JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

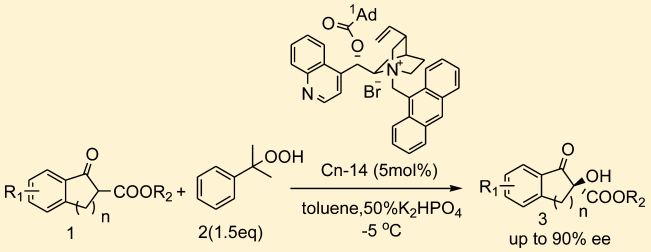
Asymmetric Direct α-Hydroxylation of β-Oxo Esters Catalyzed by Chiral Quaternary Ammonium Salts Derived from Cinchona Alkaloids

Hongjie Yao, Mingming Lian, Zhi Li, Yakun Wang, and Qingwei Meng*

State Key Laboratory of Fine Chemicals, School of Pharmaceutical Science and Technology, Dalian University of Technology, Dalian 116024, China

Supporting Information

ABSTRACT: Cinchona alkaloid-derived chiral quaternary ammonium organocatalysts were developed. The catalyst with a bulky 1-adamantoyl group at the C-9 position promoted the enantioselective α-hydroxylation of β-oxo esters and resulted in the corresponding products in 35−95% yields and 58−90% ee. The reaction was successfully scaled to a gram-quantity scale with a similar yield without loss of enantioselectivity.



INTRODUCTION

α-Hydroxydicarbonyl compounds represent a functional and common structural motif in a variety of natural products and pharmaceuticals, such as vindoline, kjellmanianone, hamigeran A, and doxycycline.[1] Moreover, optically active α-hydroxydicarbonyl compounds are important synthetic intermediates; for example, (*S*)-5-chloro-2-hydroxy-1-oxoindan-2-carboxylic acid methyl ester is the key intermediate in the manufacture of the insecticide indoxacarb.[2]

Because the cinchona alkaloids have been reported to provide moderate stereoselectivity in the asymmetric α-hydroxylation of dicarbonyl compounds,[3] the most convenient enantioselective synthesis of the α-hydroxydicarbonyl unit is through the direct oxidation of β-oxo esters by metal complexes and organocatalysts. Thus, for the past few years, efforts have been made toward the development of highly enantioselective catalysts. Metal complexes, such as the TASSOL−Ti complex,[4] the DBFOX−Ni complex,[5] and the BINAP−Pd complex,[6] have been reported to be effective catalysts for the enantioselective α-hydroxylation of β-oxo esters using oxaziridine as the oxidant. In the field of organocatalysis, Zhong et al. have used a chiral phosphoric acid as a catalyst and nitroso compounds as an oxidant to realize the highly enantioselective α-hydroxylation of β-oxo compounds.[7] However, these methodologies are limited by the use of expensive catalysts and complicated oxidants. Through our exploratory attempts, we found that lappaconitine[8] and the β-blocker inhibitor (*S*)-timolol derivatives[9] catalyzed the asymmetric α-hydroxylation reaction in moderate yields and enatioselectivities. Inspired by Maruoka's asymmetric alkylation of α-benzoyloxy β-oxo esters to produce similar chiral compounds and other catalytic asymmetric α-oxidation by phase-transfer catalysis,[10] we also developed a phase-transfer catalyst to achieve the asymmetric α-hydroxylation of β-oxo esters.[11] We used *N*-(3-trifluoromethylbenzyl)dihydrocinchoninium bromide as the catalyst under the phase-transfer catalysis conditions, which resulted in the corresponding hydroxylation products with 65−74% ee. The major issue was that the stereoselectivities of this catalyst system were moderate; it was clear to us that our catalyst system required further optimization. Herein, we report our recent progress on the asymmetric α-hydroxylation of β-oxo esters via phase-transfer catalysis. By modifying the hydroxyl and quaternary nitrogen groups of alkaloid catalysts using bulky groups, the enantioselectivity of the α-hydroxyaltion of β-oxo esters reached 90%.

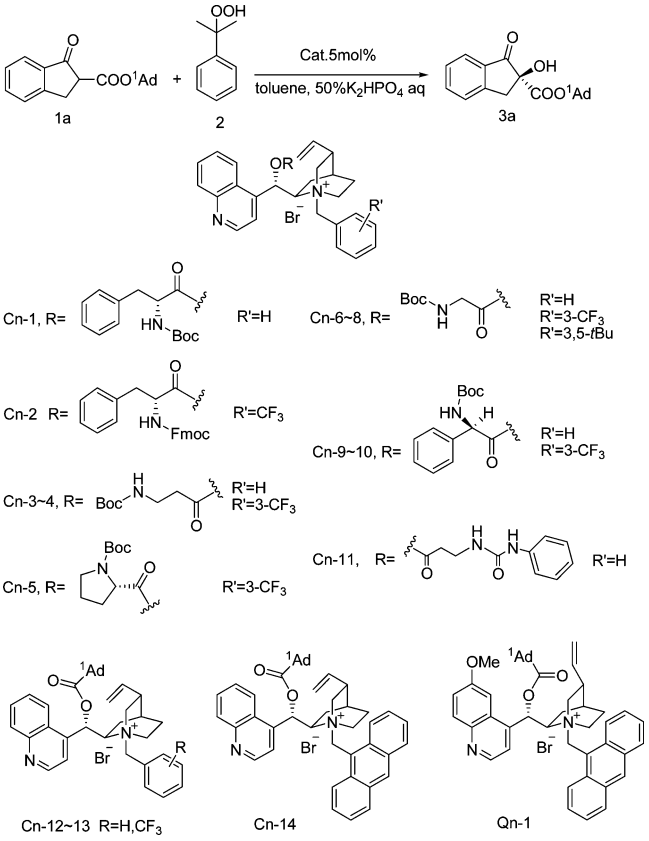
RESULTS AND DISCUSSION

The combination of small molecules with macromolecules is believed to be an effective strategy to generate a variety of new catalysts. For example, Lectka reported that active (*R*)-bromoesters catalyzed by a proline−cinchona alkaloid conjugated catalyst and 1,1,3,6-tetrabromonaphthalen-2-(1*H*)-one as the brominating agent gave yields as high as 68% and 99% ee.[12] This strategy prompted us to investigate cinchona catalysts through protection of the chiral secondary alcohol of the present phase-transfer catalysts.

Initially, we attempted the α-hydroxylation of 1-indanone-derived β-oxo ester **1a** with commercially available cumyl hydroperoxide (CHP) using Cn-1 (5 mol %) as the catalyst in combination with K_2HPO_4 (50% aq), which furnished **3a** in 83% yield with a moderate ee value of 52% (Table 1, entry 1). Prompted by this result, we undertook an initial screening of some similar catalysts with the chiral secondary alcohol protected by Boc-amino acids (phenylalanine, β-alanine, proline, glycine, and D-phenylglycine). All of the above catalysts showed similar catalytic activities (Table1, entries 1−11); among the investigated catalysts, Cn-7 gave the best performance with 85% yield and 69% ee (Table 1, entry 7). When the configuration of the amino acids was changed from L to D, the

Received: August 3, 2012
Published: October 10, 2012

Table 1. Screening of Phase-Transfer Catalysts for the Organocatalytic α-Hydroxylation of β-Oxo Ester 1a[a]



entry	catalyst	yield[b] (%)	ee[c] (%)
1	Cn-1	83	52(s)[d]
2	Cn-2	82	60
3	Cn-3	79	54
4	Cn-4	82	56
5	Cn-5	76	41
6	Cn-6	81	62
7	Cn-7	85	69
8	Cn-8	83	69
9	Cn-9	78	55
10	Cn-10	75	61
11	Cn-11	65	30
12	Cn-12	88	42
13	Cn-13	89	44
14	Cn-14	90	88
15	Qn-1	89	84

[a]The reaction was performed with 0.2 mmol of **1a**, 1.5 equiv of cumyl hydroperoxide (CHP), and 50% aq K_2HPO_4 (1 mL) in the presence of 5 mol % of catalyst in toluene (2 mL) under −5 °C for 60 h. [b]Isolated yield (**3a**). [c]The enantiomeric excess was determined by HPLC analysis of product **3a** using a chiral column (DAICEL Chiralcel AD-H) with hexane/2-propanol (80:20) as the eluent. [d]The absolute configuration was determined by comparison with the optical rotation and the HPLC retention time of an authentic sample.[14]

absolute stereochemistry of the products was not reversed, and the reaction was not improved (Table 1, entries 9 and 10 vs 1−8). In contrast, the Cn-11 with a urea substitution decreased the catalytic activity significantly (Table 1, entry 11).

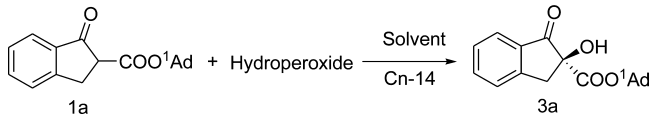
Although we did not obtain the desired effect with these catalysts, the results indicated that the esterification of the C-9 hydroxy group would affect the catalytic activity of the catalysts; we therefore introduced Cn-12, Cn-13, Cn-14, and Qn-1, in which the chiral secondary alcohol was protected by a bulky 1-adamantyl group.[13] Compared with amino acid groups, the 1-adamantyl group is expected to provide greater configurational rigidity. Both the Cn-12 and Cn-13 catalysts gave high yields but decreased the ee values (Table 1, entries 12 and 13). However, when the benzyl group was replaced with an anthracene group, the ee value was improved to 88% (Table 1, entry 14). We also evaluated the quinidine-based catalyst Qn-1 in addition to the cinchonine-based derivative Cn-14, which resulted in the corresponding hydroxylation product **3a** in 89% yield and 84% ee (Table 1, entry 15).

After a suitable catalyst was identified, further reaction optimization was undertaken. Table 2 summarizes the effect of several parameters on this reaction. We found that changing cumyl hydroperoxide (CHP) to *tert*-butyl hydroperoxide (TBHP) led to a slightly lower yield and ee value (Table 2, entry 2). Performing the reaction at either lower or higher temperature reduced the enantioselectivity of the product (Table 2, entries 3 and 4). Variation of either the oxidant used (Table 2, entry 5) or the catalyst loading (Table 2, entries 6 and 7) failed to improve the enantioselectivity. Dilution of the reaction also did not give positive results (Table 2, entries 8 and 9). We also tested other bases (Table 2, entries 10−14); for example, the base was changed from 50% K_2HPO_4 to 30% K_2CO_3, and although this change led to complete conversion, it also led to lower ee (Table 2, entry 10). The use of an organic base or a solid resulted in an obvious decrease in the product ee value (Table 2, entries 11−14). These results collectively revealed that the original reaction conditions were the best ones. Under the optimized conditions, the hydroxylation process was considerably more enantioselective in the phase-transfer catalysis method (where a relatively stable and commercially available cumyl hydroperoxide and a cinchonine-based ammonium salt at lower loading were used) at −5 °C.

The scope of the method was next probed using various β-oxo esters (Table 3). First, substituted 1-Ad esters were investigated. The reactivity of **1b** and **1c** bearing an electron-donating group afforded the corresponding products **3b** and **3c** in high yields and high enantioselectivities (Table 3, entries 2 and 3). Slightly modified conditions were needed for the 5,6-dimethoxy β-oxo ester because of its lower reactivity; however, it still gave excellent results (Table 3, entry 4). Halogen substitutions were uniformly tolerated (Table 3, entries 5−7) and afforded the oxidation products in satisfactory yields and enantioselectivities. Interestingly, although not significant, the yields and enantioselectivities of the current asymmetric oxidation using Cn-14 were influenced by the substituent on the benzene ring of the indanone derivatives (Table 3, entries 1−7). For example, a bromine substituent at the C-6 position decreased the ee value to 58% (Table3, entry 5), and a bromine substituent at the C-4 position decreased the enantioselectivity from 88 to 76% (Table 3, entry 6), whereas a methoxy substituent was less influential (Table 3, entries 2−4). These results indicate that electron-withdrawing substituents on the indanone derivatives deteriorate the observed enantioselectivities. When the 1-Ad of R_2 was changed to 2-Ad, complete conversion and a good yield were achieved, although the observed ee value decreased (Table 3, entry 8). *tert*-Butyl esters and 3-ethyl amyl esters were investigated. The α-hydroxylation of these substrates gave moderate to good yields and 78−85% ee values (Table 3, entries 9−14). Despite having results similar

dx.doi.org/10.1021/jo3016242 | J. Org. Chem. 2012, 77, 9601−9608

Table 2. Optimization of the Reaction Conditions



entry	sub (mmol)	solvent (2 mL)	oxidant (equiv)	Cn-14 (mol %)	T (°C)	base	yield[a] (%)	ee[b] (%)
1	0.2	PhMe	CHP (1.5)	5	−5	50% K_2HPO_4	90	88
2	0.2	PhMe	TBHP (1.5)	5	−5	50% K_2HPO_4	82	82
3	0.2	PhMe	CHP (1.5)	5	0	50% K_2HPO_4	92	83
4	0.2	PhMe	CHP (1.5)	5	−15	50% K_2HPO_4	78	80
5	0.2	PhMe	CHP (1.2)	5	−5	50% K_2HPO_4	83	88
6	0.2	PhMe	CHP (1.5)	2.5	−5	50% K_2HPO_4	76	80
7	0.2	PhMe	CHP (1.5)	10	−5	50% K_2HPO_4	92	85
8	0.1	PhMe	CHP (1.5)	5	−5	50% K_2HPO_4	85	87
9	0.05	PhMe	CHP (1.5)	5	−5	50% K_2HPO_4	80	80
10	0.2	PhMe	CHP (1.5)	5	−5	30% K_2CO_3	97	23
11	0.2	PhMe	CHP (1.5)	5	−5	iPr$_2$EtN (0.3 equiv)	nd	19
12	0.2	CH_2Cl_2	CHP (1.5)	5	−5	iPr$_2$EtN (0.3 equiv)	nd	21
13	0.2	PhMe	CHP (1.5)	5	−5	K_2HPO_4(0.5 g)	84	40
14	0.2	PhMe	CHP (1.5)	5	−5	K_2CO_3(0.3 g)	95	0

[a]Isolated yields. [b]The enantiomeric excess was determined by HPLC analysis of the product **3a** using a chiral column (DAICEL Chiralcel AD-H) with hexane/2-propanol (80:20) as the eluent.

to those of the 1-Ad esters, the yields and enantioselectivities were slightly lower with the *tert*-butyl esters and 3-ethyl amyl esters. These results suggest that the 1-Ad moiety was better suited to provide a good yield and selectivity than were other bulky ester groups.

The scope of the reaction was further probed using six-membered cyclic and acyclic substrates. The six-membered cyclic substrates 1-tetralone-derived β-oxo esters were not active and only gave 35% yields and moderate ee values (Table 3, entries 15 and 16). Notably, the asymmetric oxidations of such substrates, even in low yields, are typically very challenging.[15] The simple β-oxo ester **1q** could not be oxidized when THP was used as the oxygen source under the investigated reaction conditions (Table 3, entry 17), and acyclic substrate **1r** was inert under our asymmetric oxidation conditions, even when aqueous NaOH solution was used as the base (Table 3, entry 18). To test the generality of our asymmetric oxidation, **1a** was treated with CHP (1.5 equiv) on a gram-quantity scale. After only 30 h at −5 °C, the hydroxylation product was obtained in 85% yield without any loss of enantioselectivity (87% ee). The shorter reaction time was ascribed to the intensive mixing conditions under high-speed mechanical agitation (800 rpm).

CONCLUSION

In conclusion, although the application value of traditional organocatalysts was restricted, we found that the cinchona alkaloid catalysts with a bulky 1-adamantyl group at C-9 are capable of promoting the desired enantioselective α-hydroxylation of 1-indanone-derived β-oxo esters under mild conditions. High selectivity was obtained for a range of substituted indanone derivatives (58−90% ee). Another significant improvement over the literature benchmark is that the enantioselective α-hydroxylation of 1-tetralone-derived β-oxo ester (**1o** and **1p**) was also achieved. Moreover, this improved α-oxidation method for β-oxo esters was successfully scaled up to a gram-quantity in 85% yield without loss of enantioselectivity (87% ee).

EXPERIMENTAL SECTION

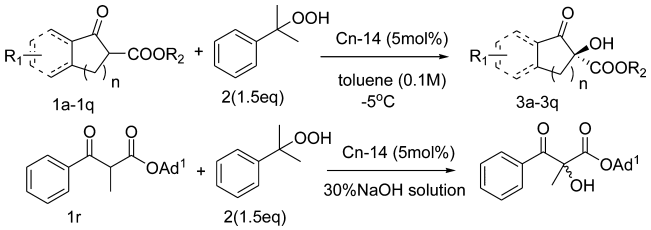
General Procedure for the Synthesis of Phase-Transfer Catalysts. The phase-transfer catalysts Cn-1 to Cn-10 were synthesized following known procedures.[12] To a flame-dried flask equipped with a magnetic stirring bar and a reflux condenser were added cinchoninium bromide, dried CH_2Cl_2 (10 mL), and the desired Boc-amino acids, dimethylaminopyridine (0.1 equiv); the solution was subsequently cooled to 0 °C. Dicyclohexylcarbodiimide (2.5 equiv) dissolved in 10 mL of CH_2Cl_2 was then added, and the reaction was allowed to warm to room temperature overnight. The reaction mixture was filtered, and the filtrate was concentrated. The residue was separated by CC (CH_2Cl_2/MeOH = 50:3) to give a solid.

O(9)-Boc-Phenylalanineyl-N-benzylcinchoninium Bromide (Cn-1): White powder (1.33 g, yield 86.8%); $[\alpha]_D^{20}$ 71.0 (c 0.10, MeOH); mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 4.3 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.64 (s, 2H), 7.59 (t, J = 9.0 Hz, 2H), 7.54 (d, J = 7.3 Hz, 1H), 7.48 (t, J = 7.2 Hz, 4H), 7.40 (d, J = 4.4 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H), 7.15 (t, J = 7.4 Hz, 2H), 6.67 (d, J = 7.1 Hz, 2H), 6.38 (d, J = 12.0 Hz, 1H), 6.11−5.90 (m, 1H), 5.47 (t, J = 11.1 Hz, 1H), 5.35 (d, J = 10.2 Hz, 1H), 5.18 (d, J = 16.9 Hz, 1H), 5.10 (dd, J = 14.4, 10.0 Hz, 1H), 4.38 (t, J = 9.8 Hz, 1H), 4.09 (d, J = 12.1 Hz, 1H), 3.45−3.33 (m, 1H), 3.14 (dd, J = 14.0, 5.3 Hz, 1H), 2.78 (dd, J = 20.9, 9.8 Hz, 1H), 2.41−2.25 (m, 2H), 1.89 (s, 1H), 1.77 (d, J = 9.9 Hz, 1H), 1.68 (s, 1H), 1.63 (s, 9H), 1.04 (s, 1H), 0.88 (t, J = 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 155.8, 149.1, 147.0, 138.8, 136.7, 135.2, 134.6, 130.7, 129.7, 129.5, 129.1, 129.0, 128.8, 127.3, 126.8, 123.6, 122.7, 119.1, 118.3, 80.2, 68.5, 65.1, 62.5, 55.9, 55.0, 54.0, 38.3, 37.2, 28.6, 27.2, 23.4, 22.2; HRMS(ES+) calcd for $[C_{40}H_{46}N_3O_4Br - Br]^+$ 632.3488, found 632.3499.

O(9)-Fmoc-Phenylalanineyl-N-(3-trifluoromethylbenzyl)-cinchoninium Bromide (Cn-2): Yellowish powder (1.1 g, yield 65.4%); $[\alpha]_D^{25}$ 31.0 (c 0.2, MeOH); mp 150−152 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 3.5 Hz, 2H), 8.62 (s, 1H), 8.06 (s, 1H), 7.96 (d, J = 7.5 Hz, 1H), 7.83 (s, 1H), 7.75 (t, J = 6.7 Hz, 3H), 7.59 (m, J = 8.7 Hz, 6H), 7.41 (dd, J = 14.2, 7.0 Hz, 2H), 7.31 (m, J = 12.6, 5.5 Hz, 6H), 7.07 (s, 2H), 6.42 (d, J = 11.8 Hz, 1H), 6.02−5.85 (m, 1H), 5.53 (s, 1H), 5.19 (dd, J = 27.4, 13.7 Hz, 1H), 4.84 (s, 1H), 4.68 (s, 1H), 4.54−4.42 (m, 1H), 4.38−4.30 (m, 1H), 4.26 (d, J = 11.7 Hz, 1H), 4.18 (t, J = 7.1 Hz, 1H), 3.41−3.18 (m,3H), 2.75−2.59 (m, 1H), 2.43 (d, J = 8.7 Hz, 1H), 2.37−2.26 (m, 1H), 2.02−1.79 (m, 3H), 1.73 (s, 1H), 1.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 156.7, 149.0, 147.4, 143.5, 143.3, 141.2, 139.1, 138.5,

dx.doi.org/10.1021/jo3016242 | J. Org. Chem. 2012, 77, 9601−9608

Table 3. Substrate Scope Evaluation[a]



entry	sub	*n*	R_1	R_2	yield[b] (%)	ee[c] %
1	**1a**	1	H	^{1}Ad	90	88
2	**1b**	1	6-MeO	^{1}Ad	85	86
3	**1c**	1	4-MeO	^{1}Ad	83	90
4[d]	**1d**	1	5,6-diMeO	^{1}Ad	61	90
5	**1e**	1	6-Br	^{1}Ad	45	58
6	**1f**	1	4-Br	^{1}Ad	73	76
7	**1g**	1	5-Cl	^{1}Ad	88	82
8	**1h**	1	H	^{2}Ad	95	75
9[e]	**1i**	1	H	*t*Bu	79	78
10	**1j**	1	4-MeO	*t*Bu	75	84
11[f]	**1k**	1	H	3-ethyl amyl	70	83
12	**1l**	1	4-MeO	3-ethyl amyl	78	82
13[d]	**1m**	1	5,6-diMeO	3-ethyl amyl	82	85
14[f]	**1n**	1	5-Cl	3-ethyl amyl	69	79
15	**1o**	2	H	methyl	35(98)	63(44)[g]
16[i]	**1p**	2	H	^{1}Ad	35	71
17[j]	**1q**	1	without benzene ring	Bn	trace	nd
18[j]	**1r**			^{1}Ad	trace	nd

[a]Unless otherwise specified, the reaction was performed with **1** (0.2 mmol) and 5 mol % of catalyst Cn-14 in a mixture of toluene (2 mL) and 50% aqueous K_2HPO_4 solution at −5 °C. [b]Isolated yields. [c]The enantiomeric excess was determined by HPLC analysis of the product using a chiral column (DAICEL Chiralcel AD-H) with hexane/2-propanol as the eluent. [d]Oxidant loading: 2.0 equiv. Reaction time: 80 h. [e]The enantiomeric excess was determined by HPLC analysis of the product using a chiral column (DAICEL Chiralcel OD-H) with hexane/2-propanol as the eluent. [f]The enantiomeric excess was determined by HPLC analysis of the product using a chiral column (DAICEL Chiralcel AS-H) with hexane/2-propanol as the eluent. [g]For cases where 30% K_2CO_3 was used as the base, the ee value and yield are given in parentheses. [i]By using 30% K_2CO_3 as base. [j]Monitored by TLC.

136.5, 134.9, 131.6, 131.3, 130.1, 129.8, 129.7, 129.0, 128.4, 127.9, 127.8, 127.3, 127.3, 127.2, 125.4, 125.3, 124.2, 123.2, 122.2, 119.9, 119.2, 118.4, 69.3, 67.3, 65.7, 61.2, 56.3, 56.1, 54.6, 47.0, 38.0, 36.7, 30.6, 26.9, 23.3, 22.6; HRMS(ES+) calcd for $[C_{51}H_{47}N_3O_4F_3Br - Br]^+$ 822.3519, found 822.3533.

O(9)-Boc-β-Alanineyl-N-benzylcinchoninium Bromide (Cn-3): White powder (1.4 g, yield 67.6%); $[\alpha]_D^{25}$ 89.0 (*c* 0.10, MeOH); mp 153−156 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 4.2 Hz, 1H), 8.80 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 5.3 Hz, 3H), 7.82 (t, *J* = 7.2 Hz, 1H), 7.48 (s, 3H), 7.43 (s, 2H), 6.30 (d, *J* = 11.6 Hz, 1H), 6.04−5.89 (m, 1H), 5.55 (s, 1H), 5.32 (dd, *J* = 45.4, 13.8 Hz, 4H), 5.15 (s, 1H), 4.88 (s, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 3.79 (t, *J* = 10.5 Hz, 1H), 3.69 (t, *J* = 11.5 Hz, 1H), 3.55 (s, 1H), 3.46 (s, 2H), 2.91 (dd, *J* = 11.1, 5.6 Hz, 3H), 2.56 (d, *J* = 8.4 Hz, 1H), 2.45−2.29 (m, 1H), 2.04 (s, 1H), 1.99 (s, 2H), 1.82 (s, 1H), 1.43 (s, 9H), 1.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 156.2, 149.3, 148.1, 140.0, 135.4, 134.3, 130.7, 130.4, 129.9, 129.2, 126.6, 124.5, 124.0, 118.5, 118.1, 79.7, 69.1, 65.2, 62.4, 56.4, 54.7, 37.5, 35.5, 28.4, 26.9, 23.4, 22.6; HRMS (ES+) calcd for $[C_{34}H_{42}N_3O_4Br - Br]^+$ 556.3175, found 556.3188.

O(9)-Boc-β-Alanineyl-N-(3-trifluoromethylbenzyl)cinchoninium Bromide (Cn-4): Yellowish powder (0.5 g, yield 63.4%); $[\alpha]_D^{25}$ 75.0 (*c* 0.10, MeOH); mp 147−149 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.2 Hz, 1H), 8.65 (t, *J* = 11.6 Hz, 1H), 8.58 (d, *J* = 6.9 Hz, 1H), 8.27 (s, 1H), 8.05 (d, J = 8.3 Hz, 1H), 7.87 (t, *J* = 7.2 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 4.1 Hz, 1H), 7.32 (d, *J* = 3.7 Hz, 1H), 6.17 (d, *J* = 11.5 Hz, 1H), 5.99 (ddd, *J* = 17.1, 10.2, 6.8 Hz, 1H), 5.50 (s, 1H), 5.44−5.25 (m, 3H), 4.80 (dd, *J* = 21.8, 11.0 Hz, 2H), 4.15−3.92 (m, 1H), 3.81−3.54 (m, 2H), 3.48 (d, *J* = 5.1 Hz, 1H), 2.97 (s, 1H), 2.89- 2.67 (m, 2H), 2.60 (d, *J* = 7.5 Hz, 1H), 2.54−2.36 (m, 1H), 2.04 (s, 1H), 1.84 (dd, *J* = 25.6, 10.2 Hz, 2H), 1.36 (s, 9H), 1.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 156.3, 149.2, 148.2, 139.9, 138.5, 135.2, 131.5, 131.2, 130.5, 130.0, 129.9, 129.2, 127.9, 127.6, 124.9, 124.5, 124.1, 122.2, 118.8, 118.0, 79.9, 69.3, 65.6, 61.3, 56.4, 55.1, 37.6, 36.5, 35.9, 28.3, 26.9, 23.4, 22.7; HRMS (ES+) calcd for $[C_{35}H_{41}N_3O_4F_3Br - Br]^+$ 624.3049, found 624.3030.

O(9)-Boc-Prolineyl-N-(3-trifluoromethylbenzyl)cinchoninium Bromide (Cn-5): Yellowish powder (1.1 g, yield 80.3%); $[\alpha]_D^{20}$ 57.0 (*c* 0.10, MeOH); mp 144−146 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 8.4 Hz, 1H), 8.93 (d, *J* = 4.5 Hz, 1H), 8.83 (d, *J* = 7.5 Hz, 1H), 8.23−8.11 (m, 2H), 8.05 (t, *J* = 7.5 Hz, 1H), 7.93−7.82 (m, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.68 (t, *J* = 7.7 Hz, 1H), 7.60 (s, 1H), 7.43 (d, *J* = 4.3 Hz, 1H), 6.54 (d, *J* = 11.6 Hz, 1H), 6.06−5.81 (m, 2H), 5.38 (d, *J* = 10.4 Hz, 1H), 5.30 (t, *J* = 8.6 Hz, 1H), 5.08 (t, *J* = 9.6 Hz, 1H), 4.60 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.30 (d, *J* = 11.6 Hz, 1H), 3.88−3.77 (m, 1H), 3.71−3.58 (m, 2H), 3.53−3.37 (m, 1H), 2.88−2.73 (m, 1H), 2.64−2.50 (m, 1H), 2.38 (dd, *J* = 23.0, 11.2 Hz, 2H), 2.24 −2.10 (m, 3H), 2.04(s, 4H), 1.84(s, 1H), 1.72 (s, 2H), 1.48 (s, 9H), 1.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 155.7, 149.0, 148.3, 139.6, 138.4, 135.6, 131.6, 131.3, 130.7, 129.9, 129.8, 129.4, 127.9, 127.6, 125.0, 124.1, 122.3, 119.1, 117.8, 81.4, 69.3, 64.9, 61.0, 60.0, 56.0, 55.2, 53.5, 47.7, 37.9, 30.3, 28.5, 28.4, 27.5, 25.2, 23.3, 22.8; HRMS (ES+) calcd for $[C_{37}H_{43}N_3O_4F_3Br - Br]^+$ 650.3206, found 650.3220.

O(9)-Boc-Glycineyl-N-benzylcinchoninium Bromide (Cn-6): White powder (0.37 g, yield 74.0%); $[\alpha]_D^{25}$ 121.0 (*c* 0.10, MeOH); mp 158−160 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 8.9 Hz, 1H), 8.19 (d, *J* = 6.7 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.00 (t, *J* = 7.6 Hz, 1H), 7.76 (t, *J* = 7.5 Hz, 1H), 7.63 (s, 1H), 7.48−7.37 (m, 2H), 7.22 (d, *J* = 3.5 Hz, 1H), 6.24 (s, 1H), 6.16 (d, *J* = 11.7 Hz, 1H), 5.92 (ddd, *J* = 16.9, 10.5, 6.1 Hz, 1H), 5.43−5.20 (m, 1H), 4.66 (s, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.12 (qd, *J* = 16.8, 6.0 Hz, 1H), 4.00−3.90 (m, 1H), 3.66 (t, *J* = 11.9 Hz, 1H), 2.81 (m, 1H), 2.47 (d, *J* = 7.8 Hz, 1H), 2.31−2.17 (m, 1H), 1.97 (s, 1H), 1.93−1.81 (m, 1H), 1.76 (d, *J* = 10.7 Hz, 1H), 1.33 (s, 9H), 1.13 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 156.9, 149.3, 147.7, 139.2, 135.7, 134.5, 130.4, 130.0, 128.9, 126.9, 124.6, 123.4, 118.4, 118.1, 80.0, 68.5, 65.5, 62.4, 56.5, 54.4, 43.7, 37.4, 28.1, 27.0, 23.4, 22.5; HRMS(ES+) calcd for $[C_{33}H_{40}N_3O_4Br - Br]^+$ 542.3019, found 542.3024.

O(9)-Boc-Glycineyl-N-(3-trifluoromethylbenzyl)cinchoninium Bromide (Cn-7): Yellowish powder (0.37g, yield 71.4%); $[\alpha]_D^{20}$ 102.0 (*c* 0.10, MeOH); mp 168−170 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (1 H, d, *J* 8.4), 8.89 (1 H, d, *J* 7.6), 8.85 (1 H, d, *J* = 4.6), 8.21 (1 H, s), 8.13 (1 H, d, *J* = 8.4), 8.04 (1 H, t, *J* = 7.7), 7.83 (1 H, t, *J* = 7.3), 7.76 (1 H, d, *J* = 7.7), 7.65 (1 H, t, *J* = 7.8), 7.56 (1 H, s), 7.40 (1 H, d, *J* = 4.4), 6.42 (1 H, d, *J* = 11.6), 5.98 (1 H, ddd, *J* = 17.1, 10.4, 6.6), 5.63 (1 H, d, *J* = 9.0), 5.58 (1 H, t, *J* = 6.1), 5.40 (1 H, d, *J* = 10.4), 5.32 (1 H, d, *J* = 17.9), 4.97 (1 H, t, *J* = 8.9), 4.53 (1 H, d, *J* = 11.7), 4.16 (1 H, dd, *J* = 16.8, 6.1), 4.07−3.99 (1 H, m), 3.94 (1 H, dd, *J* = 16.9, 5.5), 3.63 (1 H, t, *J* = 12.0), 2.70 (1 H, dd, *J* = 20.9, 9.9), 2.57 (1 H, d, *J* = 8.0), 2.43−2.30 (1 H, m), 2.06 (1 H, s), 2.02−1.94 (1 H, m), 1.81 (2 H, s), 1.38 (9 H, s), 1.32 (1 H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 156.9, 149.3, 147.9, 139.3, 138.6, 135.4, 130.6, 130.2, 129.9, 129.7, 129.1, 128.1, 127.4, 124.9, 124.8, 123.8, 122.2, 118.8, 118.4, 80.4, 68.8, 65.7, 61.1, 56.5, 55.1, 43.8, 37.5, 28.1, 27.1, 23.4,

dx.doi.org/10.1021/jo3016242 | J. Org. Chem. 2012, 77, 9601−9608

22.7; HRMS (ES+) calcd for $[C_{34}H_{39}N_3O_4F_3Br - Br]^+$ 610.2893, found 610.2891.

O(9)-Boc-Glycineyl-N-(3,5-tert-butyllbenzyl)cinchoninium Bromide (Cn-8): Yellowish powder (0.1 g, yield 15.6%); $[\alpha]_D^{25}$ 95.0 (*c* 0.10, MeOH); mp 159−161 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 4.5 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 7.85 (s, 2H), 7.76−7.64 (m, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.47 (s, 1H), 6.09 (t, *J* = 5.9 Hz, 1H), 6.01 (ddd, *J* = 17.2, 10.4, 6.9 Hz, 1H), 5.77 (d, *J* = 12.0 Hz, 1H), 5.29 (dd, *J* = 24.8, 13.8 Hz, 2H), 5.17 (s, 1H), 4.58 (d, *J* = 11.6 Hz, 2H), 4.21 (t, *J* = 5.3 Hz, 2H), 4.03−3.90 (m, 1H), 3.84 (t, *J* = 11.5 Hz, 1H), 3.14 (dd, *J* = 20.2, 9.6 Hz, 1H), 2.62 (dd, *J* = 16.6, 8.5 Hz, 1H), 2.46−2.29 (m, 1H), 1.99 (s, 1H), 1.84 (d, *J* = 7.6 Hz, 2H), 1.41 (s, 9H), 1.35 (s, 18H), 1.25 (d, *J* = 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 156.5, 152.3, 149.6, 148.2, 139.7, 135.8, 130.2, 130.1, 128.9, 128.5, 126.1, 124.6, 124.0, 124.0, 118.7, 118.5, 80.3, 69.4, 64.9, 64.3, 56.9, 56.3, 43.6, 37.8, 35.1, 31.5, 28.3, 27.2, 23.7, 22.7; HRMS (ES+) calcd for $[C_{41}H_{56}N_3O_4Br - Br]^+$ 654.4271, found 654.4272.

O(9)-Boc-D-Phenylglycineyl-N-benzylcinchoninium Bromide (Cn-9): White powder (0.6 g, yield 92.7%); $[\alpha]_D^{25}$ 56.0 (*c* 0.10, MeOH); mp 148−150 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, *J* = 8.2 Hz, 1H), 8.38 (d, *J* = 4.6 Hz, 1H), 8.33−8.26 (m, 2H), 8.11−7.98 (m, 2H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 3.4 Hz, 2H), 7.48 (ddd, *J* = 17.5, 10.9, 4.9 Hz, 6H), 7.41−7.36 (m, 2H), 6.54 (d, *J* = 4.6 Hz, 1H), 6.38 (d, *J* = 11.4 Hz, 1H), 6.02 (ddd, *J* = 17.0, 10.5, 6.3 Hz, 1H), 5.75 (t, *J* = 11.0 Hz, 1H), 5.48 (d, *J* = 10.5 Hz, 1H), 5.40 (d, *J* = 17.6 Hz, 1H), 5.29 (td, *J* = 5.4, 2.4 Hz, 2H), 5.00 (t, *J* = 9.2 Hz, 1H), 4.56 (d, *J* = 11.4 Hz, 1H), 4.20−4.00 (m, 1H), 3.82−3.69 (m, 1H), 3.54 (d, *J* = 4.8 Hz, 1H), 3.54 (d, *J* = 4.8 Hz, 1H), 2.88 (dd, *J* = 20.7, 10.0 Hz, 1H), 2.58 (dd, *J* = 16.3, 8.2 Hz, 1H), 2.31−2.15 (m, 1H), 2.02 (d, *J* = 20.6 Hz, 1H), 1.82 (s, 2H), 1.47 (s, *J* = 4.2 Hz, 9H), 1.33−1.17 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 155.9, 148.7, 148.0, 139.1, 136.2, 134.6, 132.1, 130.5, 130.5, 130.2, 129.7, 129.5, 129.5, 128.9, 128.2, 127.0, 125.1, 124.0, 118.1, 117.5, 81.3, 69.1, 65.1, 64.9, 62.0, 59.8, 56.3, 54.5, 41.9, 37.3, 30.1, 29.1, 28.2, 26.9, 23.4, 23.3, 23.0, 22.7; HRMS(ES+) calcd for $[C_{39}H_{44}N_3O_4Br - Br]^+$ 618.3332, found 618.3346.

O(9)-Boc-D-Phenylglycineyl-N-(3-trifluoromethylbenzyl)-cinchoninium Bromide (Cn-10): Yellowish powder (0.23 g, yield 53.5%); $[\alpha]_D^{25}$ 53.0 (*c* 0.10, MeOH); mp 140−143 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (1 H, d, *J* = 7.8), 8.97 (1 H, d, *J* = 6.4), 8.39 (1 H, d, *J* = 4.6), 8.24 (1 H, s), 8.12 (1 H, d, *J* = 8.4), 8.02 (1 H, t, *J* = 7.3), 7.81 (2 H, m), 7.70 (1 H, t, *J* = 7.6), 7.52−7.55 (3 H, m), 7.47 (2 H, t, *J* = 7.4), 7.40 (1 H, s), 7.38 (1 H, s), 6.59 (1 H, s), 6.59 (1 H, s), 6.55 (1 H, m) 6.03 (1 H, ddd, *J* = 17.1, 10.5, 6.5), 5.84 (1 H, d, *J* = 9.0), 5.51 (1 H, d, *J* = 10.5), 5.41 (1 H, d, *J* = 17.3), 5.26 (2 H, d, *J* = 2.3), 5.09 (1 H, d, *J* = 9.4), 4.60 (1 H, d, *J* = 11.5), 4.19 (1 H, dd, *J* = 17.9, 7.1), 3.74−3.64 (1 H, m), 3.55 (2 H, d, *J* = 4.8), 2.81−2.68 (1 H, m), 2.63 (1 H, d, *J* = 7.4), 2.31- 2.18 (1 H, m), 2.04 (3 H, d, *J* = 13.6), 1.84 (3 H, s), 1.42 (9 H, s), 1.32−1.23 (1 H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 156.0, 148.7, 148.1, 139.0, 138.9, 135.8, 132.0, 130.6, 130.2, 129.9, 129.8, 129.6, 129.5, 128.3, 128.2, 125.2, 124.0, 118.4, 117.5, 81.5, 69.3, 65.2, 65.1, 60.9, 59.7, 56.4, 55.0, 42.0, 37.4, 30.1, 29.7, 29.1, 28.2, 28.1, 27.0, 23.4, 23.3, 23.1, 22.8; HRMS(ES+) calcd for $[C_{40}H_{43}N_3O_4F_3Br - Br]^+$ 686.3206, found 686.3177.

Cn-11: The catalyst was synthesized following known procedures. To a flame-dried flask equipped with a magnetic stirring bar were added Cn-3 (0.3 g) and dried CH_2Cl_2 (10 mL), and the solution was cooled to 0 °C, then TFA (1 mL) was added slowly and the reaction kept at this temperature for 4 h. The mixture was concentrated to ∼1 mL and poured onto Et_2O (100 mL). The precipitate was filtered and was washed thoroughly with Et_2O to give the primary amine product as a white solid. Phenylcarbimide solution (75 mg, 0.629 mmol in 5 mL of dried THF) was added to a suspension of the above primary amine (270 mg) in dried THF (7.5 mL). The reaction was stirred at room temperature for 8 h, then was concentrated, and the product was purified by CC (CH_2Cl_2/MeOH = 50:3) to give a bright powder (0.16 g, yield 78.7%): $[\alpha]_D^{25}$ 44 (*c* 0.10, MeOH); mp 165−168 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (1 H, d, *J* = 4.6), 8.28 (1 H, d, *J* = 8.4), 8.14 (1 H, d, *J* = 8.4), 7.90 (1 H, t, *J* = 7.7), 7.83 (1 H, t, *J* = 7.6), 7.75 (2 H, d, *J* = 7.5), 7.71 (1 H, d, *J* = 4.7), 7.56 (1 H, d, *J* = 7.2), 7.51 (2 H, t, *J* = 7.2), 7.45 (1 H, s), 7.34 (2 H, d, *J* = 7.8), 7.19 (2 H, t, *J* = 7.9), 6.96 (1 H, t, *J* = 7.4), 6.37 (1 H, s), 6.21 (1 H, ddd, *J* = 17.3, 10.4, 7.0), 5.39 (2 H, dd, *J* = 41.7, 30.4), 4.94 (2 H, d, *J* = 5.2), 4.14 (1 H, t, *J* = 9.2), 4.03−3.92 (1 H, m), 3.87−3.73 (2 H, m), 3.63 (2 H, m), 3.16−3.00 (2 H, m), 2.99−2.89 (1 H, m), 2.72 (2 H, d, *J* = 9.4), 2.07 (1 H, s), 1.89 (2 H, d, *J* = 10.0), 1.48 (1 H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 156.6, 149.2, 147.5, 140.2, 139.5, 135.0, 134.0, 130.9, 130.0, 129.9, 129.4, 128.7, 127.9, 126.5, 123.0, 122.5, 121.7, 118.9, 118.4, 117.6, 68.9, 66.4, 63.8, 56.9, 54.7, 37.4, 36.0, 35.2, 29.7, 26.7, 23.6, 22.4; HRMS (ES+) calcd for $[C_{36}H_{39}N_4O_3Br - Br]^+$ 575.3022, found 575.3022.

The phase-transfer catalysts Cn-12 to Cn-14 and Qn-1 were synthesized by an analogous procedure as reported by Jorgensen.[13] To a flame-dried flask equipped with a magnetic stirring bar and a reflux condenser was added cinchoninium bromide or quinidium bromide (1 mmol), CH_2Cl_2 (10 mL), and adamantane carbonyl chloride (0.6 g, 3.2 mmol) was added to a suspension of the above salt; 30% w/w NaOH solution (1.4 mL) was added, and the suspension was stirred vigorously at room temperature for 30 min, during which time the solid fully dissolved. Water (10 mL) was added, and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic fractions were dried by Na_2SO_4, filtered, and concentrated to ∼1 mL and then poured onto Et_2O (30 mL). The precipitate was filtered and washed thoroughly with Et_2O to give the products as a solid. The product was purified by a neutral alumina column (CH_2Cl_2/MeOH = 20:1) to give a bright powder.

O-1-Adamantoyl-N-benzylcinchoninium Bromide (Cn-12): White powder (0.6 g, yield 98.3%); $[\alpha]_D^{20}$ 65.0 (*c* 0.10, MeOH); mp 147−149 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J* = 8.4 Hz, 1H), 8.92 (d, *J* = 4.6 Hz, 1H), 8.16 (d, *J* = 8.3 Hz, 1H), 8.02 (t, *J* = 7.6 Hz, 1H), 7.89−7.83 (m, 3H), 7.55−7.51 (m, 3H), 7.49 (d, *J* = 2.3 Hz, 1H), 7.40 (d, *J* = 4.5 Hz, 1H), 6.48 (d, *J* = 11.8 Hz, 1H), 6.01 (ddd, *J* = 17.3, 10.4, 7.0 Hz, 1H), 5.77 (t, *J* = 11.0 Hz, 1H), 5.43−5.20 (m, 3H), 4.99 (t, *J* = 9.5 Hz, 1H), 4.17 (d, *J* = 11.7 Hz, 1H), 3.78 (dt, *J* = 22.5, 11.0 Hz, 2H), 2.95 (dd, *J* = 21.2, 10.0 Hz, 1H), 2.58 (dd, *J* = 16.9, 9.0 Hz, 1H), 2.45−2.34 (m, 1H), 2.19 (s, 4H), 2.10 (s, 9H), 1.83 (dd, *J* = 32.4, 12.0 Hz, 8H), 1.44−1.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 149.0, 148.2, 140.5, 135.1, 134.0, 130.8, 130.6, 129.6, 129.4, 129.2, 126.6, 125.0, 124.2, 118.9, 117.6, 68.6, 64.9, 62.3, 56.0, 54.7, 41.1, 39.2, 39.1, 37.8, 36.2, 27.6, 26.8, 23.4, 23.0; HRMS(ES+) calcd for $[C_{37}H_{43}N_2O_2Br - Br]^+$ 547.3325, found 547.3329.

O-1-Adamantoyl-N-(3-trifluoromethylbenzyl)cinchoninium Bromide (Cn-13): Yellowish powder (0.71 g, yield 98%); $[\alpha]_D^{20}$ 64.0 (*c* 0.10, MeOH); mp 142−144 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, *J* = 8.4 Hz, 1H), 8.93 (d, *J* = 4.5 Hz, 1H), 8.56 (d, *J* = 7.5 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 8.02 (t, *J* = 7.7 Hz, 1H), 7.90−7.76 (m, 2H), 7.75−7.68 (m, 2H), 7.49 (s, 1H), 7.41 (d, *J* = 4.5 Hz, 1H), 6.76 (d, *J* = 11.9 Hz, 1H), 6.02 (ddd, *J* = 17.2, 10.4, 7.1 Hz, 1H), 5.91 (t, *J* = 11.0 Hz, 1H), 5.48−5.18 (m, 2H), 5.06 (t, *J* = 9.6 Hz, 1H), 4.20 (d, *J* = 11.8 Hz, 1H), 3.86 (t, *J* = 9.6 Hz, 1H), 3.61 (t, *J* = 11.1 Hz, 1H), 2.87 (dd, *J* = 20.9, 9.9 Hz, 1H), 2.68−2.50 (m, 1H), 2.42 (t, *J* = 12.4 Hz, 1H), 2.17 (d, *J* = 20.9 Hz, 3H), 2.08 (d, *J* = 18.9 Hz, 9H), 1.84 (dd, *J* = 34.3, 12.3 Hz, 9H), 1.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 148.8, 148.1, 140.4, 138.3, 134.8, 130.9, 130.5, 129.7, 129.6, 129.4, 127.9, 127.7, 124.9, 124.3, 119.2, 117.6, 68.6, 65.2, 61.3, 56.1, 55.0, 41.2, 39.2, 39.1, 37.9, 36.2, 27.7, 26.9, 23.4, 23.0; HRMS (ES+) calcd for $[C_{38}H_{42}F_3N_2O_2Br - Br]^+$ 615.3198, found 615.3193.

O-1-Adamantoyl-N-(9-anthracenylmethyl)cinchonium Bromide (Cn-14): Yellow powder (0.71 g, yield 97.5%); $[\alpha]_D^{20}$ 136.0 (*c* 0.10, MeOH); mp 101−103 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (d, *J* = 8.9 Hz, 1H, CH Ar), 9.03 (d, *J* = 4.2 Hz, 1H, CH Ar), 8.94 (d, *J* = 8.4 Hz, 1H, CH Ar), 8.69 (s, 1H, CH Ar), 8.26 (d, *J* = 8.3 Hz, 1H, CH Ar), 8.19- 8.11 (m, 1H, CH Ar), 8.06 (d, *J* = 8.4 Hz, 2H, 2 × CH Ar), 7.98 (t, *J* = 7.7 Hz, 1H, CH Ar), 7.89 (m, 3H, 3 × CH Ar), 7.81 (d, *J* = 4.1 Hz, 1H, CH Ar), 7.66−7.52 (m, 3H, 3 × CH Ar), 6.44 (d, *J* = 13.3 Hz, 1H, CHO), 6.01 (t, *J* = 8.9 Hz, 1H, CHN methylanthracene), 5.93 (ddd, *J* = 17.1, 10.3, 6.7 Hz, 1H, CH vinyl), 5.83 (t, *J* = 10.7 Hz, 1H, CHN methylanthracene), 5.27 (d, *J* = 10.3 Hz, 1H, CHH′ vinyl), 5.06(d, *J* = 17.1 Hz, 1H, CHH′ vinyl), 3.81

dx.doi.org/10.1021/jo3016242 | J. Org. Chem. 2012, 77, 9601−9608

(t, J = 10.1 Hz, 1H, CHN), 3.81 (t, J = 10.1 Hz, 1H, CHN), 3.18 (t, J = 11.4 Hz, 1H, CHN), 3.18 (t, J = 11.4 Hz, 1H, CHN), 2.57 (m, 3H), 2.22 (s, 6H), 2.18 (s, 6H), 2.02 (d, J = 16.4 Hz, 2H), 1.89 (dd, J = 25.3, 12.8 Hz, 8H), 1.73 (d, J = 11.9 Hz, 1H), 1.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 149.1, 148.5, 148.5, 140.7, 135.4, 134.1, 134.0, 132.7, 131.5, 130.6, 130.6, 130.3, 129.8, 129.4, 128.8, 127.6, 126.9, 126.4, 125.1, 124.9, 123.6, 122.5, 118.9, 118.5, 69.0, 65.7, 56.9, 55.3, 54.9, 41.5, 39.5, 38.8, 36.3, 27.8, 27.2, 25.9, 23.9, 23.3; HRMS (ES+) calcd for $[C_{45}H_{47}N_2O_2Br - Br]^+$ 647.3638, found 647.3646.

O-1-Adamantoyl-N-(9-anthracenylmethyl)quinidium Bromide (Qn-1): Yellow powder (0.75 g, yield 98.0%); $[\alpha]_D^{25}$ 160.0 (c 0.10, MeOH); mp 108−110 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (d, J = 8.8 Hz, 1H), 8.83 (s, 1H), 8.72 (s, 1H), 8.16 (d, J = 8.7 Hz, 2H), 8.08 (d, J = 8.2 Hz, 3H), 8.01−7.89 (m, 3H), 7.83 (d, J = 7.9 Hz, 2H), 7.76 (d, J = 4.3 Hz, 1H), 7.65−7.53 (m, 4H), 7.49 (d, J = 9.3 Hz, 1H), 6.35 (s, 1H), 6.25 (s, 1H), 5.96 (m, 2H), 5.70 (d, J = 13.4 Hz, 1H), 5.28 (d, J = 10.3 Hz, 1H), 5.08 (d, J = 17.4 Hz, 1H), 4.35 (s, 3H), 3.23 (t, J = 11.4 Hz, 1H), 2.75−2.60 (m, 1H), 2.53−2.46 (m, 1H), 2.23−1.51 (m, 24H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 175.9, 158.5, 147.1, 146.6, 144.8, 140.6, 138.8, 136.3, 133.7, 133.0, 132.8, 131.7, 131.6, 131.3, 131.0, 130.7, 129.9, 129.6, 129.4, 129.2, 128.8, 127.8, 127.7, 126.9, 126.2, 126.1, 125.9, 125.2, 125.0, 124.8, 123.5, 123.0, 122.3, 119.8, 119.0, 118.7, 116.6, 102.5, 68.5, 66.1, 59.5, 56.8, 56.2, 55.7, 55.0, 49.6, 49.0, 41.6, 40.9, 40.7, 39.2, 39.1, 38.8, 38.6, 38.2, 36.6, 36.2, 36.1, 27.8, 27.6, 27.2, 26.7, 24.0, 23.3, 11.2; HRMS (ES+) calcd for $[C_{46}H_{49}N_2O_3Br - Br]^+$ 677.3743, found 677.3774.

General Procedure for the Synthesis of β-Oxo Esters. β-Oxo esters **1a**−**1h**,[11] **1i**−**1j**,[16] and **1o**−**1r**[11] were prepared according to the literature procedure, and **1k**, **1l**, **1m**, and **1n** were synthesized in accordance with a modified literature procedure as described here: To a flask equipped with a Dean−Stark trap and reflux condenser were added β-oxo methyl ester (1.0 g), corresponding alcohol (1.2 equiv), the transesterification catalyst ZnO[17] (20 mol %), and toluene. The mixture was heated to reflux, distilling the methanol formed during the reaction. The mixture was refluxed until complete conversion was observed by TLC, then concentrated under reduced pressure, and the crude residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 3/1), then recrystallization in n-hexane to give a crystal.

*3-Ethyl Amyl-1-indanone-2-carboxylate (**1k**):* Colorless crystal (0.86 g, 59.8% yield); mp 61−63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.7 Hz, 1H), 7.61 (td, J = 7.6, 1.2 Hz, 1H), 7.52−7.46 (m, 1H), 7.42−7.34 (m, 1H), 3.64 (dd, J = 8.2, 3.9 Hz, 1H), 3.49 (dd, J = 17.1, 3.9 Hz, 1H), 3.35 (dd, J = 17.1, 8.2 Hz, 1H), 1.89−1.77 (m, 6H), 0.83 (t, J = 7.5 Hz, 9H), minor peaks due to enol observed at 3.49 (s, 1H), 1.94 (q, J = 7.5 Hz, 3H), 0.88 (t, J = 7.5 Hz, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 167.9, 153.7, 135.6, 135.2, 127.7, 126.5, 124.6, 90.2, 54.6, 30.6, 26.8, 7.6, minor peaks due to enol observed at 143.0, 129.0, 126.7, 120.5, 32.8, 27.3; HRMS (ES+) calcd for $[C_{17}H_{22}O_4 + Na]^+$ 297.1467, found 297.1462.

*3-Ethyl Amyl 4-Methoxyl-1-indanone-2-carboxylate (**1l**):* Colorless crystal (0.91 g, 65.9% yield); mp 52−53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.35−7.34 (m, 1H), 7.04 (p, J = 4.1 Hz, 1H), 3.91 (s, 3H), 3.61 (dd, J = 8.0, 3.9 Hz, 1H), 3.36 (dd, J = 17.6, 3.9 Hz, 1H), 3.26 (dd, J = 17.6, 8.0 Hz, 1H), 1.88−1.77 (m, 6H), 0.83 (t, J = 7.5 Hz, 9H), minor peaks due to enol observed at 6.92 (d, J = 8.0 Hz, 1H), 3.43 (s, 2H), 1.93 (q, J = 7.5 Hz, 6H), 0.88 (t, J = 7.5 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 168.0, 156.9, 142.6, 137.1, 129.2, 116.0, 115.3, 90.1, 55.5, 54.5, 27.5, 27.3, 26.8, 7.7, 7.6, minor peaks due to enol observed at 155.6, 138.9, 130.3, 128.8, 128.5, 114.7, 113.3, 110.9, 104.0, 36.2, 30.1, 22.5; HRMS (ES+) calcd for $[C_{18}H_{24}O_4 + Na]^+$ 327.1572, found 327.1577.

*3-Ethyl Amyl 5,6-Dimethoxy-1-indanone-2-carboxylate (**1m**):* Colorless crystal (0 8 g, 59.9% yield); mp 104−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 1H), 6.91 (s, 1H), 3.97 (s, 4H), 3.90 (s, 3H), 3.62 (dd, J = 7.8, 3.5 Hz, 1H), 3.38 (dd, J = 16.9, 3.4 Hz, 1H), 3.25 (dd, J = 16.9, 7.8 Hz, 1H), 1.92−1.78 (m, 7H), 0.84 (t, J = 7.5 Hz, 10H), minor peaks due to enol observed at 3.09−3.00 (m, 1H), 2.69−2.63 (m, 1H), 1.46 (q, J = 7.5 Hz, 3H), 0.87 (s, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.57, 168.25, 155.86, 149.67, 149.17, 128.25, 107.25, 104.78, 89.97, 56.24, 56.04, 54.78, 30.30, 26.77, 7.55, minor peaks due to enol observed at 150.36, 149.39, 129.88, 107.50, 104.17, 74.57, 36.48, 25.53; HRMS (ES+) calcd for $[C_{19}H_{26}O_5 + Na]^+$ 357.1678, found 357.1685.

*3-Ethyl Amyl 5-Chloro-1-indanone-2-carboxylate (**1n**):* Colorless crystal (0.78 g, 56.9% yield); mp 91−93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (dd, J = 8.2, 3.9 Hz, 1H), 3.47 (dd, J = 17.4, 3.8 Hz, 1H), 3.32 (dd, J = 17.4, 8.2 Hz, 1H), 1.89−1.78 (m, 6H), 0.83 (t, J = 7.5 Hz, 9H), minor peaks due to enol observed at 7.53 (d, J = 8.1 Hz, 1H), 7.42 (d, J = 1.1 Hz, 1H), 3.47 (s, 2H), 1.94 (q, J = 7.5 Hz, 6H), 0.88 (t, J = 7.5 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8, 163.7, 151.4, 138.0, 130.3, 124.8, 123.0, 121.9, 86.8, 50.9, 26.6, 23.1, 3.9, minor peaks due to enol observed at 194.8, 140.8, 123.5, 121.3, 117.7, 29.0, 23.6; HRMS (ES+) calcd for $[C_{17}H_{21}ClO_3 + Na]^+$ 331.1077, found 331.1069.

General Procedure for the Catalytic Enantioselective Hydroxylation Reaction. β-Oxo ester **1** (0.2 mmol) and catalyst Cn-14 (7.2 mg, 0.01 mmol, 5 mol %) were added to a test tube equipped with a stirring bar and dissolved in toluene (1 mL). Cumyl hydroperoxide (0.3 mmol in toluene solution, 1.5 equiv, 1 mL) was added; the resulting mixture was cooled to −5 °C before precooled 50% aq K_2HPO_4 (1 mL) was added, and the reaction was stirred at this temperature for 60 h. After completion of the reaction, the reaction mixture was diluted with Et_2O (10 mL), washed with water (3 × 5 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (silica gel; petroleum ether/EtOAc, 13:1−5:1) to afford products.

*1-Adamantyl 2-Hydroxy-1-oxoindan-2-carboxylate (**3a**):* Colorless oil (58.7 mg, 90% yield, 88% ee); $[\alpha]_D^{25}$ 12.5 (c 0.11, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (1 H, d, J = 7.7), 7.64 (1 H, dd, J = 10.9, 4.1), 7.47 (1 H, d, J = 7.7), 7.40 (1 H, t, J = 7.5), 4.10 (1 H, s), 3.66 (1 H, d, J = 17.1), 3.21 (1 H, d, J = 17.1), 2.11 (3 H, s), 1.96 (6 H, d, J = 2.9), 1.59 (6 H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 170.2, 152.4, 135.8, 134.0, 127.9, 126.3, 125.0, 83.9, 80.6, 40.9, 39.6, 35.9, 30.8. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1 mL/min, 254 nm, τ_R (major) = 12.0 min, τ_R (minor) = 20.7 min.

*1-Adamantyl 6-Methoxyl-2-hydroxy-1-indanone-2-carboxylate (**3b**):* Colorless oil (60.7 mg, 85% yield, 86% ee); $[\alpha]_D^{20}$ 17.3 (c 0.10, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (1 H, d, J = 8.2), 7.26−7.19 (2 H, m), 4.11 (1 H, s), 3.84 (3 H, s), 3.58 (1 H, d, J = 16.8), 3.13 (1 H, d, J =16.8), 2.12 (3 H, s), 1.98 (6 H, d, J = 2.5), 1.60 (6 H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 170.3, 159.6, 145.3, 135.1, 127.0, 125.1, 106.1, 83.8, 81.2, 55.6, 40.9, 39.0, 35.9, 30.8. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 24.8 min, τ_R (minor) = 48.1 min.

*1-Adamantyl 4-Methoxyl-2-hydroxy-1-indanone-2-carboxylate (**3c**):* Colorless solid (59.2 mg, 83% yield, 90% ee); $[\alpha]_D^{25}$ 32.2 (c 0.08, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 1.5 Hz, 1H), 7.36 (s, 1H), 7.10−7.07 (m, 1H), 4.04 (s, 1H), 3.91 (s, 3H), 3.59 (d, J = 17.5 Hz, 1H), 3.07 (d, J = 17.6 Hz, 1H), 2.11 (s, 3H), 1.98 (d, J = 2.8 Hz, 6H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6, 170.4, 156.6, 141.4, 135.3, 129.4, 116.4, 116.0, 83.8, 80.3, 55.6, 40.9, 36.4, 35.9, 30.8. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane/i-PrOH = 98/2, 1 mL/min, 254 nm, τ_R (major) = 28.5 min, τ_R (minor) = 32.8 min.

*1-Adamantyl 5,6-Dimethoxy-2-hydroxy-1-indanone-2-carboxylate (**3d**):* Colorless solid (42.5 mg, 61% yield, 90% ee); $[\alpha]_D^{25}$ 56.3 (c 0.08, MeOH); ^{1}H NMR (400 MHz, $CHCl_3$) δ 7.19 (1 H, s), 6.89 (1 H, s), 4.02 (1 H, s), 3.99 (3 H, s), 3.92 (3 H, s), 3.57 (1 H, d, J = 16.9), 3.12 (1 H, d, J = 16.9), 2.13 (3 H, s), 2.00 (6 H, s), 1.61 (6 H, s); ^{13}C NMR (100 MHz, $CHCl_3$) δ 199.8, 170.5, 156.4, 149.8, 148.2, 126.6, 107.2, 105.3, 83.7, 80.8, 56.3, 56.1, 41.0, 39.3, 35.9, 30.8. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/i-PrOH = 80/20, 1 mL/min, 254 nm, τ_R (major) = 23.6 min, τ_R (minor) = 42.6 min.

*1-Adamantyl 6-Bromo-2-hydroxy-1-indanone-2-carboxylate (**3e**):* Colorless oil (35.8 mg, 45% yield, 58% ee); $[\alpha]_D^{25}$ −15.5 (c 0.084, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 77.91 (1 H, d, J =

dx.doi.org/10.1021/jo3016242 | J. Org. Chem. 2012, 77, 9601−9608

1.3), 7.74 (1 H, dd, J = 8.1, 1.7), 7.36 (1 H, d, J = 8.1), 4.07 (1 H, s), 3.59 (1 H, d, J = 17.3), 3.15 (1 H, d, J = 17.3), 2.13 (3 H, s), 1.96 (6 H, d, J = 2.5), 1.60 (6 H, s); ^{13}C NMR (100 MHz, $CHCl_3$) δ 200.1, 169.7, 150.8, 138.5, 135.8, 127.8, 127.8, 122.0, 84.3, 80.7, 40.9, 39.2, 35.8, 30.8. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 80/20, 1 mL/min, 254 nm, τ_R (major) = 11.1 min, τ_R (minor) = 21.8 min.

*1-Adamantyl 4-Bromo-2-hydroxy-1-indanone-2-carboxylate (**3f**):* Colorless oil (58.2 mg, 73% yield,76% ee); $[\alpha]_D^{25}$ 34.5 (*c* 0.116, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 7.98 (d, J = 7.7 Hz, 1H), 7.74 (d, J = 7.5 Hz, 1H), 7.46 (t, J = 7.7 Hz, 1H), 6.67 (br s, 1H), 3.45 (d, J = 17.5 Hz, 1H), 2.99 (d, J = 17.5 Hz, 1H), 2.05 (br s, 3H), 1.88 (br s, 6H), 1.53 (br s, 6H); ^{13}C NMR (100 MHz, DMSO) δ 201.3, 169.8, 151.7, 138.9, 136.3, 130.9, 123.9, 121.6, 82.0, 80.4, 42.5, 41.0, 35.8, 30.6. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 16.4 min, τ_R (minor) = 19.5 min.

*1-Adamantyl 5-Chloro-2-hydroxy-1-indanone-2-carboxylate (**3g**):* White solid (64.1 mg, 88% yield, 82% ee); $[\alpha]_D^{25}$ 41.7 (*c* 0.156, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (1 H, d, J = 8.2 Hz), 7.47 (1 H, s), 7.39 (1 H, d, J = 8.2 Hz), 4.14 (1 H, s), 3.63 (1 H, d, J = 17.3 Hz), 3.20 (1 H, d, J = 17.3 Hz), 2.12 (3 H, s), 1.97 (6 H, s), 1.60 (6 H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 169.8, 153.7, 142.4, 132.5, 128.8, 126.5, 126.1, 84.2, 80.5, 40.9, 39.3, 35.8, 30.8. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 80/20, 1 mL/min, 254 nm, τ_R (major) = 12.5 min, τ_R (minor) = 22.1 min.

*2-Adamantyl 2-Hydroxy-1-indanone-2-carboxylate (**3h**).* Colorless solid (62.1 mg, 95% yield, 75% ee); $[\alpha]_D^{25}$ 3.2(*c* 0.16, MeOH); ^{1}H NMR (400 MHz, $CHCl_3$) δ 7.80 (1 H, d, J = 7.7 Hz), 7.71−7.61 (1 H, m), 7.50 (1 H, d, J = 7.7 Hz), 7.42 (1 H, t, J = 7.5 Hz), 4.95 (1 H, s), 4.15 (1 H, s), 3.71 (1 H, d, J = 17.0 Hz), 3.30 (1 H, d, J = 17.0 Hz), 1.87 (2 H, d, J = 28.3 Hz), 1.81−1.21 (12 H, m); ^{13}C NMR (100 MHz, $CHCl_3$) δ 201.2, 170.6, 152.0, 135.9, 134.1, 128.0, 126.3, 125.0, 81.0, 79.7, 39.6, 37.1, 36.1, 36.0, 31.7, 31.5, 31.3, 26.8, 26.7. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 80/20, 1 mL/min, 254 nm, τ_R (major) = 11.3 min, τ_R (minor) = 14.4 min.

*tert-Butyl 2-Hydroxy-1-indanone-2-carboxylate (**3i**):* Colorless solid (38.7 mg, 79% yield, 78% ee); $[\alpha]_D^{25}$ 10.3 (*c* 0.15, MeOH); ^{1}H NMR (400 MHz, $CHCl_3$) δ 7.79 (d, J = 7.7 Hz, 1H), 7.65 (td, J = 7.6, 1.2 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 4.08 (s, 1H), 3.65 (d, J = 17.1 Hz, 1H), 3.22 (d, J = 17.1 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CHCl_3$) δ 201.4, 170.5, 152.3, 135.8, 133.9, 127.9, 126.3, 125.0, 83.9, 80.6, 39.5, 27.7. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 6.5 min, τ_R (minor) = 7.1 min.

*tert-Butyl 4-Methoxyl-2-hydroxy-1-indanone-2-carboxylate (**3j**):* Colorless solid (41.1 mg, 75% yield, 84% ee); $[\alpha]_D^{25}$ 31.9 (*c* 0.16, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 2.3 Hz, 1H), 7.37 (s, 1H), 7.11−7.09 (m, 1H), 4.02 (s, 1H), 3.91 (s, 4H), 3.58 (d, J = 17.6 Hz, 1H), 3.08 (d, J = 17.6 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 170.7, 156.6, 141.3, 135.2, 129.4, 116.5, 116.0, 83.9, 80.3, 55.6, 36.3, 27.7. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 12.4 min, τ_R (minor) = 11.1 min.

*3-Ethyl Amyl 2-Hydroxy-1-indanone-2-carboxylate (**3k**):* Colorless oil (40.1 mg, 70% yield, 83% ee); $[\alpha]_D^{25}$ −5.2 (*c* 0.14, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.7 Hz, 1H), 7.64 (td, J = 7.6, 1.1 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 4.08 (s, 1H), 3.64 (d, J = 17.1 Hz, 1H), 3.25 (d, J = 17.0 Hz, 1H), 1.70 (q, J = 7.5 Hz, 6H), 0.65 (t, J = 7.5 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 170.1, 152.2, 135.8, 134.2, 128.0, 126.2, 124.9, 92.1, 80.8, 39.7, 26.9, 7.4; HRMS (ES+) calcd for $[C_{17}H_{22}O_4 + Na]^+$ 313.1416, found 313.1428. HPLC conditions: Chiralcel AS-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 13.4 min, τ_R (minor) = 10.8 min.

*3-Ethyl Amyl 4-Methoxyl-2-hydroxy-1-indanone-2-carboxylate (**3l**):* Colorless oil (49.7 mg, 78% yield, 82% ee); $[\alpha]_D^{25}$ 20.0 (*c* 0.12, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (1 H, d, J = 1.4 Hz), 7.37 (1 H, s), 7.11−7.07 (1 H, m), 4.03 (1 H, s), 3.91 (4 H, s), 3.59 (1 H, d, J = 17.4 Hz), 3.09 (1 H, d, J = 17.4 Hz), 1.71 (6H, q, J = 7.4 Hz), 0.67 (9 H, t, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 166.5, 152.9, 137.4, 131.8, 125.7, 112.6, 112.3, 88.3, 76.9, 51.9, 32.7, 23.2, 3.7; HRMS (ES+) calcd for $[C_{18}H_{24}O_5 + Na]^+$ 343.1521, found 343.1533. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 26.1 min, τ_R (minor) = 19.6 min.

*3-Ethyl Amyl 5,6-Dimethoxy-2-hydroxy-1-indanone-2-carboxylate (**3m**):* Colorless oil (51.7 mg, 82% yield, 85% ee); $[\alpha]_D^{25}$ 7.1 (*c* 0.08, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 1H), 6.89 (s, 1H), 4.06 (s, 1H), 4.00 (s, 1H), 3.92 (s, 3H), 3.56 (d, J = 16.8 Hz, 1H), 3.15 (d, J = 16.9 Hz, 1H), 1.73 (q, J = 7.5 Hz, 6H), 0.70 (t, J = 7.5 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8, 170.4, 156.4, 149.8, 148.1, 126.7, 107.1, 105.2, 91.9, 80.9, 56.3, 56.1, 39.4, 26.8, 7.4; HRMS(ES+) calcd for $[C_{19}H_{26}O_6 + Na]^+$ 373.1627, found 373.1642. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 42.7 min, τ_R (minor) = 36.0 min.

*3-Ethyl Amyl 5-Chloro-2-hydroxy-1-indanone-2-carboxylate (**3n**):* Colorless oil (44.7 mg, 69% yield, 79% ee); $[\alpha]_D^{25}$ 25.0 (*c* 0.12, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (1 H, d, J = 8.2 Hz), 7.48 (1 H, s), 7.40 (1 H, d, J = 7.4 Hz), 4.08 (1 H, s), 3.61 (1 H, d, J = 17.3 Hz), 3.23 (1 H, d, J = 17.3 Hz), 1.71 (6 H, q, J = 7.5 Hz), 0.67 (9 H, t, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 169.7, 153.5, 142.4, 132.6, 128.8, 126.5, 126.0, 92.5, 80.7, 39.3, 26.9, 7.4; HRMS (ES+) calcd for $[C_{17}H_{21}ClO_4 + Na]^+$ 347.1026, found 347.1019. HPLC conditions: AS-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 11.6 min, τ_R (minor) = 9.1 min.

*Methyl 2-Hydroxy-1-tetralone-2-carboxylate (**3o**):* Colorless solid (15.7 mg, 35% yield, 63% ee); $[\alpha]_D^{25}$ 20.0 (*c* 0.015, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (1 H, d, J = 7.9 Hz), 7.53 (1 H, t, J = 7.5 Hz), 7.34 (1 H, t, J = 7.5 Hz), 7.26 (1 H, d, J = 7.7 Hz), 4.36 (1 H, s), 3.74 (3 H, s), 3.13 (2 H, m), 2.71 (1 H, dt, J = 13.6, 5.1 Hz), 2.25 (1 H, ddd, J = 13.6, 8.9, 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 171.1, 144.0, 134.4, 130.2, 129.0, 128.2, 127.0, 77.7, 53.0, 32.7, 25.6. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 9.6 min, τ_R (minor) = 10.9 min.

*1-Adamantyl 2-Hydroxy-1-tetralone-2-carboxylate (**3p**):* Colorless solid (26.7 mg, 35% yield, 71% ee); $[\alpha]_D^{25}$ −34.8 (*c* 0.023, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (1 H, d, J = 7.9 Hz), 7.53−7.46 (1 H, m), 7.33 (1H, dt, J = 13.0, 4.6 Hz), 7.28−7.20 (1 H, m), 3.15−3.05 (2 H, m), 2.63 (1 H, m), 2.26−2.16 (1 H, m), 2.11 (3 H, s), 2.00 (6 H, s), 1.60 (6 H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 169.7, 143.8, 134.0, 130.7, 128.8, 127.9, 126.8, 83.4, 77.8, 41.0, 35.9, 32.9, 31.7, 30.8, 25.7. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane/*i*-PrOH = 90/10, 1 mL/min, 254 nm, τ_R (major) = 14.6 min, τ_R (minor) = 24.9 min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Characterization data (including ^{1}H NMR, ^{13}C NMR, and HPLC spectra) for catalysts, β-oxo esters **1k**, **1l**, **1m**, and **1n** and all products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mengqw@dlut.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We would likely to thank the National Natural Science Foundation of China (No. 21176041) and the State Key Laboratory of Fine Chemicals for their support.

■ REFERENCES

(1) Christoffers, J.; Baro, A.; Werner, T. *Adv. Synth. Catal.* **2004**, *346*, 143.
(2) McCann, S. F.; Annis, G. D.; Shapiro, R.; Piotrowski, D. W.; Lahm, G. P.; Long, J. K.; Lee, K. C.; Hughes, M. M.; Myers, B. J.; Griswold, S. M.; Reeves, B. M.; March, R. W.; Sharpe, P. L.; Lowder, P.; Barnette, W. E.; Wing, K. D. *Pest Manage. Sci.* **2001**, *57*, 153−164.
(3) Acocella, M. R.; Bella, M.; Jørgensen, K. A. *J. Org. Chem.* **2004**, *69*, 8165−8167.
(4) Toullec, P. Y.; Bonaccorsi, C.; Mezzetti, A.; Togni, A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5810−5814.
(5) Ishimaru, T.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanemasa, S. *J. Am. Chem. Soc.* **2006**, *128*, 16488−16489.
(6) Smith, A. M. R.; Billen, D.; Hii, K. K. *Chem. Commun.* **2009**, 3925−3927.
(7) Lu, M.; Zhu, D.; Lu, Y. P.; Zeng, X. F.; Tan, B.; Xu, Z. J.; Zhong, G. F. *J. Am. Chem. Soc.* **2009**, *131*, 4562−4563.
(8) Gong, B.; Meng, Q. W.; Su, T.; Lian, M. M.; Wang, Q.; Gao, Z. X. *Synlett* **2009**, *16*, 2659−2662.
(9) Cai, Y. C.; Lian, M. M.; Li, Z.; Meng, Q. W. *Tetrahedron* **2012**, *38*, 7973−7977.
(10) (a) Hashimoto, T.; Sasaki, K.; Fukumoto, K.; Murase, Y.; Abe, N.; Ooi, T.; Maruoka, K. *Chem. Asian J.* **2010**, *5*, 562−570. (b) Sano, D.; Nagata, K.; Itoh, T. *Org. Lett.* **2008**, *10*, 1593−1595. (c) Erik, F. J.; Lisette, P.; Marcello, C.; Johannes, B.; Arne, G. *Tetrahedron: Asymmetry* **1995**, *6*, 1123−1132.
(11) Lian, M. M.; Li, Z.; Meng, Q. W.; Gao, Z. X. *Eur. J. Org. Chem.* **2010**, *34*, 6525−6530.
(12) Wolfer, J.; Weatherwax, A.; Taggi, A. E.; Lectka, T. *J. Org. Chem.* **2006**, *71*, 8946−8949.
(13) Poulsen, T. B.; Bernardi, L.; Bell, M.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 6551−6554.
(14) Ishimaru, T.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanemasa, S. *J. Am. Chem. Soc.* **2006**, *128*, 16488−16489.
(15) (a) Ishimaru, T.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanemasa, S. *J. Am. Chem. Soc.* **2006**, *128*, 16488−16489. (b) Smith, A. M. R.; Rzepa, H. S.; White, A. J. P.; Billen, D.; Hii, K. K. *J. Org. Chem.* **2010**, *75*, 3085−3096. (c) Cao, S. H.; Shi, M. *Tetrahedron: Asymmetry* **2010**, *21*, 2675−2680. (d) Lian, M. M.; Li, Z.; Meng, Q. W.; Gao, Z. X. *Eur. J. Org. Chem.* **2010**, *34*, 6525−6530.
(16) Nakajima, M.; Yamamoto, S.; Yamaguchi, Y.; Nakamura, S.; Hashimoto, S. *Tetrahedron* **2003**, *59*, 7307−7313.
(17) Pericas, A.; Shafir, A.; Vallribera, A. *Tetrahedron* **2008**, *64*, 9258−9263.