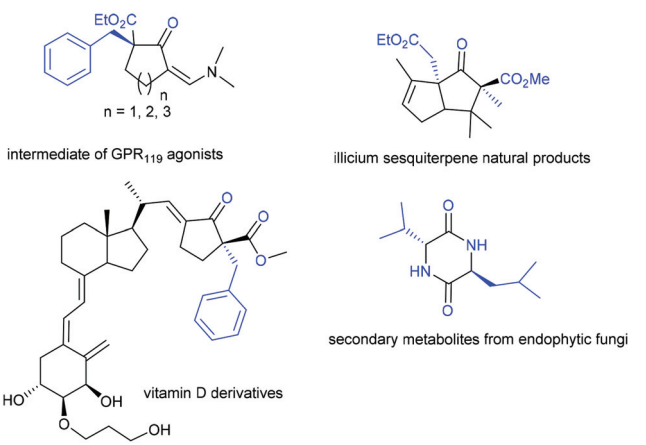
Without employing any transition metal, a highly enantioselective α-alkylation of cyclic β-keto esters and β-keto amides has been realized by phase-transfer catalysis. This improved procedure is applicable to different kinds of halides with cinchona derivatives and gives the corresponding products in excellent enantiopurities (up to 98% ee) and good yields (up to 98%). Moreover, the reaction was scalable and the phase-transfer catalyst was recyclable. This provided an alternative and competitive method to the asymmetric α-alkylation of β-dicarbonyl compounds.

Introduction

Enantioselective construction of quaternary carbon centers represents a challenging and demanding area in asymmetric catalysis.[1] Furthermore, β-dicarbonyl compounds have become interesting substrates because they had various opportunities for further structural manipulation, especially for the asymmetric process.[2] Optically active α-alkylated β-dicarbonyl moieties are common structural motifs in a wide range of natural products and pharmaceuticals, such as the tricyclic pyrazolopyrimidines (potent and selective GPR119 agonists),[3] the methylvitamin D derivatives,[4] the illicium sesquiterpene natural products,[5] and the secondary metabolites from endophytic fungi[6] (Scheme 1). Moreover, the structural motifs provided a reliable route for the asymmetric synthesis of β-amino acid derivatives and other useful building blocks.[2b,7] Thus, the development of green and highly enantioselective α-alkylation of β-dicarbonyl compounds with a broad substrate scope is necessary and meaningful. Until now, the enantioselective alkylation of α-substituted β-keto esters has been realized by palladium catalysis[8] and enamine catalysis.[9] On the other hand, asymmetric phase-transfer catalysis could provide a simple and efficient solution to this problem, because it is far from being an effective and sustainable method.[10] In 1998, Manabe synthesized a novel phosphonium salt and applied it to the asymmetric phase-transfer alkylation of β-keto esters, and the corresponding products were obtained with up to 50% ee.[11] The binaphthalene-derived quaternary ammonium salt developed by Maruoka has been demonstrated as an efficient catalyst for the alkylation of cyclic β-keto esters with *tert*-butoxy groups.[12] However, the use of cinchona alkaloid-derived ammonium salts as phase-transfer organocatalysts has been limited. In 2002, Dehmlow and co-workers used the cinchona-derived ammonium salts for the alkylation of 2-oxocyclopentanecarboxylate, achieving the enantioselectivities in the range of 7–52%.[13] Then Kim and co-workers developed a bulkier catalyst that improved the selectivity. All of the corresponding β-keto esters were isolated with moderate enantioselectivities (44–84% ee) for all cases except when *p*-nitrobenzyl bromide



Scheme 1 Some examples of α-alkylated β-dicarbonyl compounds as key structures of natural products or as synthetic intermediates.

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was employed as the alkylating reagent (65–99% ee).[14] In 2011, Chinchilla developed dimeric cinchona ammonium salts as the PTC for the enantioselective alkylation of 2-alkoxy carbonyl-1-indanones with activated bromides with high yields and moderate ee values (up to 55%).[15] Although successful catalytic systems have been reported, a highly efficient method for the α-alkylation of β-dicarbonyl compounds with high enantioselectivities for a broad scope of substrates remains to be developed.

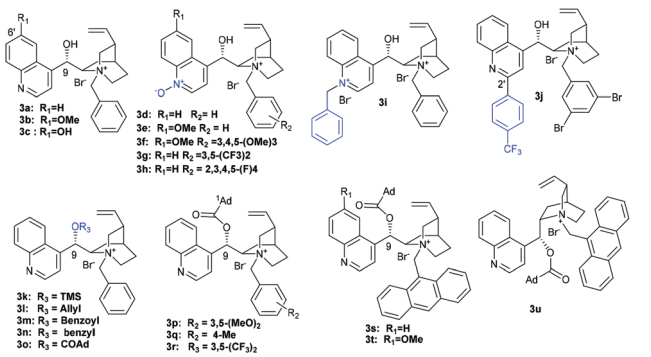
Considering our interest in the development of the efficient and practical enantioselective α-functionalization of β-dicarbonyl compounds by phase-transfer catalysis,[16] our initial work focused on the structural modification of the cinchona alkaloids and a series of phase-transfer catalysts (PTC) derived from cinchonine and quinidine were screened. First, the simplest PTC **3a** provided **2a** with 51% ee after 24 hours (Table 1, entry 1). PTC **3b**, with a methoxyl group at the C-6′ position, led to a slightly lower enantioselectivity (Table 1, entry 2). PTC **3c**, which has hydroxy groups at both the C-9 and C-6′ positions, showed poor results (Table 1, entry 3). The *N*-oxide PTC **3d** and **3f** were tested, and the reactions proceeded faster (80–85% yield, 12 h) with higher enantioselectivities (51–54% ee) (Table 1, entries 4 and 5). A series of *N*-oxide PTC derived from cinchona alkaloids were then screened.[16e,g] PTC **3f** and **3g** did not reveal good results (Table 1, entries 6 and 7). Interestingly, 2,3,4,5-$(F)_4$ groups in the benzyl position showed higher ee values (61%) compared with the 3,5-$(CF_3)_2$ groups, and the configuration of **2b** was inverted (Table 1, entry 8). These findings indicated that the electron cloud density of the benzyl groups at the bridgehead nitrogen atom had a significant influence on the reactivity and enantioselectivity. The doubly quaternized PTC **3i**[17] and the C-2′-arylated phase-transfer catalysts PTC **3j** were also tested,[16d,18] but the enantioselectivities of **2a** were not noticeably improved (Table 1, entries 9 and 10). In further studies, we discovered that the most important functional group for achieving a high ee value and yield was not only the benzyl group at the bridgehead nitrogen atom, but also the chiral secondary alcohol moiety at the C-9 position of the alkaloid (Scheme 2). The catalysts with 9-OH protected trimethylsilyl (**3k**), benzoyl (**3m**), and benzyl (**3n**) groups gave **2a** in high yields, but with low enantioselectivities (Table 1, entries 11, 13 and 14). Notably, an obvious improvement of enantioselectivity had been achieved by protecting the 9-OH by the allyl group (Table 1, entry 12). To our delight, the catalyst **3o** which the C-9 hydroxy protected by a bulky 1-adamantyl group afforded **2a** with a higher enantioselectivity (66% ee). Compared with other protecting groups, the 1-adamantyl group was expected to provide greater configurational rigidity. Both the catalysts **3p** and **3q** gave high yields and increased ee values (Table 1, entries 16 and 17). PTC **3r**, with electron-withdrawing groups ($-CF_3$) at the 3 and 5 positions, showed lower enantioselectivity (53% ee). Moreover, we found that the ee value was improved to 93% by introducing a 9-anthracenylmethyl group[19] (Table 1, entry 19). The quinidine-derived PTC **3t** resulted in the corresponding product **2a** in 93% yield and 92% ee (Table 1, entry 19). Notably, the cinchonidine-derived PTC **3u** afforded high reactivity and selectivity (94% yield, 81% ee) and provided the expected *R*-product (Table 1, entry 21).

After PTC **3s** had been identified as a suitable catalyst, further reaction optimizations were undertaken. Table 2 summarizes the effects of several parameters on this reaction. First, we screened several bases in toluene in the presence of PTC **3s** (Table 2, entries 1–9). The use of aq. 10% KOH, aq. 30% Cs_2CO_3 and aq. 10% CsOH provided faster reaction rates,

Table 1 Screening of cinchona alkaloid derivatives for α-alkylation of β-keto ester **1a**[a]

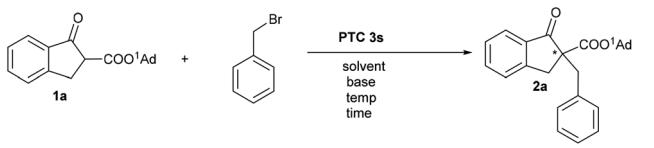
Entry	Cat.	*t* [h]	Yield[b] [%]	ee[c] [%]
1	**3a**	24	65	51 (*S*)
2	**3b**	24	78	47 (*S*)
3	**3c**	24	51	25 (*S*)
4	**3d**	12	80	54 (*S*)
5	**3e**	12	85	51 (*S*)
6	**3f**	12	95	42 (*S*)
7	**3g**	24	51	13 (*S*)
8	**3h**	24	76	61 (*R*)
9	**3i**	24	91	56 (*S*)
10	**3j**	12	92	54 (*S*)
11	**3k**	12	89	11(*S*)
12	**3l**	12	93	61(*S*)
13	**3m**	12	87	52 (*S*)
14	**3n**	12	91	39 (*S*)
15	**3o**	12	92	66 (*S*)
16	**3p**	12	95	72 (*S*)
17	**3q**	12	91	69 (*S*)
18	**3r**	12	76	53 (*S*)
19	**3s**	12	96	93 (*S*)
20	**3t**	12	93	92 (*S*)
21	**3u**	12	94	81 (*R*)

[a] The reactions were performed with **1a** (0.1 mmol), benzyl bromide (0.13 mmol), catalyst (0.005 mmol), and 30% K_2CO_3 (0.5 mL) in toluene (4 mL) at room temperature. [b] Yields shown are of isolated products. [c] Determined by chiral HPLC (Chiralcel AD-H).



Scheme 2 Quaternary ammonium salts employed for the α-alkylation of β-keto ester **1a**.

Table 2 Optimization of the reaction conditions for the α-alkylation of β-keto ester **1a** with PTC **3s**[a]



Entry	Solvent	Base	T [°C]	t [h]	Yield[b] [%]	ee[c] [%]
1	$PhCH_3$	10% KOH	25	3	95	86
2	$PhCH_3$	30% Cs_2CO_3	25	6	93	91
3	$PhCH_3$	10% CsOH	25	6	95	92
4	$PhCH_3$	30% K_2CO_3	25	6	94	93
5	$PhCH_3$	50%K_2HPO_4	25	12	85	89
6[d]	$PhCH_3$	iPr_2EtN	25	24	Trace	ND
7[d]	$PhCH_3$	K_2CO_3	25	6	95	90
8[d]	$PhCH_3$	KOH	25	2	94	89
9	$CHCl_3$	30% K_2CO_3	25	12	78	67
10	$PhCH_3/CHCl_3$ (7/3)	30% K_2CO_3	25	12	95	92
11	$PhCF_3$	30% K_2CO_3	25	12	97	85
12	Et_2O	30% K_2CO_3	25	6	98	<5
13	DMF	30% K_2CO_3	25	24	67	25
14	THF	30% K_2CO_3	25	24	87	67
15	$PhCH_3$	30% K_2CO_3	0	18	98 (**97**)[e]	97 (**98**)[e]
16	$PhCH_3$	30% K_2CO_3	−10	24	85	96

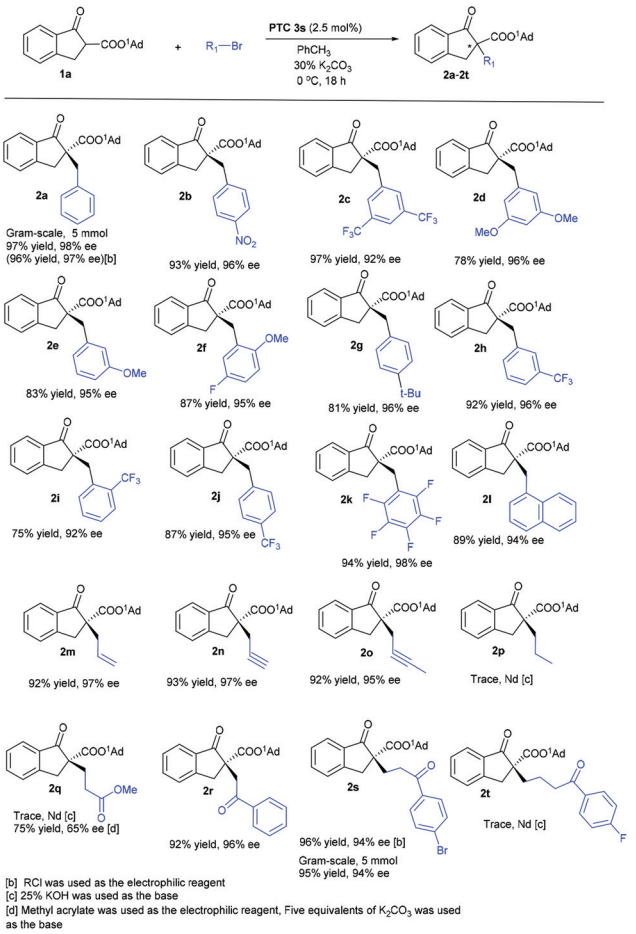
[a] Unless otherwise specified, the reactions were performed with **1a** (0.1 mmol), benzyl bromide (0.13 mmol), PTC **3s** (0.005 mmol), and base (0.2 mL) in solvent (5 mL). [b] Yields shown are of isolated products. [c] Determined by chiral HPLC (Chiralcel AD-H). [d] 3 equivalents of the base. [e] The reactions were performed with **1a** (0.2 mmol), benzyl bromide (0.26 mmol), PTC **3s** (0.005 mmol), and 30% K_2CO_3 (0.5 mL) in toluene (5 mL).

but the enantioselectivities were lower than those achieved with aq. 30% K_2CO_3 (Table 2, entries 1–4). The weaker base aq. 50% K_2HPO_4 provided lower yield and enantioselectivity (Table 2, entry 5). The organic base $^iPr_2EtN$ was also tested, but only a trace amount of **2a** was formed (Table 2, entry 6). Solid inorganic bases (KOH and K_2CO_3) can accelerate the reaction rate, but the enantioselectivities were unsatisfactory (Table 2, entries 7 and 8). Next we screened the effect of the solvent. $CHCl_3$ afforded poor results (78% yield, 67% ee) after 12 h, but the ee value was improved to 92% when $PhMe/CHCl_3$ = 7 : 3 was used as the component solvent (Table 2, entries 9 and 10). Using $PhCF_3$ as the solvent resulted in excellent yield (97%), but the enantioselectivity was decreased (Table 2, entry 11). High polar solvents (Et_2O, THF and DMSO) were also tested, but the results were poor (Table 2, entries 12–14). It is worth mentioning that the enantioselectivity was improved to 97% when the reaction temperature was decreased to 0 °C. Then the enantioselectivity of the reaction could be increased to 98% ee by enhancing the substrate concentration from 0.02 M to 0.04 M and the loading of catalyst **3s** could be reduced to 2.5 mol% (Table 2, entry 15). Finally we reduced the temperature to −10 °C, but the enantioselectivity of **2a** was not improved (Table 2, entry 16).

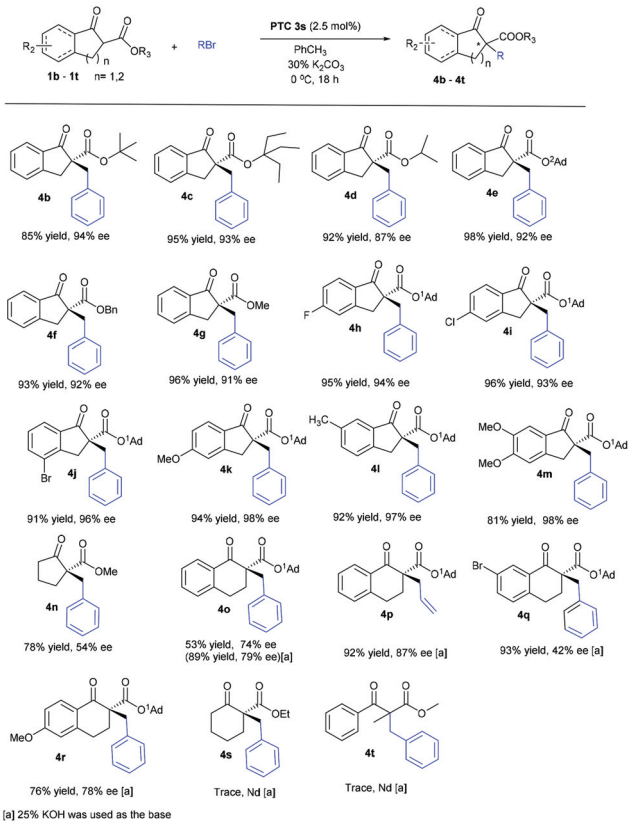
With the optimized conditions in hand, we next explored the substrate scope to demonstrate the generality in this asymmetric α-alkylation. First, we investigated the influence of the electrophiles. Benzyl chloride can also react with **1a** and provide **2a** with 96% yield and 97% ee. A thoughtful study incorporating substituents at *ortho*, *para* and *meta* positions (both electron-donating or electron-withdrawing) had been carried out. Benzyl bromides with a variety of substituents on the aromatic rings, such as nitro, trifluoromethyl, methoxyl, *tert*-butyl, and fluorine groups, were nicely converted into the corresponding products **2b–2k** in good yields (75–97%) with 92–98% ee. 1-(Bromomethyl)naphthalene, allyl bromide and propargyl bromide were proved to be excellent electrophiles for this reaction. Moreover, the substituted propargyl derivatives can react with **1a** and the product **2o** was obtained with good enantioselectivity (95%). However, bromopropane could not react with **1a** even when 25% KOH was used as the base. Interestingly, when methyl acrylate was introduced, the Michael adduct **2q** was obtained in 75% yield with 65% ee. Further research has found that phenacyl bromide was a good electrophile, and the α-alkylated product **2r** was obtained with 92% yield and 96% ee. To our knowledge, this type of chiral product could be only achieved by α-photoalkylation through enamine catalysis.[9a,d] The β-haloketone was also tested and it showed promising results. Unfortunately, the γ-haloketone did not perform well and **2t** was not obtained even when aq. 25% KOH was used. After all, various halides can act as the electrophiles, showing promising results (Scheme 3).

Next, we investigated the influence of the β-keto esters. First, we tested the steric influence of the ester group. Tertiary and secondary alcohol derived β-keto esters **1b–1e** gave excellent enantioselectivities (87–94% ee). To our delight, methyl ester **1g** with small steric hindrance afforded the corresponding product **4j** with 91% ee and 96% yield. A series of 1-indanone-derived adamantyl β-keto esters were then investigated. A variety of substrates with substituents on the aromatic rings, such as Cl, F, Br, methyl and methoxy groups, were nicely converted into the corresponding products (**4h–4m**) in good yields (81–96%) with 93–98% ee. The cyclopentanone derived β-keto ester **1n** appeared to be a candidate for this alkylation, but the enantioselectivity was moderate. β-Keto esters **1o–1r** derived from 1-tetralone were then examined. A stronger base (25% KOH) was needed to promote reactions and the corresponding products **4o–4r** were obtained in 76–93% yield with 42–87% ee. Unfortunately, **4s** and **4t** could not be obtained even when 25% KOH was used. Ultimately, these results showed a significant improvement in the enantioselectivities and substrate scopes for the phase-transfer catalyzed asymmetric α-alkylation of β-keto esters[12–15] (Scheme 4).

Compared with the β-keto esters, β-keto amides are still challenging substrates, possibly due to the lower acidity of the α-hydrogen.[20] There are no examples for the asymmetric α-alkylation of β-keto amides by phase transfer catalysis as far as we know. Thus, after investigation of the β-keto esters, the α-alkylation of β-keto amide **5a** was examined. To our delight, the simple phase transfer catalyst **3a** provided **6a** with 74% ee in toluene (Table 3, entry 1). The stronger bases (30% Cs_2CO_3 and 10% KOH) could accelerate the reaction and improve the



Scheme 3 Substrate scope of the α-alkylation for different electrophiles. Reaction conditions (unless otherwise specified): The reactions were performed with **1** (0.2 mmol), halohydrocarbon (0.26 mmol), PTC **3s** (0.005 mmol), and 30% K_2CO_3 (0.5 mL) in toluene (5 mL) at 0 °C for 18 h.

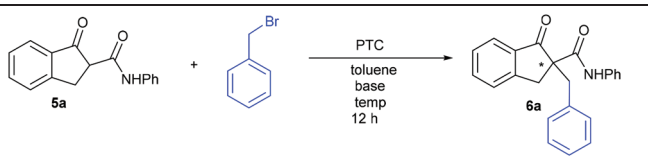


Scheme 4 Substrate scope of the α-alkylation for different β-keto esters. Reaction conditions (unless otherwise specified): The reactions were performed with β-keto ester (0.2 mmol), benzyl bromide (0.26 mmol), PTC **3s** (0.005 mmol), and 30% K_2CO_3 (0.5 mL) in toluene (5 mL) at 0 °C for 18 h.

enantioselectivities (Table 3, entries 2 and 3). However, other types of catalysts such as **3d**, **3i**, **3j**, and **3s** afforded poor ee values, although the yields of the products were excellent (Table 3, entries 5–8). These results showed that the enantioselectivity of the product **6a** was hypersensitive for the unique structural characteristics of the phase transfer catalysts. Further studies showed that the ee value could be improved to 87% when the reaction temperature was decreased to 0 °C (Table 3, entry 9). The use of a solid inorganic base KOH can accelerate the reaction rate, and the enantioselectivity was slightly decreased (Table 3, entry 11).

Under the standard conditions, the scope of β-keto amides was examined. **5a** was nicely converted into **6a** in 93% yield with 87% ee. However, when 3,5-trifluoromethyl benzyl bromide was used, the ee value of **6b** was decreased to 57%. 3,5-Methoxyl benzyl bromide could not participate in this reaction. **5d** with methyl and phenyl in the *N*-position afforded **6d** in 78% yield with 58% ee. Compound **5e**, with 4-*tert*-butylphenyl in the *N*-position, afforded **6e** with 26% ee. **5f**, which bears

Table 3 Optimization of the reaction conditions for the α-alkylation of β-keto amide **5a** [a]



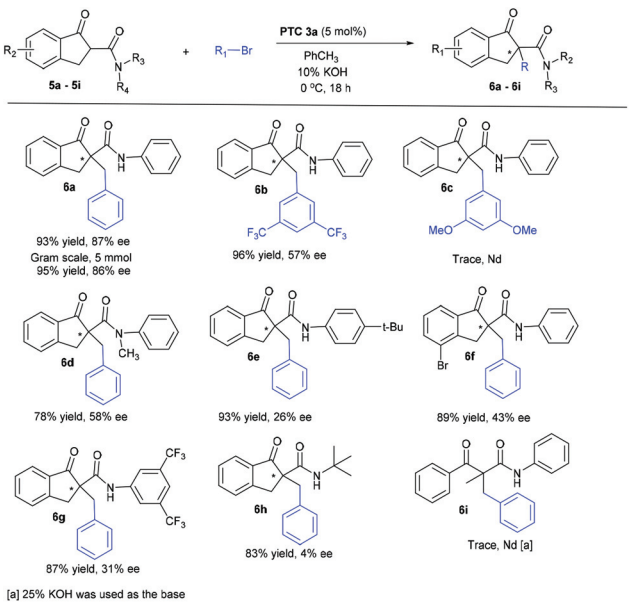
Entry	Cat.	Base	T [°C]	Yield[b] [%]	ee[c] [%]
1	**3a**	30% K_2CO_3	25	56	74
2	**3a**	30% Cs_2CO_3	25	89	76
3	**3a**	10% KOH	25	97	78
4	**3b**	10% KOH	25	87	65
5	**3d**	10% KOH	25	89	23
6	**3i**	10% KOH	25	76	15
7	**3j**	10% KOH	25	93	27
8	**3s**	10% KOH	25	96	34
9[d]	**3a**	10% KOH	0	93	87
10[d]	**3a**	10% KOH	−10	78	86
11	**3a**	KOH[e]	0	96	85

[a] Unless otherwise specified, the reactions were performed with **5a** (0.1 mmol), benzyl bromide (0.13 mmol), PTC (0.005 mmol), and base (0.5 mL) in solvent (5 mL). [b] Yields shown are of isolated products. [c] Determined by chiral HPLC (Chiralcel AD-H). [d] Reaction time: 18 h. [e] 3 equivalents of the base.

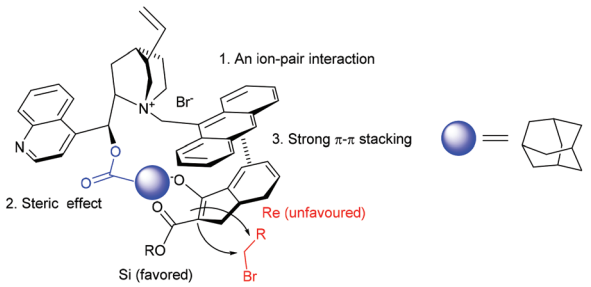
a Br-atom at the 5-position, afforded **6f** with 43% ee (Scheme 5). **5g** with electron withdrawing groups CF_3 at the 3,5-position afforded **6g** in good yield (87%), but the enantioselectivity was moderate (31%). We also tested the β-keto amide **5h** with the aliphatic amido group. Unfortunately, the corresponding product **6h** was obtained in 83% yield with only 4% ee. The simple acyclic β-keto amide **5i** could not react with benzyl bromide even when aqueous 25% KOH solution was used as the base. Although the results were not fully satisfactory, we still developed the first enantioselective α-alkylation of β-keto amides by phase-transfer catalysis.

It is interesting to remark that gram-scale syntheses of α-alkylated β-dicarbonyl compounds **2a**, **2k**, and **6a** were carried out, and the reactions were completed with good enantioselectivities and yields (Schemes 3 and 5). Moreover, the ammonium salt **3s** can be recovered by filtration (once the reaction was completed, after separation of the base by liquid separation, evaporation of the solvent and addition of ethyl ether) in 87% yield. The recovered ammonium salt has been reused up to three times in the model reaction (Table 2, entry 1), giving rise to almost identical yields and enantioselectivities.

On the basis of previous studies,[16b,19,21,22,23] a plausible transition state was proposed. An enolate–PTC complex needs to be formed upon deprotonation of **1**. Three different types of interactions could occur. (1) An ion pair interaction between the substrate and the PTC. (2) The steric hindrance between the substrate and the rigid 1-adamantoyl group. (3) Finally, π–π stacking interactions between the PTC and the substrate. An anthracene ring can be involved in stronger π–π stacking interactions with substrate **1** than a benzene ring. With this transition state, only the *Si* face of the enolate is available for reaction (Scheme 6).



Scheme 5 Substrate scope of the α-alkylation for the β-keto amides. Reaction conditions (unless otherwise specified): The reactions were performed with **5** (0.2 mmol), halohydrocarbon (0.26 mmol), PTC **3a** (0.005 mmol), and 10% KOH (0.5 mL) in toluene (5 mL) at 0 °C for 18 h.



Scheme 6 Model of a possible transition state for the reaction.

Conclusions

In conclusion, we have developed the highly enantioselective α-alkylation of β-keto esters and β-keto amides catalyzed by cinchona alkaloid derived phase transfer catalysts. Under mild conditions, high enantioselectivities (up to 98%) and good yields (up to 99%) were obtained for a range of substituted indanone and 1-tetralone derivatives, and a variety of halides can act as the electrophiles. This simple and effective α-alkylation is a useful synthetic strategy for construction of fully substituted stereogenic centers. Further investigations on expanding this enantioselective α-alkylation to other useful compounds are currently underway.

Experimental

General information

Unless otherwise stated, all the commercial reagents and solvents were used without further additional purification. Analytical TLC was visualized with UV light at 254 nm. Thin layer chromatography was carried out on TLC aluminum sheets with silica gel 60 F254. Purification of the reaction products was carried out with chromatography on silica gel 60 (200–300 mesh). ^{1}H NMR (400 MHz) spectra were obtained at 25 °C; ^{13}C NMR (100 MHz) were recorded on a VARIAN INOVA-400 M at 25 °C. Chemical shifts are reported as δ (ppm) values relative to TMS as an internal standard. HRMS spectra were obtained on a Bruker 7-Tesla FT-ICR MS equipped with an electrospray source. Melting points were determined with a hot plate apparatus. The enantiomeric excesses (ee) were determined by HPLC. Cinchona alkaloid catalysts **3a**, **3c**, **3i**, **3j**, and **3k–3u** were prepared according to our previous papers.[16a,d] The *N*-oxide catalysts **3d–3h** were prepared according to the previous paper.[16f] β-Keto esters **1a–1t** and β-keto amides **5a–5i** were prepared according to the literature procedure.[16a,d]

General procedure for the asymmetric α-alkylation of β-keto esters

The reaction was conducted with substrates **1a–1t** (0.2 mmol) and RBr (0.26 mmol) in the presence of PTC **3s** (2.5 mol%) in a mixture containing $PhCH_3$ (5 mL) and K_2CO_3 (0.5 mL, aq. 30%) at 0 °C. After completion of the reaction (confirmed by

TLC analysis), the mixture was diluted with EtOAc (30 mL), washed with water (3 × 20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel; petroleum ether/ethyl acetate = 30 : 1–10 : 1) to give the asymmetric products. The ee of the product was determined by chiral HPLC.

(*S*)-1-Adamantyl 2-benzyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2a). (White solid, m. p. 103–106 °C; 97% yield, 98% ee); $[\alpha]_D^{25}$ 154.6 (*c* 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.53 (td, *J* = 7.5, 1.2 Hz, 1H), 7.40–7.30 (m, 2H), 7.23–7.10 (m, 5H), 3.58 (d, *J* = 17.1 Hz, 1H), 3.47 (d, *J* = 14.1 Hz, 1H), 3.28 (d, *J* = 14.1 Hz, 1H), 3.13 (d, *J* = 17.2 Hz, 1H), 2.19–2.00 (m, 9H), 1.63 (t, *J* = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.74, 169.43, 153.41, 136.90, 135.44, 135.01, 130.01, 128.19, 127.42, 126.62, 126.11, 124.49, 82.10, 62.55, 40.97, 39.30, 36.08, 35.69, 30.82. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 8.3 min, τ_R (minor) = 6.5 min. HRMS calcd for $[C_{27}H_{28}O_3 + Na]^+$ requires *m*/*z* 423.1936, found *m*/*z* 423.1932.

(*S*)-1-Adamantyl 2-(4-nitrobenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2b). (Colorless oil, 93% yield, 96% ee); $[\alpha]_D^{25}$ 106.2 (*c* 0.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.7 Hz, 2H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.55 (td, *J* = 7.5, 1.3 Hz, 1H), 7.36 (dd, *J* = 8.2, 3.6 Hz, 4H), 3.68–3.46 (m, 2H), 3.37 (d, *J* = 14.1 Hz, 1H), 3.06 (d, *J* = 17.2 Hz, 1H), 2.17–2.01 (m, 9H), 1.61 (t, *J* = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.99, 168.93, 152.89, 146.81, 144.83, 135.43, 135.15, 130.88, 127.79, 126.15, 124.62, 123.36, 82.63, 61.96, 40.95, 38.91, 35.98, 35.88, 30.79. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 15.4 min, τ_R (minor) = 13.9 min. HRMS calcd for $[C_{27}H_{27}NO_5 + Na]^+$ requires *m*/*z* 468.1787, found *m*/*z* 468.1782.

(*S*)-1-Adamantyl 2-(3,5-trifluoromethylbenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2c). (Colorless oil, 97% yield, 92% ee); $[\alpha]_D^{25}$ 56.7 (*c* 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.69 (s, 3H), 7.58 (td, *J* = 7.5, 1.1 Hz, 1H), 7.45–7.34 (m, 2H), 3.65 (dd, *J* = 15.7, 4.5 Hz, 2H), 3.26 (d, *J* = 14.2 Hz, 1H), 3.03 (d, *J* = 17.1 Hz, 1H), 2.20–2.01 (m, 9H), 1.64 (d, *J* = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.56, 168.53, 152.72, 139.66, 135.49, 134.91, 131.38 (q, *J* = 33.2 Hz), 130.11, 127.87, 126.14, 124.73, 123.21 (q, *J* = 272.7 Hz), 120.67–120.74 (m), 82.90, 62.18, 40.92, 39.12, 36.03, 35.98, 30.83. ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.89 (s, 6F). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 98/2, 1 mL min^{-1}, 254 nm, τ_R (major) = 6.4 min, τ_R (minor) = 5.7 min. HRMS calcd for $[C_{29}H_{26}F_6O_3 + Na]^+$ requires *m*/*z* 559.1684, found *m*/*z* 559.1688.

(*S*)-1-Adamantyl 2-(3,5-methoxybenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2d). (White solid, m. p. 101–104 °C; 78% yield, 96% ee); $[\alpha]_D^{25}$ 80.1 (*c* 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.54 (td, *J* = 7.5, 1.3 Hz, 1H), 7.42–7.30 (m, 2H), 6.32 (d, *J* = 2.2 Hz, 2H), 6.25 (t, *J* = 2.3 Hz, 1H), 3.69 (s, 6H), 3.55 (d, *J* = 17.3 Hz, 1H), 3.40 (d, *J* = 14.1 Hz, 1H), 3.23 (d, *J* = 14.1 Hz, 1H), 3.12 (d, *J* = 17.2 Hz, 1H), 2.09 (dd, *J* = 39.7, 3.2 Hz, 9H), 1.62 (t, *J* = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.84, 169.43, 160.45, 153.63, 139.27, 135.45, 135.03, 127.42, 126.20, 124.42, 107.97, 98.78, 82.08, 62.39, 55.21, 40.96, 39.48, 36.06, 35.64, 30.80. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 9.4 min, τ_R (minor) = 7.6 min. HRMS calcd for $[C_{29}H_{32}O_5 + Na]^+$ requires *m*/*z* 483.2147, found *m*/*z* 483.2143.

(*S*)-1-Adamantyl 2-(3-methoxybenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2e). (White solid, m. p. 104–106 °C; 83% yield, 95% ee); $[\alpha]_D^{25}$ 83.2 (*c* 0.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.68 (m, 1H), 7.50 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.41–7.28 (m, 2H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.82–6.48 (m, 3H), 3.70 (s, 3H), 3.55 (d, *J* = 17.2 Hz, 1H), 3.42 (d, *J* = 14.1 Hz, 1H), 3.23 (d, *J* = 14.0 Hz, 1H), 3.10 (d, *J* = 17.2 Hz, 1H), 2.18–1.96 (m, 9H), 1.61 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.76, 169.42, 159.34, 153.51, 138.51, 135.43, 135.02, 129.14, 127.42, 126.15, 124.47, 122.41, 115.48, 112.24, 82.10, 62.49, 55.10, 40.96, 39.30, 36.07, 35.68, 30.81. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 12.9 min, τ_R (minor) = 9.7 min. HRMS calcd for $[C_{28}H_{30}O_4 + Na]^+$ requires *m*/*z* 453.2042, found *m*/*z* 453.2048.

(*S*)-1-Adamantyl 2-(5-fluoro-2-methoxybenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2f). (Colorless oil, 87% yield, 95% ee); $[\alpha]_D^{25}$ 86.1 (*c* 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84–7.63 (m, 1H), 7.51 (td, *J* = 7.4, 1.2 Hz, 1H), 7.39–7.29 (m, 2H), 6.97–6.58 (m, 3H), 3.68 (s, 3H), 3.59–3.43 (m, 2H), 3.23 (d, *J* = 14.2 Hz, 1H), 3.07 (d, *J* = 17.2 Hz, 1H), 2.20–1.99 (m, 9H), 1.61 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.71, 169.63, 156.61 (d, *J* = 238.2 Hz), 153.68, 135.34, 134.87, 127.39, 127.31, 127.28, 126.00, 124.42, 118.11 (d, *J* = 23.3 Hz), 113.64 (d, *J* = 22.7 Hz) 110.97 (d, *J* = 8.4 Hz), 82.06, 62.33, 55.59, 40.97, 36.07, 35.77, 32.57, 30.81. ^{19}F NMR (376 MHz, $CDCl_3$) δ −123.98 (s, 1F). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 12.3 min, τ_R (minor) = 9.2 min. HRMS calcd for $[C_{28}H_{29}FO_4 + Na]^+$ requires *m*/*z* 471.1948, found *m*/*z* 471.1950.

(*S*)-1-Adamantyl 2-(4-(*tert*-butyl)benzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2g). (Colorless oil, 81% yield, 96% ee); $[\alpha]_D^{25}$ 97.5 (*c* 0.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.51 (td, *J* = 7.4, 1.2 Hz, 1H), 7.41–7.28 (m, 2H), 7.23–7.04 (m, 4H), 3.51 (dd, *J* = 44.5, 15.6 Hz, 2H), 3.13 (dd, *J* = 15.7, 11.7 Hz, 2H), 2.07 (dd, *J* = 40.4, 3.1 Hz, 9H), 1.61 (s, 6H), 1.24 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.67, 169.39, 153.48, 149.37, 135.36, 134.93, 133.93, 129.62, 127.36, 126.14, 125.09, 124.54, 82.05, 62.82, 40.97, 38.92, 36.09, 35.80, 34.34, 31.31, 30.82. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 7.6 min, τ_R (minor) = 6.0 min. HRMS calcd for $[C_{31}H_{36}O_3 + Na]^+$ requires *m*/*z* 479.2562, found *m*/*z* 479.2561.

(*S*)-1-Adamantyl 2-(3-trifluoromethylbenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2h). (Colorless oil, 92% yield, 96% ee); $[\alpha]_D^{25}$ 71.3 (*c* 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.56–7.45 (m, 2H), 7.43–7.28 (m, 5H), 3.69–3.50 (m, 2H), 3.23 (d, *J* = 14.1 Hz, 1H), 3.05 (d,

J = 17.2 Hz, 1H), 2.17–2.01 (m, 9H), 1.66–1.58 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.16, 168.95, 153.07, 137.96, 135.25, 135.16, 133.33, 130.45 (q, J = 32.1 Hz), 128.66, 127.64, 126.68 (q, J = 3.6 Hz), 126.73–126.52 (m), 126.12, 124.60, 124.04 (q, J = 272.3 Hz), 123.70–123.36 (m), 82.49, 62.38, 40.94, 39.17, 36.03, 30.82. ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.62 (s, 3F). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 5.6 min, τ_R (minor) = 4.9 min. HRMS calcd for $[C_{28}H_{27}F_3O_3 + Na]^+$ requires m/z 491.1810, found m/z 491.1808.

(*S*)-1-Adamantyl 2-(2-trifluoromethylbenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2i). (Colorless oil, 75% yield, 92% ee); $[\alpha]_D^{25}$ 85.6 (c 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.78 (m, 1H), 7.65–7.60 (m, 1H), 7.55 (td, J = 7.5, 1.2 Hz, 1H), 7.41–7.29 (m, 3H), 7.26 (d, J = 4.2 Hz, 2H), 3.83 (dd, J = 15.8, 1.5 Hz, 1H), 3.62 (d, J = 17.3 Hz, 1H), 3.45 (d, J = 15.6 Hz, 1H), 2.84 (d, J = 17.3 Hz, 1H), 1.98 (d, J = 3.0 Hz, 9H), 1.59 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.73, 169.24, 153.70, 136.65, 136.63, 136.61, 136.60, 135.23, 135.09, 131.78, 130.24, 129.47 (q, J = 29.2 Hz), 127.54, 126.56, 126.12, 124.67, 124.34 (q, J = 274.0 Hz), 82.36, 62.14, 40.81, 36.00, 30.76. ^{19}F NMR (376 MHz, $CDCl_3$) δ −58.97 (s, 3F). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 6.7 min, τ_R (minor) = 5.5 min. HRMS calcd for $[C_{28}H_{27}F_3O_3 + Na]^+$ requires m/z 491.1810, found m/z 491.1807.

(*S*)-1-Adamantyl 2-(4-trifluoromethylbenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2j). (Colorless oil, 87% yield, 95% ee); $[\alpha]_D^{25}$ 92.3 (c 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.8 Hz, 1H), 7.56–7.51 (m, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.38–7.27 (m, 4H), 3.64–3.44 (m, 2H), 3.29 (d, J = 14.1 Hz, 1H), 3.05 (d, J = 17.2 Hz, 1H), 2.15–1.98 (m, 9H), 1.61 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.24, 169.09, 153.09, 141.18, 141.17, 135.25, 135.23, 130.32, 128.93 (q, J = 32.4 Hz), 127.64, 126.14, 125.22–125.01 (m), 124.60, 124.13 (q, J = 271.9 Hz), 82.43, 62.22, 40.95, 38.91, 36.01, 30.80. ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.50 (s, 3F). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 8.7 min, τ_R (minor) = 7.6 min. HRMS calcd for $[C_{28}H_{27}F_3O_3 + Na]^+$ requires m/z 491.1810, found m/z 491.1805.

(*R*)-1-Adamantyl 2-(2,3,4,5,6-pentafluorobenzyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2k). (Colorless oil, 94% yield, 98% ee); $[\alpha]_D^{25}$ −128.5 (c 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, chloroform-d) δ 7.75 (d, J = 7.6 Hz, 1H), 7.57 (td, J = 7.5, 1.3 Hz, 1H), 7.48–7.33 (m, 2H), 3.86–3.51 (m, 2H), 3.34 (dt, J = 14.6, 1.8 Hz, 1H), 3.04 (d, J = 17.2 Hz, 1H), 2.06 (dd, J = 45.1, 3.1 Hz, 9H), 1.61 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.97, 168.64, 152.40, 147.92–146.00 (m), 145.26–143.22 (m), 139.71–137.95 (m), 137.04–135.77 (m), 135.34, 134.75, 127.82, 126.00, 124.67, 112.31–108.10 (m), 82.78, 60.98, 40.84, 36.58, 36.00, 30.82. ^{19}F NMR (376 MHz, $CDCl_3$) δ −138.43 (dd, J = 22.6, 8.1 Hz), −155.47 (t, J = 20.9 Hz), −162.21 (dd, J = 21.1, 14.3 Hz). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 6.9 min, τ_R (minor) = 8.1 min. HRMS calcd for $[C_{27}H_{23}F_5O_3 + Na]^+$ requires m/z 513.1465, found m/z 513.1468.

(*S*)-1-Adamantyl 2-(naphthalenyl-2methyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2l). (White solid, m. p. 123–126 °C; 89% yield, 94% ee); $[\alpha]_D^{25}$ 66.9 (c 0.46, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.3 Hz, 1H), 7.90–7.65 (m, 3H), 7.59–7.44 (m, 3H), 7.39–7.29 (m, 3H), 7.26 (d, J = 7.7 Hz, 1H), 4.12 (d, J = 15.3 Hz, 1H), 3.77–3.60 (m, 2H), 3.04 (d, J = 17.1 Hz, 1H), 2.21–1.96 (m, 10H), 1.63 (d, J = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.95, 169.71, 153.67, 135.15, 135.00, 133.73, 133.38, 132.91, 128.80, 127.40, 127.28, 127.07, 126.09, 126.07, 125.48, 125.30, 124.57, 123.80, 82.21, 62.67, 40.92, 36.09, 36.06, 34.49, 30.81. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 9.1 min, τ_R (minor) = 6.6 min. HRMS calcd for $[C_{31}H_{30}O_3 + Na]^+$ requires m/z 473.2093, found m/z 473.2095.

(*S*)-1-Adamantyl 2-allyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2m). (Colorless oil, 92% yield, 97% ee); $[\alpha]_D^{25}$ 78.6 (c 0.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.7 Hz, 1H), 7.62 (td, J = 7.5, 1.3 Hz, 1H), 7.53–7.35 (m, 2H), 5.77–5.60 (m, 1H), 5.22–4.99 (m, 2H), 3.60 (d, J = 17.2 Hz, 1H), 3.11 (d, J = 17.2 Hz, 1H), 2.90–2.77 (m, 1H), 2.63–2.51 (m, 1H), 2.19–2.02 (m, 9H), 1.63 (t, J = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.67, 169.48, 153.28, 135.42, 135.14, 133.20, 127.55, 126.31, 124.60, 118.98, 81.91, 60.80, 41.02, 38.86, 36.18, 36.08, 30.80. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 98/2, 0.9 mL min^{-1}, 254 nm, τ_R (major) = 9.7 min, τ_R (minor) = 8.8 min. HRMS calcd for $[C_{23}H_{26}O_3 + Na]^+$ requires m/z 373.1780, found m/z 373.1782.

(*S*)-1-Adamantyl 2-propargyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2n). (Colorless oil, 93% yield, 97% ee); $[\alpha]_D^{25}$ 84.5 (c 0.36, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.7 Hz, 1H), 7.64 (td, J = 7.5, 1.2 Hz, 1H), 7.51 (d, J = 7.7 Hz, 1H), 7.46–7.35 (m, 1H), 3.65 (d, J = 17.2 Hz, 1H), 3.37 (d, J = 17.2 Hz, 1H), 2.96 (dd, J = 16.9, 2.7 Hz, 1H), 2.81 (dd, J = 16.9, 2.6 Hz, 1H), 2.19–2.02 (m, 9H), 1.82 (t, J = 2.6 Hz, 1H), 1.61 (t, J = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.54, 168.66, 153.54, 135.33, 135.30, 127.62, 126.22, 124.72, 82.39, 79.72, 70.24, 59.84, 40.91, 36.92, 36.01, 30.78, 23.60. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 98/2, 1 mL min^{-1}, 254 nm, τ_R (major) = 11.9 min, τ_R (minor) = 10.9 min. HRMS calcd for $[C_{23}H_{24}O_3 + Na]^+$ requires m/z 371.1623, found m/z 371.1625.

(*S*)-1-Adamantyl 2-methyl-propargyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2o). (Colorless oil, 92% yield, 95% ee); $[\alpha]_D^{25}$ 87.2 (c 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, chloroform-d) δ 7.69 (d, J = 7.6 Hz, 1H), 7.54 (td, J = 7.5, 1.2 Hz, 1H), 7.46–7.26 (m, 2H), 3.54 (d, J = 17.1 Hz, 1H), 3.26 (d, J = 17.1 Hz, 1H), 2.89–2.52 (m, 2H), 1.98 (dd, J = 41.6, 3.1 Hz, 9H), 1.59–1.41 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.04, 167.97, 152.67, 134.50, 134.05, 126.39, 125.12, 123.58, 81.05, 73.23, 59.38, 39.91, 35.97, 35.02, 29.76, 23.11. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 9.8 min,

τ_R (minor) = 7.2 min. HRMS calcd for $[C_{24}H_{26}O_3 + Na]^+$ requires *m*/*z* 385.1780, found *m*/*z* 385.1784.

(*S*)-1-Adamantyl 2-(3-methoxy-3-oxopropyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2q). (Colorless oil, 75% yield, 65% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.7 Hz, 1H), 7.61 (td, *J* = 7.5, 1.2 Hz, 1H), 7.50–7.35 (m, 2H), 3.65 (s, 4H), 3.02 (d, *J* = 17.2 Hz, 1H), 2.55–2.29 (m, 3H), 2.24–2.09 (m, 4H), 2.02 (d, *J* = 3.0 Hz, 6H), 1.65–1.54 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.36, 173.37, 169.45, 152.73, 135.28, 135.25, 127.76, 126.29, 124.73, 82.17, 60.36, 51.71, 41.01, 37.44, 36.04, 30.80, 29.74. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 11.8 min, τ_R (minor) = 10.0 min. HRMS calcd for $[C_{24}H_{28}O_5 + Na]^+$ requires *m*/*z* 419.1834, found *m*/*z* 419.1837.

(*S*)-1-Adamantyl 2-oxo-2-phenylethyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2r). (Colorless oil, 92% yield, 96% ee); $[\alpha]_D^{25}$ 112.6 (*c* 0.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01–7.91 (m, 2H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.59 (dt, *J* = 21.9, 7.4 Hz, 2H), 7.51–7.35 (m, 4H), 4.16 (d, *J* = 18.4 Hz, 1H), 4.00 (d, *J* = 17.4 Hz, 1H), 3.31 (d, *J* = 18.4 Hz, 1H), 3.11 (d, *J* = 17.5 Hz, 1H), 2.10–1.95 (m, 9H), 1.57 (t, *J* = 2.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.32, 197.12, 168.52, 153.95, 136.47, 135.24, 135.11, 133.38, 128.64, 128.08, 127.51, 126.28, 124.64, 82.05, 59.29, 43.64, 40.83, 38.42, 36.04, 30.77. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 11.8 min, τ_R (minor) = 10.0 min. HRMS calcd for $[C_{28}H_{28}O_4 + Na]^+$ requires *m*/*z* 451.1885, found *m*/*z* 451.1883.

(*S*)-1-Adamantyl 2-(3-(4-bromophenyl)-3-oxopropyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2s). (White solid, m. p. 129–131 °C; 96% yield, 94% ee); $[\alpha]_D^{25}$ 104.3 (*c* 0.41, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 18.2, 8.1 Hz, 3H), 7.68–7.55 (m, 3H), 7.51–7.37 (m, 2H), 3.67 (d, *J* = 17.1 Hz, 1H), 3.29–2.95 (m, 3H), 2.33 (dt, *J* = 9.7, 5.8 Hz, 2H), 2.08 (dd, *J* = 37.8, 3.0 Hz, 9H), 1.61 (t, *J* = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.74, 198.36, 169.86, 152.66, 135.39, 135.31, 135.28, 131.86, 129.70, 128.20, 127.81, 126.37, 124.74, 82.15, 60.18, 41.06, 38.29, 36.03, 34.13, 30.79, 29.14. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 17.5 min, τ_R (minor) = 15.8 min. HRMS calcd for $[C_{29}H_{29}BrO_4 + Na]^+$ requires *m*/*z* 543.1147, found *m*/*z* 543.1150.

(*S*)-1-*tert*-Butyl 2-benzyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4b). (Colorless oil, 85% yield, 94% ee); $[\alpha]_D^{25}$ 84.5 (*c* 0.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.53 (td, *J* = 7.4, 1.2 Hz, 1H), 7.38–7.31 (m, 2H), 7.22–7.12 (m, 5H), 3.59 (d, *J* = 17.2 Hz, 1H), 3.46 (d, *J* = 14.1 Hz, 1H), 3.29 (d, *J* = 14.1 Hz, 1H), 3.15 (d, *J* = 17.2 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.69, 169.76, 136.83, 135.40, 135.04, 129.98, 128.19, 127.44, 126.63, 126.11, 124.50, 82.08, 62.42, 39.38, 35.66, 27.78. HPLC conditions: Chiralcel AS-H column (250 × 4.6 mm), hexane/i-PrOH = 99/1, 1 mL min^{-1}, 254 nm, τ_R (major) = 7.4 min, τ_R (minor) = 6.5 min. HRMS calcd for $[C_{21}H_{22}O_3 + Na]^+$ requires *m*/*z* 345.1467, found *m*/*z* 345.1469.

(*S*)-3-Ethyl 3-pentanyl 2-benzyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4c). (Colorless oil, 95% yield, 93% ee); $[\alpha]_D^{25}$ 44.2 (*c* 0.36, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.51 (td, *J* = 7.5, 1.2 Hz, 1H), 7.39–7.30 (m, 2H), 7.21–7.07 (m, 5H), 3.53 (d, *J* = 17.1 Hz, 1H), 3.41 (d, *J* = 3.3 Hz, 2H), 3.16 (d, *J* = 17.1 Hz, 1H), 1.75 (q, *J* = 7.5 Hz, 6H), 0.70 (t, *J* = 7.5 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.90, 169.62, 153.41, 136.75, 135.78, 134.94, 130.14, 128.19, 127.42, 126.58, 126.02, 124.38, 90.14, 62.47, 38.80, 35.76, 26.82, 7.51. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 99/1, 1 mL min^{-1}, 254 nm, τ_R (major) = 5.9 min, τ_R (minor) = 5.3 min. HRMS calcd for $[C_{24}H_{28}O_3 + Na]^+$ requires *m*/*z* 387.1936, found *m*/*z* 387.1939.

(*S*)-1-Isopropyl 2-benzyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4d). (Colorless oil, 92% yield, 87% ee); $[\alpha]_D^{25}$ 123.8 (*c* 0.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.54 (td, *J* = 7.5, 1.3 Hz, 1H), 7.41–7.31 (m, 2H), 7.24–7.10 (m, 5H), 5.04 (p, *J* = 6.3 Hz, 1H), 3.64 (d, *J* = 17.2 Hz, 1H), 3.50 (d, *J* = 14.1 Hz, 1H), 3.30 (d, *J* = 14.1 Hz, 1H), 3.17 (d, *J* = 17.2 Hz, 1H), 1.21 (dd, *J* = 6.3, 2.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.34, 170.22, 153.29, 136.58, 135.23, 135.18, 129.98, 128.22, 127.54, 126.73, 126.18, 124.59, 69.44, 61.79, 39.57, 35.51, 21.59, 21.48. HPLC conditions: Chiralcel AS-H column (250 × 4.6 mm), hexane/i-PrOH = 99/1, 1 mL min^{-1}, 254 nm, τ_R (major) = 10.5 min, τ_R (minor) = 9.1 min. HRMS calcd for $[C_{20}H_{20}O_3 + Na]^+$ requires *m*/*z* 331.1310, found *m*/*z* 331.1306.

(*S*)-2-Adamantyl 2-benzyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4e). (White solid, m. p. 97–100 °C; 98% yield, 92% ee); $[\alpha]_D^{25}$ 102.9 (*c* 0.28, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.51 (td, *J* = 7.5, 1.2 Hz, 1H), 7.41–7.26 (m, 2H), 7.21–7.07 (m, 5H), 4.93 (s, 1H), 3.68–3.46 (m, 2H), 3.37 (d, *J* = 14.1 Hz, 1H), 3.17 (d, *J* = 17.2 Hz, 1H), 1.92–1.61 (m, 12H), 1.41 (d, *J* = 12.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.40, 170.03, 153.33, 136.73, 135.53, 135.11, 130.02, 128.28, 127.53, 126.69, 126.15, 124.52, 78.38, 62.08, 39.04, 37.26, 36.20, 36.18, 35.62, 31.75, 31.71, 31.58, 27.05, 26.88. HPLC conditions: Chiralcel OJ-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 5.8 min, τ_R (minor) = 5.0 min. HRMS calcd for $[C_{27}H_{28}O_3 + Na]^+$ requires *m*/*z* 423.1936, found *m*/*z* 423.1933.

(*S*)-2-Adamantyl 2-benzyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4f). (Colorless oil, 93% yield, 92% ee); $[\alpha]_D^{25}$ 103.2 (*c* 0.52, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80–7.73 (m, 1H), 7.56 (td, *J* = 7.4, 1.2 Hz, 1H), 7.39–7.30 (m, 5H), 7.30–7.24 (m, 2H), 7.21–7.03 (m, 5H), 5.25–5.09 (m, 2H), 3.66 (d, *J* = 17.3 Hz, 1H), 3.55 (d, *J* = 14.0 Hz, 1H), 3.34 (d, *J* = 14.0 Hz, 1H), 3.20 (d, *J* = 17.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.95, 170.51, 153.16, 136.31, 135.52, 135.33, 135.17, 129.97, 128.53, 128.30, 128.19, 127.86, 127.67, 126.81, 126.24, 124.71, 67.32, 61.86, 39.72, 35.40. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 13.0 min, τ_R (minor) = 10.8 min. HRMS calcd for $[C_{24}H_{20}O_3 + Na]^+$ requires *m*/*z* 379.1310, found *m*/*z* 379.1312.

(*S*)-Methyl 2-benzyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4g). (Colorless oil, 96% yield, 91% ee); $[\alpha]_D^{25}$ 154.6 (*c* 0.37,

$CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 1H), 7.56 (ddd, J = 8.4, 7.3, 1.2 Hz, 1H), 7.47–7.32 (m, 2H), 7.27–7.09 (m, 5H), 3.74 (s, 3H), 3.65 (d, J = 17.4 Hz, 1H), 3.52 (d, J = 14.0 Hz, 1H), 3.31 (d, J = 14.0 Hz, 1H), 3.20 (d, J = 17.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.14, 171.22, 153.17, 136.31, 135.35, 135.13, 129.96, 128.31, 127.66, 126.85, 126.24, 124.70, 61.69, 52.92, 39.77, 35.38. HPLC conditions: Chiralcel AS-H column (250 × 4.6 mm), hexane/i-PrOH = 99/1, 1 mL min^{-1}, 254 nm, τ_R (major) = 19.2 min, τ_R (minor) = 16.9 min. HRMS calcd for $[C_{18}H_{16}O_3 + Na]^+$ requires m/z 303.0997, found m/z 303.0995.

(*S*)-1-Adamantyl 2-benzyl-5-fluorine-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4h). (White solid, m. p. 165–168 °C; 95% yield, 94% ee); $[\alpha]_D^{25}$ 112.2 (c 0.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 8.3, 5.3 Hz, 1H), 7.25–7.08 (m, 5H), 7.07–6.93 (m, 2H), 3.55 (d, J = 17.4 Hz, 1H), 3.43 (d, J = 14.0 Hz, 1H), 3.30 (d, J = 14.1 Hz, 1H), 3.11 (d, J = 17.4 Hz, 1H), 2.15–2.03 (m, 9H), 1.64 (t, J = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.85, 169.16, 168.52, 165.97, 156.38, 156.28, 136.63, 131.86, 131.85, 129.97, 128.26, 126.80, 126.73, 126.69, 115.82 (d, J = 23.9 Hz), 112.81 (d, J = 22.4 Hz), 82.32, 62.84, 40.97, 39.21, 36.05, 35.52, 35.50, 30.82. ^{19}F NMR (376 MHz, $CDCl_3$) δ −102.06 (s, 1F). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 7.9 min, τ_R (minor) = 6.5 min. HRMS calcd for $[C_{27}H_{27}FO_3 + Na]^+$ requires m/z 441.1842, found m/z 441.1845.

(*S*)-1-Adamantyl 2-benzyl-5-chloro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4i). (White solid, m. p. 164–167 °C; 96% yield, 93% ee); $[\alpha]_D^{25}$ 87.8 (c 0.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.2 Hz, 1H), 7.36–7.28 (m, 2H), 7.17 (q, J = 7.2, 6.5 Hz, 5H), 3.54 (d, J = 17.4 Hz, 1H), 3.42 (d, J = 14.1 Hz, 1H), 3.30 (d, J = 14.1 Hz, 1H), 3.10 (d, J = 17.4 Hz, 1H), 2.15–2.02 (m, 9H), 1.63 (t, J = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.34, 169.07, 154.82, 141.52, 136.55, 133.96, 129.98, 128.29, 126.78, 126.34, 125.51, 82.38, 62.70, 40.97, 39.18, 36.04, 35.33, 30.82. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 7.9 min, τ_R (minor) = 6.6 min. HRMS calcd for $[C_{27}H_{27}ClO_3 + Na]^+$ requires m/z 457.1546, found m/z 457.1548.

(*S*)-1-Adamantyl 2-benzyl-5-chloro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4j). (White wax, 91% yield, 96% ee); $[\alpha]_D^{25}$ 95.2 (c 0.32, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, J = 7.7, 2.0 Hz, 2H), 7.27–7.10 (m, 6H), 3.53 (d, J = 17.7 Hz, 1H), 3.44 (d, J = 14.0 Hz, 1H), 3.30 (d, J = 14.0 Hz, 1H), 3.07 (d, J = 17.7 Hz, 1H), 2.20–2.01 (m, 9H), 1.64 (t, J = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.05, 168.88, 152.99, 137.73, 137.41, 136.35, 129.97, 129.21, 128.29, 126.78, 123.25, 121.59, 82.47, 62.74, 40.96, 39.32, 36.84, 36.05, 30.83. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 6.9 min, τ_R (minor) = 5.4 min. HRMS calcd for $[C_{27}H_{27}BrO_3 + Na]^+$ requires m/z 501.1041, found m/z 501.1044.

(*S*)-1-Adamantyl 2-benzyl-5-methoxyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4k). (Light yellow solid, m. p. 133–135 °C; 94% yield, 98% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.5 Hz, 1H), 7.19 (d, J = 3.2 Hz, 5H), 6.91–6.69 (m, 2H), 3.84 (s, 3H), 3.59–3.36 (m, 2H), 3.25 (d, J = 14.1 Hz, 1H), 3.06 (d, J = 17.2 Hz, 1H), 2.10 (dd, J = 32.9, 3.1 Hz, 9H), 1.63 (t, J = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.67, 169.68, 165.52, 156.48, 137.12, 130.00, 128.61, 128.17, 126.55, 126.20, 115.55, 109.19, 81.98, 62.76, 55.60, 40.98, 39.30, 36.09, 35.61, 30.82. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 14.9 min, τ_R (minor) = 10.3 min. HRMS calcd for $[C_{28}H_{30}O_4 + Na]^+$ requires m/z 453.2042, found m/z 453.2045.

(*S*)-1-Adamantyl 2-benzyl-6-methyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4l). (White wax, 92% yield, 97% ee); $[\alpha]_D^{25}$ 88.5 (c 0.64, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.31 (d, J = 1.7 Hz, 1H), 7.24–7.08 (m, 6H), 3.58–3.37 (m, 2H), 3.24 (d, J = 14.1 Hz, 1H), 3.05 (d, J = 17.0 Hz, 1H), 2.35 (s, 3H), 2.06 (dd, J = 38.1, 4.5 Hz, 9H), 1.61 (d, J = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.77, 169.56, 150.82, 137.31, 137.01, 136.32, 135.59, 130.02, 128.17, 126.56, 125.75, 124.40, 82.00, 62.85, 40.97, 39.31, 36.09, 35.32, 30.82, 21.06. Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1.2 mL min^{-1}, 254 nm, τ_R (major) = 5.5 min, τ_R (minor) = 4.3 min. HRMS calcd for $[C_{28}H_{30}O_3 + Na]^+$ requires m/z 437.2093, found m/z 437.2091.

(*S*)-1-Adamantyl 2-benzyl-5,6-dimethoxyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4m). (Yellow wax, 81% yield, 98% ee); $[\alpha]_D^{25}$ 134.6 (c 0.65, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, J = 10.2 Hz, 6H), 6.76 (s, 1H), 3.91 (d, J = 7.1 Hz, 6H), 3.55–3.36 (m, 2H), 3.27 (d, J = 14.1 Hz, 1H), 3.02 (d, J = 16.9 Hz, 1H), 2.20–2.03 (m, 9H), 1.64 (d, J = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.22, 169.79, 155.68, 149.42, 149.00, 137.08, 129.98, 128.14, 128.12, 126.55, 106.97, 104.77, 81.96, 62.77, 56.18, 56.05, 40.99, 36.09, 30.81. Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1.2 mL min^{-1}, 254 nm, τ_R (major) = 9.9 min, τ_R (minor) = 8.4 min. HRMS calcd for $[C_{29}H_{32}O_5 + Na]^+$ requires m/z 483.2147, found m/z 483.2150.

(*S*)-Methyl-1-benzyl-2-oxocyclopentane-1-carboxylate (4n). (Colorless oil, 78% yield, 54% ee); $[\alpha]_D^{25}$ 7.86 (c 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 3H), 7.14 (dd, J = 7.9, 1.6 Hz, 2H), 3.74 (s, 3H), 3.23 (d, J = 13.7 Hz, 1H), 3.13 (d, J = 13.7 Hz, 1H), 2.56–2.29 (m, 2H), 2.13–1.86 (m, 3H), 1.62 (dd, J = 8.8, 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.86, 171.37, 136.51, 130.14, 128.41, 126.89, 61.52, 52.67, 39.16, 38.39, 31.69, 19.46. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 98/2, 0.6 mL min^{-1}, 254 nm, τ_R (major) = 13.4 min, τ_R (minor) = 13.9 min. HRMS calcd for $[C_{14}H_{16}O_3 + Na]^+$ requires m/z 255.0997, found m/z 255.0992.

(*S*)-1-Adamantyl 2-benzyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4o). (White wax, 89% yield, 79% ee); $[\alpha]_D^{25}$ −4.4 (c 0.81, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 7.9, 1.5 Hz, 1H), 7.48–7.40 (m, 1H), 7.34–7.14 (m, 7H), 3.51 (d, J = 13.6 Hz, 1H), 3.25 (d, J = 13.7 Hz, 1H), 3.12 (ddd, J = 17.1, 12.1, 4.8 Hz, 1H), 2.92–2.76 (m, 1H), 2.43 (ddd, J = 13.7, 4.8, 3.2 Hz, 1H), 2.27–2.07 (m, 4H), 1.99–1.91 (m, 6H), 1.61 (d, J = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.05, 170.43, 142.87, 136.92, 133.07, 132.81, 130.96, 128.55, 127.97, 127.84, 126.55, 82.34, 59.18, 40.97, 39.60, 36.01, 30.86, 30.76, 26.20.

HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 11.2 min, τ_R (minor) = 11.8 min. HRMS calcd for $[C_{28}H_{30}O_3 + Na]^+$ requires *m*/*z* 437.2093, found *m*/*z* 437.2089.

(*S*)-1-Adamantyl 2-allyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4p). (Colorless oil, 92% yield, 87% ee); $[\alpha]_D^{25}$ −12.7 (*c* 0.24, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.12–7.98 (m, 1H), 7.45 (td, *J* = 7.5, 1.4 Hz, 1H), 7.36–7.17 (m, 2H), 5.86 (ddt, *J* = 17.3, 10.1, 7.3 Hz, 1H), 5.25–4.98 (m, 2H), 3.19–2.83 (m, 2H), 2.67 (d, *J* = 7.3 Hz, 2H), 2.43 (dt, *J* = 13.7, 4.5 Hz, 1H), 2.18–1.90 (m, 10H), 1.59 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.49, 170.43, 142.95, 133.80, 133.13, 132.56, 128.61, 127.75, 126.61, 118.54, 82.11, 57.74, 41.06, 38.69, 36.04, 31.00, 30.76, 26.04. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 5.3 min, τ_R (minor) = 4.9 min. HRMS calcd for $[C_{24}H_{28}O_3 + Na]^+$ requires *m*/*z* 387.1936, found *m*/*z* 387.1941.

(*S*)-1-Adamantyl 2-benzyl-7-bromine-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4q). (White solid, m. p. 152–154 °C; 93% yield, 42% ee); $[\alpha]_D^{25}$ −3.5 (*c* 0.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 2.2 Hz, 1H), 7.54 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.31–7.17 (m, 5H), 7.07 (d, *J* = 8.2 Hz, 1H), 3.53 (d, *J* = 13.7 Hz, 1H), 3.21 (d, *J* = 13.6 Hz, 1H), 3.12–2.95 (m, 1H), 2.87–2.71 (m, 1H), 2.42 (dd, *J* = 13.8, 1.7 Hz, 1H), 2.21–2.08 (m, 3H), 1.96 (d, *J* = 2.9 Hz, 7H), 1.62 (d, *J* = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.73, 170.14, 141.62, 136.62, 135.84, 134.28, 130.95, 130.54, 130.40, 128.04, 126.66, 120.59, 82.72, 59.07, 41.00, 39.53, 35.99, 30.77, 30.72, 25.81. HPLC conditions: Chiralcel OJ-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 6.5 min, τ_R (minor) = 4.8 min. HRMS calcd for $[C_{28}H_{29}BrO_3 + Na]^+$ requires *m*/*z* 515.1198, found *m*/*z* 515.1196.

(*S*)-1-Adamantyl 2-benzyl-6-methoxyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (4r). (Light yellow solid, m. p. 87–89 °C; 76% yield, 78% ee); $[\alpha]_D^{25}$ −18.1 (*c* 0.42, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.8 Hz, 1H), 7.28–7.21 (m, 4H), 7.20–7.12 (m, 1H), 6.86–6.77 (m, 1H), 6.59 (d, *J* = 2.5 Hz, 1H), 3.82 (s, 3H), 3.47 (d, *J* = 13.6 Hz, 1H), 3.21 (d, *J* = 13.6 Hz, 1H), 3.06 (td, *J* = 12.2, 6.0 Hz, 1H), 2.76 (dt, *J* = 17.2, 4.1 Hz, 1H), 2.38 (dd, *J* = 4.7, 3.4 Hz, 1H), 2.14–1.86 (m, 10H), 1.59 (d, *J* = 3.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.68, 170.61, 163.33, 145.45, 137.09, 130.93, 130.34, 127.95, 126.48, 126.33, 113.22, 112.22, 82.17, 58.94, 55.39, 41.03, 39.72, 36.05, 30.80, 30.78, 26.60. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1 mL min^{-1}, 254 nm, τ_R (major) = 7.5 min, τ_R (minor) = 7.1 min. HRMS calcd for $[C_{29}H_{32}O_4 + Na]^+$ requires *m*/*z* 467.2198, found *m*/*z* 467.2195.

General procedure for the asymmetric α-alkylation of β-keto amides

The reaction was conducted with substrates **5a–5i** (0.2 mmol) and RBr (0.26 mmol) in the presence of PTC **3a** (2.5 mol%) in a mixture containing $PhCH_3$ (5 mL) and KOH (0.5 mL, aq. 10%) at 0 °C. After completion of the reaction (confirmed by TLC analysis), the mixture was diluted with EtOAc (30 mL), washed with water (3 × 20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography to give the asymmetric products. The ee of the product was determined by chiral HPLC.

2-Benzyl-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (6a). (White solid, m. p. 152–154 °C; 93% yield, 87% ee); $[\alpha]_D^{25}$ −13.8 (*c* 0.26, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.67–7.51 (m, 3H), 7.48–7.32 (m, 4H), 7.27–7.04 (m, 6H), 3.98 (d, *J* = 18.0 Hz, 1H), 3.44–3.18 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.08, 167.47, 153.34, 137.71, 136.15, 135.09, 135.03, 129.93, 128.99, 128.23, 127.71, 127.33, 126.51, 124.50, 124.37, 120.01, 62.09, 45.58, 34.90. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1.2 mL min^{-1}, 254 nm, τ_R (major) = 12.9 min, τ_R (minor) = 16.5 min. HRMS calcd for $[C_{23}H_{19}NO_2 + Na]^+$ requires *m*/*z* 364.1313, found *m*/*z* 364.1310.

2-(3,5-Trifluoromethylbenzyl)-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (6b). (Colorless oil, 96% yield, 57% ee); $[\alpha]_D^{25}$ −3.5 (*c* 0.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H), 7.85–7.30 (m, 11H), 7.18–7.08 (m, 1H), 3.96 (d, *J* = 18.1 Hz, 1H), 3.51–3.32 (m, 2H), 3.17 (d, *J* = 18.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.43, 166.72, 152.61, 137.62, 137.19, 136.70, 134.77, 131.49 (q, *J* = 33.5 Hz), 129.95, 129.08, 128.16, 126.54, 124.77, 124.71, 123.05 (q, *J* = 273.0 Hz), 122.00–120.79 (m), 119.99, 61.38, 44.88, 35.27. ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.96 (s, 6F). HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1 mL min^{-1}, 254 nm, τ_R (major) = 4.6 min, τ_R (minor) = 5.6 min. HRMS calcd for $[C_{25}H_{17}F_6NO_2 + Na]^+$ requires *m*/*z* 500.1061, found *m*/*z* 500.1064.

2-Benzyl-1-oxo-*N*-phenyl-*N*-methyl-2,3-dihydro-1*H*-indene-2-carboxamide (6d). (White wax, 78% yield, 58% ee); $[\alpha]_D^{25}$ −16.2 (*c* 0.21, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 7.1 Hz, 2H), 7.04–6.77 (m, 12H), 3.53–3.34 (m, 3H), 3.30–3.14 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.39, 171.52, 151.31, 137.10, 135.69, 130.61, 127.55, 126.67, 126.38, 125.24, 123.50, 60.42, 42.47, 40.39, 37.09. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 13.6 min, τ_R (minor) = 11.5 min. HRMS calcd for $[C_{24}H_{21}NO_2 + Na]^+$ requires *m*/*z* 378.1470, found *m*/*z* 378.1467.

2-Benzyl-1-oxo-*N*-(4-*tert*-butyl-phenyl)-2,3-dihydro-1*H*-indene-2-carboxamide (6e). (White wax, 93% yield, 26% ee); $[\alpha]_D^{25}$ −4.2 (*c* 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.56 (td, *J* = 7.5, 1.2 Hz, 1H), 7.51–7.43 (m, 2H), 7.41–7.28 (m, 4H), 7.22–7.05 (m, 5H), 3.95 (d, *J* = 18.0 Hz, 1H), 3.47–3.08 (m, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.14, 167.36, 153.40, 147.34, 136.11, 135.20, 135.11, 135.08, 129.96, 128.24, 127.68, 127.31, 126.52, 125.81, 124.49, 119.83, 62.10, 45.52, 34.87, 34.42, 31.41. HPLC conditions: Chiralcel OJ-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1 mL min^{-1}, 254 nm, τ_R (major) = 10.4 min, τ_R (minor) = 16.1 min. HRMS calcd for $[C_{27}H_{27}NO_2 + Na]^+$ requires *m*/*z* 420.1939, found *m*/*z* 420.1943.

4-Bromine 2-Benzyl-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (6f). (White wax, 89% yield, 43% ee); $[\alpha]_D^{25}$ −4.0 (*c* 0.35, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.71

(dd, J = 20.5, 7.6 Hz, 2H), 7.61–7.47 (m, 2H), 7.34 (t, J = 7.9 Hz, 2H), 7.25–7.02 (m, 7H), 3.90 (d, J = 18.5 Hz, 1H), 3.45–3.11 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.52, 166.89, 152.92, 138.79, 137.56, 136.93, 134.60, 129.85, 129.39, 129.01, 128.30, 127.48, 124.51, 123.22, 121.92, 120.03, 62.35, 45.65, 36.20. HPLC conditions: Chiralcel OJ-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1 mL min^{-1}, 254 nm, τ_R (major) = 11.5 min, τ_R (minor) = 16.6 min. HRMS calcd for $[C_{23}H_{18}BrNO_2 + Na]^+$ requires m/z 442.0419, found m/z 442.0423.

2-Benzyl-1-oxo-*N*-(3,5-ditrifluoromethyl-phenyl)-2,3-dihydro-1*H*-indene-2-carboxamide (6g). (White wax, 87% yield, 31% ee); $[\alpha]_D^{25}$ −3.8 (c 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 8.02 (d, J = 1.4 Hz, 2H), 7.78 (d, J = 7.7 Hz, 1H), 7.67–7.59 (m, 2H), 7.49–7.33 (m, 2H), 7.24–7.15 (m, 3H), 7.10–7.01 (m, 2H), 3.93 (d, J = 18.0 Hz, 1H), 3.44–3.13 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.71, 168.29, 153.03, 138.97, 136.53, 134.50, 132.32 (q, J = 33.4 Hz), 129.86, 128.32, 127.96, 127.62, 126.56, 124.68, 123.08 (q, J = 272.5 Hz), 119.77 (d, J = 3.6 Hz), 117.77–117.26 (m), 61.90, 45.82, 35.06. ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.99 (s, 6F). HPLC conditions: Chiralcel OJ-H column (250 × 4.6 mm), hexane/i-PrOH = 95/5, 1 mL min^{-1}, 254 nm, τ_R (major) = 12.4 min, τ_R (minor) = 9.4 min. HRMS calcd for $[C_{25}H_{17}F_6NO_2 + Na]^+$ requires m/z 500.1061, found m/z 500.1064.

2-Benzyl-1-oxo-*N*-(*tert*-butyl)-2,3-dihydro-1*H*-indene-2-carboxamide(6h). (White wax, 83% yield, 4% ee); $[\alpha]_D^{25}$ −0.1 (c 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 7.6 Hz, 1H), 7.53 (td, J = 7.5, 1.3 Hz, 1H), 7.41–7.28 (m, 2H), 7.20–7.04 (m, 6H), 3.89 (d, J = 18.0 Hz, 1H), 3.29 (d, J = 13.5 Hz, 1H), 3.20–2.99 (m, 2H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.50, 168.29, 153.56, 135.72, 135.62, 135.34, 129.96, 128.04, 127.41, 127.03, 126.45, 124.20, 61.95, 51.25, 45.22, 34.91, 28.62. HPLC conditions: Chiralcel OJ-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL min^{-1}, 254 nm, τ_R (major) = 6.6 min, τ_R (minor) = 5.9 min. HRMS calcd for $[C_{21}H_{23}NO_2 + Na]^+$ requires m/z 344.1626, found m/z 344.1628.

Conflicts of interest

There are no conflicts to declare.

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