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Asymmetric Direct α-Hydroxylation of β-Oxo Esters by Phase-Transfer Catalysis Using Chiral Quaternary Ammonium Salts

Mingming Lian,[a] Zhi Li,[a] Jian Du,[a] Qingwei Meng,*[a] and Zhanxian Gao[a]

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The first enantioselective direct α-hydroxylation of β-oxo esters was developed by using phase-transfer catalysis. 1-Indanone-derived 1-adamantyl (1-Ad) β-oxo esters, in the presence of commercially available cumyl hydroperoxide and a cinchonine-based ammonium salt, resulted in the corresponding products with 69–91 % yield and 65–74 % *ee*. The reaction had also been successfully scaled-up to a gram quantity, and a similar yield was obtained without loss of the enantioselectivity.

Introduction

The development of novel and efficient catalytic methodologies for the stereoselective preparation of chiral α-hydroxy β-oxo esters is an important synthetic target.[1] This functional moiety is a common structural motif in a variety of natural products and pharmaceuticals, such as vindoline and its analogues, kjellmanianone, hamigeran A and doxycycline, etc. Moreover, optically active chiral hydroxy-containing compounds constitute an important class of synthetic intermediates, for example, in the synthesis of the insecticide indoxacarb by the Dupont group.[2]

Despite the importance of this moiety in organic synthesis, to the best of our knowledge, there are only a few examples that could give asymmetric products. The first highly enantioselective α-hydroxylation of β-oxo esters was described by Togni and Mezzetti in 2004,[3] using oxaziridine as oxidant in the presence of a TASSOL-Ti complex. Later, Toru and Shibata,[4] adopted a DBFOX-Ni complex with another oxaziridine. Recently, Hii reported the use of dimethyldioxirane (DMD) as an effective oxidant in the presence of a dicationic BINAP-Pd catalyst,[5] and more recently Shi[6] found Cu^{I} complexes could also catalyze this asymmetric reaction. In the fields of organocatalysis, Zhong reported another efficient catalytic system based on a Brønsted acid derived from chiral BINOL that mediates indirect α-oxidation of β-oxo esters with nitrosobenzene as the electrophile.[7] In addition to acids, chiral bases could be used as effective catalysts. In this context, the Dupont group, Jørgensen, and we have reported that alkaloids and their derivatives, such as cinchona, cinchona analogues and lappaconitine, catalyze the α-hydroxylation reaction with satisfactory stereoselectivity.[8] Recently, Maruoka used an asymmetric alkylation of α-benzoyloxy β-oxo esters to produce similar chiral compounds by phase-transfer catalysis, another good strategy.[9] Although several examples of catalytic enantioselective α-hydroxylation of β-oxo esters have already been reported, there are still challenging issues that need to be addressed, particularly in the area of organocatalysis. These challenges include enantioselectivity, safety of oxidant, efficiency and ease of catalyst preparation, and reaction scale-up.

Results and Discussion

Here, we performed the first direct oxidation of β-oxo esters to α-hydroxy compounds using phase-transfer catalysis, which is a clean and efficient process in organocatalysis. In our ongoing research, we anticipated that a phase-transfer catalytic hydroxylation of β-oxo ester could provide an elegant approach to satisfy the desired stereochemical requirement, since this method is frequently used to obtain chiral derivatives.[10] To the best of our knowledge, there have been no reported attempts to construct a C–O bond and simultaneously create a tetrasubstituted stereogenic center at the α position of β-oxo esters when a chiral phase-transfer catalyst (PTC) was employed.

Initially,[11] we attempted the reaction of 1-indanone-derived β-oxo ester **1a** with commercially available cumyl hydroperoxide (CHP) **2** using **Cn-1** (5 mol-%), in combination with K_2HPO_4 (50 % aq.) for enantioselective hydroxylation, which furnished **3a** in 75 % yield with a good *ee* value of 54 % (Table 1, Entry 1). Prompted by this result, we undertook an initial screening of the most widely used modified cinchona catalysts, but those catalysts bearing a hindering 9-anthracenylmethyl group at the quinuclidine nitrogen atom (Corey's catalyst, **Cn-22**, Table 1, Entry 22) or a

[a] State Key Laboratory of Fine Chemicals,
School of Pharmaceutical Science and Technology,
Dalian University of Technology,
158 Zhongshan Road, Dalian 116012, P. R. China
E-mail: Mengqw@dlut.edu.cn

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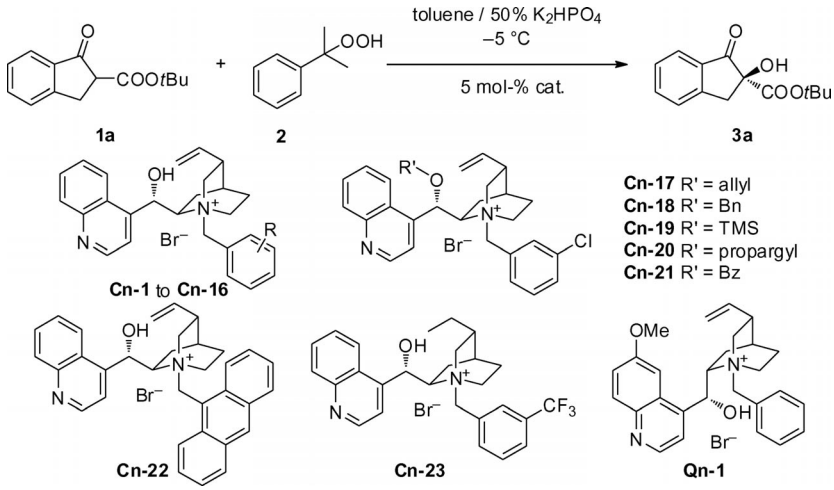
Table 1. Screening of phase-transfer catalysts for the organocatalytic α-hydroxylation of β-oxo ester **1a**.[a]



Entry	Catalyst	R	Yield[b] [%]	*ee*[c] [%]
1	**Cn-1**	H	75	54 (*S*)[d]
2	**Cn-2**	4-MeO	76	44 (*S*)
3	**Cn-3**	3,5-$(MeO)_2$	70	42 (*S*)
4	**Cn-4**	4-F	74	50 (*S*)
5	**Cn-5**	4-F_3C	68	47 (*S*)
6	**Cn-6**	2-O_2N	63	43 (*S*)
7	**Cn-7**	3-O_2N	74	54 (*S*)
8	**Cn-8**	4-O_2N	63	36 (*S*)
9	**Cn-9**	2-Cl	64	49 (*S*)
10	**Cn-10**	3-Cl	72	56 (*S*)
11	**Cn-11**	4-Cl	69	48 (*S*)
12	**Cn-12**	3-Br	73	58 (*S*)
13	**Cn-13**	4-Br	68	50 (*S*)
14	**Cn-14**	3-I	68	60 (*S*)
15	**Cn-15**	3-F_3C	71	60 (*S*)
16	**Cn-16**	3,5-$(F_3C)_2$	80	55 (*S*)
17	**Cn-17**	–	>99	37 (*S*)
18	**Cn-18**	–	>99	37 (*S*)
19	**Cn-19**	–	80	38 (*S*)
20	**Cn-20**	–	>99	35 (*S*)
21	**Cn-21**	–	73	56 (*S*)
22	**Cn-22**	–	44	54 (*S*)
23	**Cn-23**	–	71	62 (*S*)
24	**Qn-1**	–	64	–32 (*R*)

[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 the product **3a** using a chiral column (DAICEL Chiralcel OD-H) with hexane/2-propanol (90:10) as the eluent. [d] The absolute configuration was determined by comparison with the optical rotation and the HPLC retention time of an authentic sample.[4]

strong electron-withdrawing group (**Cn-5**, Table 1, Entry 5), rendered only poor results. **Cn-22** gave a low yield for the hydroxylation product with an acceptable *ee* value. In contrast, **Cn-5** gave a higher yield, but a reduced enantioselectivity. These phenomena indicated that the sterically more hindered 9-anthracenylmethyl derivative was less reactive, and the substituent on the phenyl ring in this reaction system was crucial to obtain high yields and enantioselectivities. To optimize the ability of cinchonine-derived quaternary ammonium salts to catalyze the α-hydroxylation reaction, a series of catalysts were synthesized, and the corresponding outcomes are summarized in Table 1.

We first found that the benzyl ring bearing one substituent at the *meta* position was crucial to achieve a better result. For example, the introduction of *m*-NO_2 and *m*-Cl moieties gave **3a** with comparable yields (74 and 72%, respectively) and *ee* values of 54 and 56%, respectively (Table 1, Entries 7, 10).

The regioisomeric catalysts (*p*-NO_2, *o*-NO_2 or *p*-Cl, *o*-Cl derivatives, Table 1, Entries 8, 6, 11, 9) proved to be ineffective for achieving good enantioselectivities, and **Cn-3** with two electron-donating groups such as methoxy in both *meta* positions gave a significantly lower *ee* value (Table 1, Entry 3). Changing the position of the electron-donating

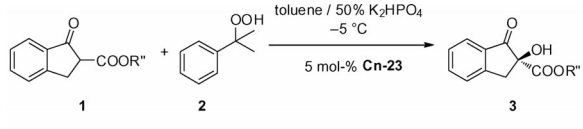
group to *para* did not give a higher selectivity (Table 1, Entry 2). Next, screening of the *meta*-halogenated PTCs was performed (Table 1, Entries 10, 12). Chlorinated and brominated PTCs (**Cn-10**, **Cn-12**) smoothly promoted the reaction to give **3a** with 56 and 58% *ee*, respectively. The same tendency was observed with a regioisomeric PTC (*p*-Br derivative, **Cn-13**), which proved to be ineffective for achieving a reasonable enantioselectivity (Table 1, Entry 13). However, a steady improvement in enantiocontrol was obtained by the *m*-I and *m*-CF_3 derivatives (**Cn-14**, **Cn-15**) both of which gave the best results for the asymmetric oxidation of **1a** with 60% *ee*, and the latter bearing a stronger electron-withdrawing group gave a better yield (Table 1, Entries 14, 15). We also examined the double-substituent catalyst **Cn-16**, which resulted in a higher yield than **Cn-15** did, but lowered the selectivity as shown in Entry 16. These findings indicate that the *meta*-substituted derivatives are quite effective in this asymmetric induction. Although the role of the halogen or CF_3 group in the *meta* position of the phenyl ring of the PTC is not clear at present, it seems to be dependent on the steric effect rather than the electronic effect in this asymmetric induction in comparison with the results when using other types of PTCs.

Further studies found that the most important functional group for achieving high *ee* values was not only the benzyl group at the bridgehead nitrogen atom of cinchonine but also the chiral secondary alcohol moiety at C-9 of the alkaloid. The hydroxy group had a significant influence on the yield and enantioselectivity, as shown in Entries 17–20. The catalysts with the chiral secondary alcohol protected by allyl (**Cn-17**), benzyl (**Cn-18**) and propargyl (**Cn-20**) groups gave very high yields, but rather low enantioselectivities. Notably, a slight improvement of enantioselectivity with a moderate sacrifice in the yield had been achieved by replacing the 9-OH group by a benzoic acid ester (**Cn-21**, Table 1, Entry 21), but the increase was not significant. Yield and *ee* value were similar to those of **Cn-1**.

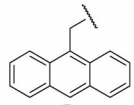
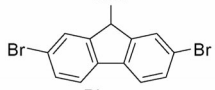
Finally, dihydrocinchonine-derived ammonium salts (**Cn-23**) bearing an *m*-F_3C-benzyl group were introduced, and this kind of modification increased the enantioselectivity with a comparable yield to **Cn-15**. We also investigated other cinchona alkaloid-derived PTCs, and the chiral ammonium salt of quinine **Qn-1** was found to be inferior to cinchonine derivatives showing very low selectivity.

To the best of our knowledge, numerous studies indicate that a bulky *tert*-butyl ester group in β-dicarbonyl compounds is crucial for obtaining good enantioselectivity in the field of phase-transfer catalysis.[10a,10b,12] However, there are only a few cases being successfully performed by using small ester groups.[10c,10e] Because of this uncertainty, we investigated the limitations of the ester group of indanone derivatives in this novel asymmetric process (Table 2). As stated above, a bulky ester group in β-dicarbonyl compounds was found to be essential for good selectivity, and our study further demonstrated that the enantioselectivities were strongly influenced by the degree of substitution in the ester group. For example, small primary alcohol derived β-oxo esters, such as **1c**, gave poor selectivity, but the bulkier primary ester group such as 9-anthracenylmethyl did not promote a higher selectivity either (Table 2, Entries 3, 4). Changing the primary esters to a secondary one boosted the enantiocontrol dramatically, and the corresponding hydroxylation products of **3e** and **3g** were isolated in 44 and 41% *ee*, respectively (Table 2, Entries 5, 7). It should be mentioned that 2-Ad derivatives performed extremely well and gave an impressive yield with a good *ee* value (Table 2, Entry 6). Fortunately, the trend seemed to hold true for tertiary esters **1h** and **1i** (Table 2, Entries 8, 9), which resulted in high enantioselectivities, especially when **1j** (bearing an 1-Ad group) was used as the substrate, producing **3j** in good yield and an impressive 72% *ee* (Table 2, Entry 10). This indicated that the 1-Ad moiety not only enhanced the reaction rate but also affected the stereochemical outcome of the reaction.

Table 2. Effect of the ester group on the 1-indanone derivatives.[a]

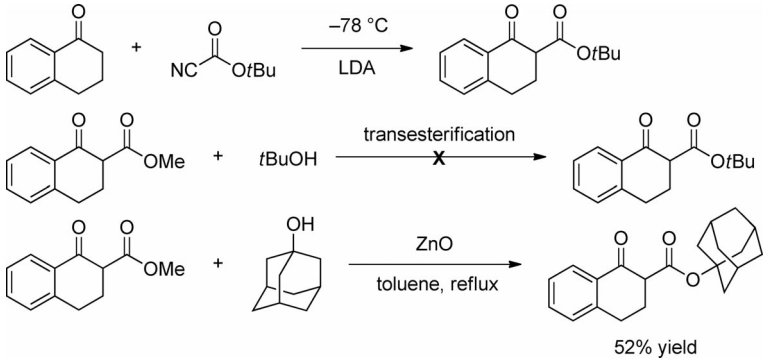


1 2 3

Entry	Sub.	R"	Product	Yield[b] [%]	*ee*[c] [%]
1	**1a**	*t*Bu	**3a**	71	62 (*S*)[d]
2	**1b**	Me	**3b**	55	5 (*S*)
3	**1c**	Bn	**3c**	58	17 (*S*)
4	**1d**		**3d**	80	21
5	**1e**	*i*Pr	**3e**	74	44 (*S*)
6	**1f**	2-Ad	**3f**	>99	66
7	**1g**		**3g**	53	41
8	**1h**		**3h**	68	55
9	**1i**		**3i**	48	57
10	**1j**	1-Ad	**3j**	88	72 (*S*)

[a] The reaction was performed with 0.2 mmol of **1** by using the same conditions described in Table 1. [b] Isolated yields. [c] The enantiomeric excess was determined by HPLC analysis of the product using a chiral column (DAICEL Chiralcel OD-H or AD-H) with hexane/2-propanol as the eluent (see the Supporting Information for details). [d] The absolute configuration of the product was determined by comparison of the optical rotation and the HPLC retention time of the corresponding ester with literature values.[4,7]

It is worth mentioning that compound **1j** was easier to access by a transesterification than thr corresponding *tert*-butyl ester, due to the decreased volatility of 1-Ad alcohol. For example, the 1-tetralone-derived *tert*-butyl β-oxo ester was only obtained by a *C*-acylation of 1-tetralone with *tert*-butyl cyanoformate under severe reaction conditions developed by Jørgensen.[10b] We attempted the synthesis of 1-tetralone-derived *tert*-butyl β-oxo ester by transesterification of the corresponding methyl ester, but the expected



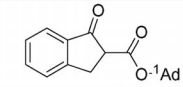
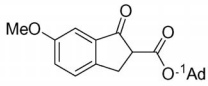
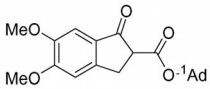
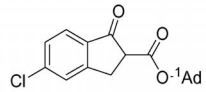
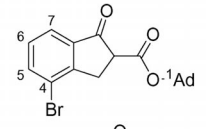
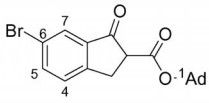
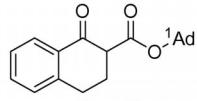
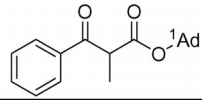
Scheme 1. Preparation of 1-Ad β-oxo esters by transesterification.

bulky ester was not detected, and easy access to these esters seemed to be limited to indanone derivatives. However, when using 1-Ad alcohol instead of *tert*-butyl alcohol as reagent in the transesterification reaction, the easy reaction could be efficiently carried out according to a reported protocol[13] by using a catalytic amount of ZnO in refluxing toluene, which led to a good yield of 52% (Scheme 1).

The next experiment with respect to the substituent on the benzene ring was performed (Table 3). Various substituted 1-Ad esters reacted with CHP in the presence of 5 mol-% of **Cn-23** without considerably affecting the enantioselectivity. First, we investigated the reactivity of **1k** bearing an electron-donating group, which afforded the corresponding product **3k** in high yield and enantioselectivity (Table 3, Entry 2). A much longer reaction time was needed for 5,6-dimethoxy β-oxo ester due to its inherently lower reactivity, but it still gave excellent results (Table 3, Entry 3). Halogen substitutions were uniformly well tolerated (Table 3, Entries 4–6), which afforded the oxidation products in good yields and enantioselectivities. Interestingly, although similar successful results were obtained with **Cn-16** and **Cn-23** under the biphasic reaction conditions (Table 3, Entry 1), the selectivity obtained with **Cn-16** as catalyst was strongly influenced by the substituent on the benzene ring (Table 3, Entries 1–6). For example, a bromine atom in 6-positon decreased the *ee* value to 37% (Table 3, Entry 6), whereas a bromine atom at the 4-position increased the selectivity from 57 to 65% (Table 3, Entry 5). These results indicate that a substituent in 4-position of the indanone derivative has a bad influence on the selectivity with **Cn-23**, whereas a substituent in 6-position dramatically lowers the selectivity with **Cn-16**, which has two *m*-CF_3 groups on the benzyl moiety.

In order to investigate the possible extensions of this reaction to other kinds of β-oxo esters, the oxidation of an acyclic or six-membered cyclic substrate with a 1-Ad ester group was tested. The 1-tetralone-derived β-oxo ester was not active enough, suggesting a stronger base should be used to promote the reaction. After screening of the bases under our optimized conditions, asymmetric hydroxylation of **1p** was quite ineffective and yielded products with low *ee* values (Table 3, Entry 7). The inherently lower reactivity of acyclic substrates inhibited the compound from being oxidized under the reported method, even when using an aqueous NaOH solution as the bulk base. Under these conditions the oxidizer mostly decomposed (Table 3, Entry 8). These results revealed that our protocol was dependent on the indanone derivatives.

Table 3. Enantioselective hydroxylation of β-oxo esters.[a]

Entry	Sub.		Product	Base	Yield[b] [%]	*ee*[c,d] [%]
1		**1j**	**3j**	K_2HPO_4 50%	88	72 (68)
2		**1k**	**3k**	K_2HPO_4 50%	91	68 (47)
3[e]		**1l**	**3l**	K_2HPO_4 50%	89	74 (59)
4		**1m**	**3m**	K_2HPO_4 50%	86	74 (60)
5		**1n**	**3n**	K_2HPO_4 50%	80[f]	57 (65)
6		**1o**	**3o**	K_2HPO_4 50%	69	69 (37)
7		**1p**	**3p**	K_3PO_4 50%	82	21
8		**1q**	**3q**	–	trace	nd

[a] Unless otherwise specified, the reaction was carried out in the presence of 5 mol-% **Cn-23** under the reaction conditions described in Table 1. [b] Isolated yields by using **Cn-23** as catalyst. [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 (see the Supporting Information for details). [d] By using **Cn-16** as catalyst, the *ee* values are given in parentheses. [e] Reaction time: 80 h. [f] Isolated yields by using **Cn-16** as catalyst.

To test the scale-up potential of our methodology, **1m** was treated with CHP (1.25 equiv.) on a gram-quantity scale under the same conditions of catalyst loading (5 mol-%). Surprisingly, after only 30 h at –5 °C, the hydroxylation product was obtained in 80% yield without any loss of enantioselectivity (75% *ee*). The shorter reaction time was ascribed to the intensive mixing conditions by high-speed mechanical agitation (800 rpm).

For the hydroxylation reaction to occur with the observed selectivity, an enolate–PTC complex needs to be formed, in which only the *Si* face of the enolate is available for reaction. To this effect, three sites of interaction between substrate and catalyst have to exist: (i) Coulombic interaction (ion pairing); (ii) hydrogen bonding between the proton of the hydroxy group at C-9 of the PTC and the ester group of the substrate; (iii) π–π stacking of the benzyl moiety and the aromatic portion of the substrate. A model of the transition state, depicted in Figure 1, may explain the importance of the chiral secondary alcohol moiety at the C-9 position of the alkaloid (Table 1, Entries 17–20). The last interaction could explain the decrease in stereoselectivity, when **1n** was used as the substrate. The unfavorable effect is probably due to the fact that the 3′-CF_3 group of **Cn-23** sterically repels the aromatic ring of the enolate, bearing a substituent in 4 position (Table 3, Entry 5), which disturbs the π–π interaction. This activation model may also explain the dramatic decrease in stereoselectivity, when **Cn-16** (instead of **Cn-23**) was used to catalyze the indanone derivatives bearing a substituent in 6-position (Table 3, Entries 2, 3, 6).

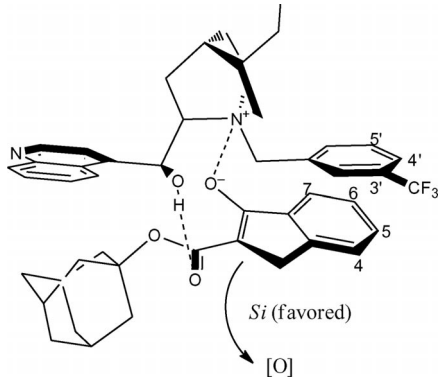


Figure 1. Model of a possible transition-state of the reaction.

Conclusions

We have developed the first enantioselective phase-transfer-catalyzed direct oxidation of 1-Ad β-oxo esters with commercially available CHP. Under mild conditions, high selectivities were obtained for a range of substituted indanone derivatives. Moreover, this new methodology was successfully amplified to a gram-quantity scale. This method should be of great value in terms of simplicity and ready availability of the respective catalysts.

Experimental Section

General Procedure for the Catalytic Enantioselective Hydroxylation Reaction

1-Adamantyl 2-Hydroxy-1-oxoindan-2-carboxylate (3j): 1-Ad β-oxo ester **1j** (62.3 mg, 0.2 mmol) and catalyst **Cn-23** (5.3 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 M in toluene solution, 1.5 equiv., 1 mL) was added, and the resulting mixture was cooled to –5 °C before precooled 50% K_2HPO_4 (aq.) (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, 10:1) to afford **3j** (57.4 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 7.6 Hz, 1 H), 7.65 (t, J = 7.4 Hz, 1 H), 7.50–7.37 (m, 2 H), 4.07 (s, 1 H), 3.66 (d, J = 17.1 Hz, 1 H), 3.22 (d, J = 17.1 Hz, 1 H), 2.08 (d, J = 25.9 Hz, 3 H), 1.96 (s, 6 H), 1.59 (s, 7 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.52, 170.24, 152.39, 135.85, 133.98, 127.92, 126.28, 125.05, 83.92, 80.53, 40.89, 39.58, 35.85, 30.79 ppm. HRMS (ES^-): calcd. for $C_{20}H_{21}O_4$ [M – H]$^-$, 325.1440; found 325.1453. $[\alpha]_D^{20}$ = 21.4 (c = 1.08, $CHCl_3$, 73% *ee*). The *ee* value was determined by HPLC using a Chiralcel AD-H column [hexane/2-propanol (90:10)]; flow rate = 1.0 mL/min; 254 nm; τ_{major} = 12.9 min, τ_{minor} = 21.3 min (73% *ee*).

Supporting Information (see footnote on the first page of this article): Experimental procedures, characterization of the prepared compounds, copies of NMR spectra, and chiral HPLC spectra of the hydroxylation products.

Acknowledgments

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[1] J. Christoffers, A. Baro, T. Werner, *Adv. Synth. Catal.* **2004**, *346*, 143–151.
[2] S. F. McCann, G. D. Annis, R. Shapiro, D. W. Piotrowski, G. P. Lahm, J. K. Long, K. C. Lee, M. M. Hughes, B. J. Myers, S. M. Griswold, B. M. Reeves, R. W. March, P. L. Sharpe, P. Lowder, W. E. Barnette, K. D. Wing, *Pest Manag. Sci.* **2001**, *57*, 153–164.
[3] P. Y. Toullec, C. Bonaccorsi, A. Mezzetti, A. Togni, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5810–5814.
[4] T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru, S. Kanemasa, *J. Am. Chem. Soc.* **2006**, *128*, 16488–16489.
[5] a) A. M. R. Smith, D. Billen, K. K. Hii, *Chem. Commun.* **2009**, 3925–3927; b) A. M. Smith, H. S. Rzepa, A. J. White, D. Billen, K. K. Hii, *J. Org. Chem.* **2010**, *75*, 3085–3096.
[6] J.-J. Jiang, J. Huang, D. Wang, M.-X. Zhao, F.-J. Wang, M. Shi, *Tetrahedron: Asymmetry* **2010**, *21*, 794–799.
[7] M. Lu, D. Zhu, Y. P. Lu, X. F. Zeng, B. Tan, Z. J. Xu, G. F. Zhong, *J. Am. Chem. Soc.* **2009**, *131*, 4562–4563.
[8] a) E. Taylor, G., WO Patent WO/2003/040,083, **2003**; b) M. R. Acocella, O. G. Mancheno, M. Bella, K. A. Jørgensen, *J. Org. Chem.* **2004**, *69*, 8165–8167; c) B. Gong, Q. W. Meng, T. Su, M. M. Lian, Q. Wang, Z. X. Gao, *Synlett* **2009**, 2659–2662.

[9] T. Hashimoto, K. Sasaki, K. Fukumoto, Y. Murase, N. Abe, T. Ooi, K. Maruoka, *Chem. Asian J.* **2010**, *5*, 562–570.
[10] a) T. B. Poulsen, L. Bernardi, M. Bell, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2006**, *45*, 6551–6554; b) T. B. Poulsen, L. Bernardi, J. Aleman, J. Overgaard, K. A. Jørgensen, *J. Am. Chem. Soc.* **2007**, *129*, 441–449; c) E. J. Park, M. H. Kim, D. Y. Kim, *J. Org. Chem.* **2004**, *69*, 6897–6899; d) T. A. Moss, B. Alonso, D. R. Fenwick, D. J. Dixon, *Angew. Chem. Int. Ed.* **2010**, *49*, 568–571; e) D. Y. Kim, E. J. Park, *Org. Lett.* **2002**, *4*, 545–547; f) E. V. Dehmlow, S. Duttmann, B. Neumann, H. G. Stammler, *Eur. J. Org. Chem.* **2002**, 2087–2093; g) M. Bella, S. Kobbelgaard, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 3670–3671.
[11] The screening detials of solvents, hydroperxoides, and temperature are listed in the Supporting Information.
[12] a) T. Ooi, T. Miki, M. Taniguchi, M. Shiraishi, M. Takeuchi, K. Maruoka, *Angew. Chem. Int. Ed.* **2003**, *42*, 3796–3798; b) T. Hashimoto, K. Sasaki, K. Fukumoto, Y. Murase, N. Abe, T. Ooi, K. Maruoka, *Chem. Asian J.* **2010**, *5*, 562–570.
[13] A. Pericas, A. Shafir, A. Vallribera, *Tetrahedron* **2008**, *64*, 9258–9263.

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