DOI: 10.1002/asia.200900344

Phase-Transfer-Catalyzed Asymmetric Alkylation of α-Benzoyloxy-β-keto Esters: Stereoselective Construction of Congested 2,3-Dihydroxycarboxylic Acid Esters

Takuya Hashimoto,[a] Keigo Sasaki,[a] Kazuhiro Fukumoto,[a] Yuichi Murase,[a] Naoyuki Abe,[a] Takashi Ooi,[b] and Keiji Maruoka*[a]

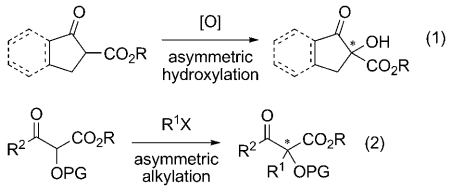
Dedicated to the 150th anniversary of Japan–UK diplomatic relations

Abstract: Highly enantioselective phase-transfer-catalyzed alkylation of *tert*-butyl 2-benzoyloxy-3-oxobutanoate was realized by the use of an *N*-spiro chiral quaternary ammonium salt, as a complementary approach to the asymmetric hydroxylation of α-alkyl-β-keto esters. The synthetic utility of the alkylated compounds is highlighted by the diastereoselective reduction and alkylation of the remaining ketone moiety to give various enantiomerically enriched congested 2,3-dihydroxycarboxylic acid esters.

Keywords: alkylation · asymmetric synthesis · diastereoselectivity · hydroxylation · phase-transfer catalysis

Introduction

Catalytic asymmetric α-hydroxylation of β-keto esters has been developed in the past decade as an efficient means to provide densely oxygenated chiral α-hydroxycarboxylic acid derivatives, which are potentially valuable intermediates for the synthesis of natural products and biologically active compounds [Eq. (1)].[1] Examples include chiral Lewis acid catalyzed α-hydroxylation using oxaziridine or dioxirane as an oxygen source,[2] and organocatalytic α-hydroxylation using hydroperoxides.[3] More recently, chiral Brønsted acid catalyzed addition of nitrosobenzene to β-keto esters has appeared as an alternative approach.[4]



Despite these advances, most of these methods are only applicable to cyclic β-keto esters, and the use of acyclic β-keto esters generally leads to either poor yields or modest selectivity. In this context, we became interested in a complementary strategy for the synthesis of enantiomerically enriched acyclic α-alkyl-α-hydroxy-β-keto esters by relying on the phase-transfer-catalyzed asymmetric alkylation of acyclic α-hydroxy-β-keto ester derivatives [Eq. (2)].[5] As the hydroxy moiety is incorporated into the α position of the β-keto ester in advance and the subsequent alkylation under phase-transfer conditions is set as a crucial asymmetric induction step, a variety of enantioenriched compounds are easily accessible just by changing the alkyl halides while anticipating a similar level of enantioselectivity.

We report herein the detailed study of this phase transfer catalyzed asymmetric alkylation, building on the well-established catalytic activity of binaphthyl-modified chiral quaternary ammonium bromides **1** under phase-transfer conditions.[6] Diastereoselective transformation of the remaining ketone moiety is also investigated to highlight the synthetic utility of so-obtained α-alkyl-α-hydroxy-β-keto esters.

[a] Dr. T. Hashimoto, K. Sasaki, K. Fukumoto, Y. Murase, N. Abe, Prof. Dr. K. Maruoka
Department of Chemistry
Graduate School of Science
Kyoto University
Sakyo, Kyoto, 606-8502 (Japan)
Fax: (+81) 75-753-4041
E-mail: maruoka@kuchem.kyoto-u.ac.jp

[b] Prof. Dr. T. Ooi
Department of Applied Chemistry
Graduate School of Engineering
Nagoya University
Chikusa, Nagoya 464-8603 (Japan)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/asia.200900344.

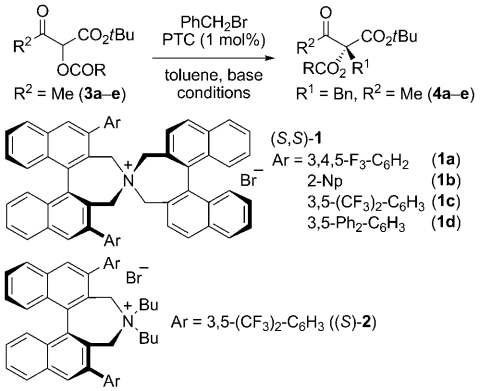
Results and Discussion

Phase-Transfer-Catalyzed Asymmetric Alkylation of α-Benzoyloxy-β-keto Esters

As a suitable substrate for our synthetic plan, we focused on the use of α-acyloxy-β-keto esters, in view of the ease of deprotection of the acyl moiety after the reaction. These substrates can be easily prepared from the corresponding β-keto ester in two steps by following the procedure developed by Wessjohann and co-workers (Scheme 1).[7]

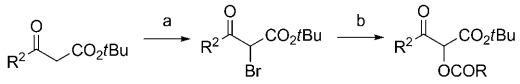
We commenced our study by investigating asymmetric benzylation of *tert*-butyl 2-benzoyloxy-3-oxobutanoate (**3a**) catalyzed by 1 mol% *N*-spiro chiral quaternary ammonium bromide **1a** in the presence of 25% aqueous KOH in relation to our extensive research on the use of **1** for asymmetric phase-transfer-catalyzed alkylation of various β-keto esters (Table 1).[8] Gratifyingly, asymmetric benzylation proceeded smoothly at 0°C to provide the alkylated compound **4a** in 72% yield with 79% *ee* (Table 1, entry 1). Further experiments with the catalysts (*S*,*S*)-**1b–d** revealed the highest efficiency for (*S*,*S*)-**1c**, with which the benzylated product was obtained in a highest *ee* value of 85% (Table 1, entries 2–4). The use of phase-transfer catalyst (*S*)-**2**, which has one binaphthyl unit, gave the product in 66% yield and disappointingly low enantioselectivity (Table 1, entry 5).[9] After setting (*S*,*S*)-**1c** as the optimal catalyst, the reaction was then performed at lower temperature, anticipating an increase of the enantioselectivity. As expected, **4a** was obtained in 90% *ee* by carrying out the reaction at −20°C (Table 1, entry 6).

Table 1. Phase-transfer-catalyzed alkylation of *tert*-butyl 2-acyloxy-3-oxobutanoates with benzyl bromide.[a]



Entry	PTC	Base	R	*T* [°C], *t* [h]	Yield [%][b]	*ee* [%][c]
1	**1a**	25% KOH[d]	Ph (**3a**)	0, 9	72	79
2	**1b**	25% KOH	Ph	0, 9	72	60
3	**1c**	25% KOH	Ph	0, 10	76	85
4	**1d**	25% KOH	Ph	0, 9	83	62
5	**2**	25% KOH	Ph	0, 11	66	35
6	**1c**	25% KOH	Ph	−20, 12	79	90
7	**1c**	25% KOH	4-ClC_6H_4 (**3b**)	−20, 31	79	89
8	**1c**	25% KOH	4-$MeOC_6H_4$ (**3c**)	−20, 12	68	87
9	**1c**	25% KOH	2-Np (**3d**)	−20, 7	63	89
10	**1c**	25% KOH	*t*Bu (**3e**)	−20, 2	57	77
11	**1c**	KOH[e]	Ph	−20, 12	91	90
12	**1c**	Cs_2CO_3[f]	Ph	−20, 96	49	89
13	**1c**	KOH[g]	Ph	−40, 98	95	94

[a] Performed with *tert*-butyl 2-acyloxy-3-oxobutanoate (0.20 mmol) and benzyl bromide (0.24 mmol) in the presence of 1 mol% of catalyst (*S*,*S*)-**1** or (*S*)-**2** in toluene (2.0 mL) under the given reaction conditions. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] 25% aqueous KOH (0.50 mL). [e] Powdered KOH (0.30 mmol). [f] Powdered Cs_2CO_3 (1.0 mmol). [g] Powdered KOH (1.0 mmol).



Scheme 1. Reagents and conditions: a) *N*-bromosuccinimide, acetone, 74%; b) RCO_2Na, DMF, 74% (R = Ph, R^2 = Me).

At this stage, the relationship of acyl groups and *ee* values was examined by using substrates bearing different acyl groups. Whereas the attachment of other aryl groups did not affect the selectivity (Table 1, entries 7–9), the use of pivaloyloxy-substituted β-keto ester **3e** led to the lower enantioselectivity (Table 1, entry 10). For substrates bearing smaller acyl groups, rapid hydrolysis of the acyl moiety was a significant problem, furnishing the alkylated compounds in low yields (data not shown).

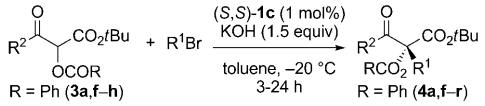
As we observed some amounts of deacylated side product derived from **4a** in the experiments above (e.g., Table 1, entry 6), we conducted the reaction under the influence of solid KOH (1.5 equiv) to minimize such competitive side reactions (Table 1, entry 11). As a result, the benzylated compound was obtained in 91% yield without affecting the enantioselectivity.

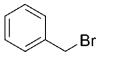
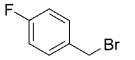
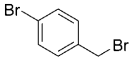
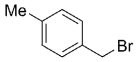
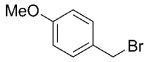
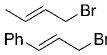
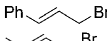
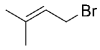
Abstract in Japanese:
近年、光学活性α-アルキル-α-ヒドロキシ-β-ケトエステルの合成法としてα-アルキル-β-ケトエステルのα位不斉ヒドロキシル化反応が注目されている。今回我々はその相補的なアプローチとして、相間移動条件下でのα-ベンゾイロキシ-β-ケトエステルの不斉アルキル化反応の開発を行った。また得られた光学活性α-アルキル-α-ヒドロキシ-β-ケトエステルの合成展開として、ケトン部位のジアステレオ選択的な変換反応を検討し、多様な立体的に込み入ったα,β-ジヒドロキシカルボン酸エステルの合成法を見出した。

The use of Cs_2CO_3 as base resulted in poor reactivity, leading to moderate conversion after prolonged reaction time (Table 1, entry 12). Although a further increase of the enantioselectivity could be achieved by conducting the reaction at −40 °C at the expense of the reaction time and the amount of base (Table 1, entry 13), we employed the reaction conditions in Table 1, entry 11 for further investigations, having practical aspects in mind.

With the optimized conditions in hand, we surveyed the scope and limitations of this asymmetric alkylation of α-benzoyloxy-β-keto esters (Table 2). The use of substituted benzyl bromides was initially evaluated. Irrespective of the electronic properties of the aromatic rings, alkylated compounds were obtained in good yields with the selectivity ranging from 88% to 92% *ee* (Table 2, entries 1–5). Allylic substrates were also suitable for this reaction, furnishing the products in good yields and enantioselectivities (Table 2, entries 6–10). Curiously, the reaction with propargyl bromide led to the significant decrease of the enantiomeric excess (Table 2, entry 11). Our focus then moved to the employment of other α-benzoyloxy-β-keto esters as nucleophiles. Asymmetric benzylation of 2-benzoyloxy-3-oxopentanoate **3f** furnished the alkylated compound in 88% yield with slightly diminished *ee* value of 79% (Table 2, entry 12). The use of α-benzoyloxy-β-keto ester **3g** bearing propyl group as R^2, resulted in the further decrease of the enantioselectivity (Table 2, entry 13). An attempt to extend this method in the reaction with the malonate **3h** having two different ester moieties led to the formation of the alkylated compound with moderate enantioselectivity (Table 2, entry 14).[10]

Table 2. Phase-transfer-catalyzed alkylation of α-benzoyloxy-β-keto esters and alkyl halides.[a]

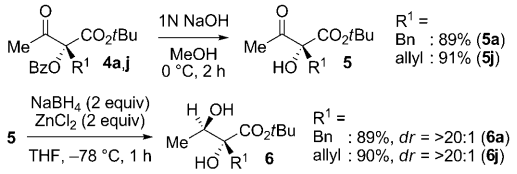


Entry	R^1Br	R^2	Yield [%][b]		*ee* [%][c]
1		Me (**3a**)	91	**4a**	90
2		Me	86	**4f**	92
3		Me	91	**4g**	91
4		Me	79	**4h**	89
5		Me	92	**4i**	88
6		Me	85	**4j**	91
7[d]		Me	90	**4k**	91
8		Me	88	**4l**	90
9		Me	89	**4m**	87
10		Me	41	**4n**	83
11		Me	29	**4o**	61
12		Et (**3f**)	88	**4p**	79
13		Pr (**3g**)	40	**4q**	73
14[e]		OMe (**3h**)	94	**4r**	31

[a] Performed with **3** (0.2 mmol) and R^1Br (0.24 mmol) in the presence of 1 mol% of catalyst (*S*,*S*)-**1c** and powdered KOH (0.3 mmol) in toluene (2 mL) at −20 °C. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis or GC analysis. [d] Crotyl bromide used as a *E*/*Z* mixture (5:1). [e] Performed at 0 °C.

Stereoselective Construction of Congested 2,3-Dihydroxycarboyxlic Acid Esters

To underline the synthetic value of so-obtained enantioenriched α-hydroxy-β-keto esters, removal of the benzoyl moiety and subsequent diastereoselective reduction of the remaining ketone moiety were initially examined (Scheme 2). As the benzoyl group could be easily cleaved under the basic hydrolytic conditions, the reduction of the ketone moiety was then implemented following the literature procedure.[11] Thus, treatment of the hydrolysis products **5** with the 1:1 mixture of $NaBH_4$ and $ZnCl_2$ gave the esters **6** bearing the 2,3-tertiary–secondary diol moiety in good yields with uniformly high diastereoselectivity.[12]

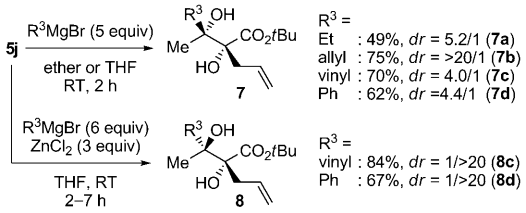


Scheme 2. Deprotection and diastereoselective reduction.

We then investigated the nucleophilic addition of Grignard reagents to the ketone moiety to find an access to the esters with highly congested vicinal tertiary–tertiary diols.[13] In this regard, subjecting the deacylated compound **5j** (see Scheme 2) to an excess of Grignard reagent furnished the *cis*-2,3-dihydroxy esters **7a–d** in good yields with moderate to excellent diastereoselectivities (Scheme 3).[12]

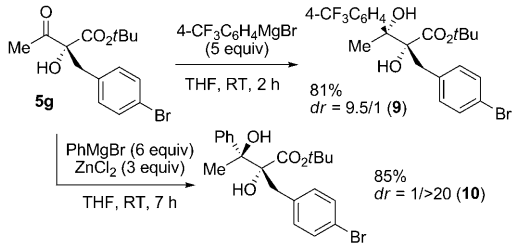
Intriguingly, the stereochemical outcome could be inverted by premixing Grignard reagent with $ZnCl_2$ in a ratio of 2:1,[14] giving the opposite *trans* isomer **8** in greater than 1:20 diastereomeric ratio.[12] Such a phenomenon could only be observed in the case of the reactions using vinyl and aryl Grignard reagents.

The relative as well as the absolute configurations of these congested 2,3-dihydroxycarboyxlic acid esters were de-



Scheme 3. Diastereoselective addition of Grignard reagents.

termined unambiguously by X-ray crystallographic analyses of the arylated compounds derived from **5g** (Scheme 4 and Figure 1).[15]



Scheme 4. Determination of the stereochemistry by X-ray crystallographic analyses.

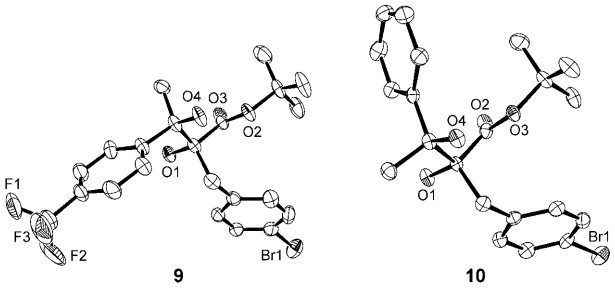


Figure 1. ORTEP plots at 50% probability of **9** (left) and **10** (right).

Conclusions

In conclusion, we obtained α-alkyl-α-hydroxy-β-keto esters with high enantioselectivities by employing the phase-transfer-catalyzed asymmetric alkylation of α-benzoyloxy-β-keto esters as a key asymmetric C–C bond forming step. The synthetic application of the so-obtained alkylated compounds allowed facile access to a variety of densely functionalized 2,3-dihydroxy esters in a highly diastereoselective fashion by the judicious choice of the reaction conditions.

Experimental Section

General information: Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer. ^{1}H NMR spectra were measured on a JEOL JNM-FX400 (400 MHz) spectrometer. Data are reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard in $CDCl_3$, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, tt = triplet of triplets, m = multiplet, br = broad, app = apparent), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on a JEOL JNM-FX400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the residual solvent as an internal standard. Analytical gas–liquid phase chromatography (GLC) was performed on Shimadzu GC-14B instruments equipped with a flame ionization detector using an Astec Chiraldex B-DM (30 m × 0.25 mm) column. High-performance liquid chromatography (HPLC) was performed on Shimadzu 10 A instruments at 220 nm using 4.6 nm × 25 cm Daicel Chiralpak and Chiralcel. High-resolution mass spectrometry (HRMS) was performed on Brucker microTOF instrument. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel 60 (Merck, 230–400 mesh). Toluene was purchased from Wako Chemical Co. Other simple chemicals were purchased and used as received. $ZnCl_2$ was fused under vacuum prior to use.

Preparation of *tert*-butyl 2-benzoyloxy-3-oxobutanoate (3a): To a solution of *tert*-butyl 2-bromo-3-oxobutanoate (2.11 g, 8.9 mmol) DMF (18 mL), prepared according to a literature method,[7] was added sodium benzoate (1.93 g, 13.4 mmol), and the mixture was stirred at room temperature for 2 h. The resulting solution was then diluted with water and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **3a** as a white solid [74% (1.83 g)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (2H, m, ArH), 7.62 (1H, tt, J = 1,5, 7.6 Hz, ArH), 7.48 (2H, app t, J = 7.6 Hz, ArH), 5.63 (1H, s, BzOCH), 2.42 (3H, s, CH_3CO), 1.52 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.9, 165.1, 163.4, 133.7, 130.1, 128.7, 128.5, 84.1, 78.6, 27.9, 27.3 ppm; IR (neat): $\tilde{\nu}$ = 2980, 1726, 1603, 1452, 1366, 1256, 1148, 1113, 1069, 1026, 841, 779, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{15}H_{18}O_5$: m/z 301.1046 $[M+Na]^+$, found: m/z 301.1047 $[M+Na]^+$.

***tert*-Butyl 2-benzoyloxy-3-oxopentanoate (3f)**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (2H, m, ArH), 7.61 (1H, tt, J = 1.5, 7.6 Hz, ArH), 7.48 (2H, app t, J = 7.7 Hz, ArH), 5.64 (1H, s, BzOCH), 2.77 (2H, q, J = 7.3 Hz, CH_2CH_3), 1.51 (9H, s, *t*Bu), 1.52 ppm (3H, t, J = 7.3 Hz, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.0, 165.2, 163.6, 133.7, 130.0, 128.7, 128.5, 83.9, 78.1, 33.3, 27.9, 7.3 ppm; IR (neat): $\tilde{\nu}$ = 2980, 1601, 1452, 1261, 1236, 1125, 1109, 1026, 839, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{16}H_{20}O_5$: m/z 315.1203 $[M+Na]^+$, found: m/z 315.1191 $[M+Na]^+$.

***tert*-Butyl 2-benzoyloxy-3-oxohexanoate (3g)**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (2H, m, ArH), 7.61 (1H, tt, J = 1.5, 7.4 Hz, ArH), 7.48 (2H, app t, J = 7.7 Hz, ArH), 5.63 (1H, s, BzOCH), 2.72 (2H, t, J = 7.1 Hz, $CH_2CH_2CH_3$), 1.70 (2H, m, $CH_2CH_2CH_3$), 1.51 (9H, s, *t*Bu), 0.96 ppm (3H, t, J = 7.3 Hz, $CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.2, 165.1, 163.5, 133.7, 130.0, 128.7, 128.5, 83.9, 78.3, 41.7, 27.9, 16.6, 13.5 ppm; IR (neat): $\tilde{\nu}$ = 2974, 1726, 1452, 1369, 1256, 1113, 1070, 1026, 841, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{17}H_{22}O_5$: m/z 329.1359 $[M+Na]^+$, found: m/z 329.1351 $[M+Na]^+$.

***tert*-Butyl methyl 2-(benzoyloxy)malonate (3h)**: To a stirred solution of *tert*-butyl methyl malonate (338 μL, 2.0 mmol) and *N*-bromosuccinimide (356 mg, 2.05 mmol) in benzene (5.0 mL) was added 2,2′-azobis(isobutyronitrile) (32.8 mg, 0.20 mmol) at room temperature. The reaction mixture was then heated at reflux for 4 h, poured into water, and extracted with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. To this residue were added DMF (3 mL) and sodium benzoate (432 mg, 3.0 mmol) at room temperature. After stirring for 4 h, the resulting mixture was poured into water and extracted with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with hexane/AcOEt = 10:1) to give **3h** as a colorless oil (455 mg, 1.55 mmol, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (2H, m, ArH), 7.60 (1H, tt, J = 1.6, 7.6 Hz, ArH), 7.47 (2H, t, J = 8.0 Hz, ArH), 5.68 (1H, s, CHOBz), 3.86 (3H, s, OCH_3), 1.52 ppm (9H, s,*t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 165.1, 163.3, 133.7, 130.1, 128.6, 128.5, 84.0, 72.5, 53.0, 27.8 ppm; IR (neat): $\tilde{\nu}$ = 2982, 1769, 1730, 1236, 1150, 1113, 1024, 841, 748, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{15}H_{18}NaO_6$: m/z 317.0996 $[M+Na]^+$, found: 317.0995 $[M+Na]^+$.

General procedure for the catalytic asymmetric alkylation of *tert*-butyl 2-benzoyloxy-3-oxoalkanoate under phase-transfer conditions (Table 2): To a solution of phase transfer catalyst (*S*,*S*)-**1c** (2.2 mg, 0.002 mmol) and 3 (0.20 mmol) in toluene (2 mL) was added the corresponding alkyl halide and the mixture was cooled to −20 °C. Freshly powdered KOH (19.8 mg, 0.3 mmol) was added to the mixture, and the reaction mixture was vigorously stirred until the completion of the reaction. The mixture was then

poured into saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give the alkylated compound.

***tert*-Butyl (*R*)-2-benzoyloxy-2-benzyl-3-oxobutanoate (4a)**: Prepared according to the general procedure with benzyl bromide (28.5 μL, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 12 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4a** as a colorless oil [91% (67.6 mg), 90% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 22.3 min (major) and 25.0 min (minor)). $[\alpha]_D^{28} = -46.5$ ($c = 1.0$, $CHCl_3$; 90% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.00 (2H, m, ArH), 7.61 (1H, app t, $J = 7.6$ Hz, ArH), 7.46 (2H, app t, $J = 7.8$ Hz, ArH), 7.21–7.22 (3H, m, ArH), 7.12 (2H, m, ArH), 3.65 (2H, s, $PhCH_2$), 2.25 (3H, s, $COCH_3$), 1.40 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 202.2$, 165.3, 165.2, 134.4, 133.5, 130.2, 129.8, 129.3, 128.5, 128.3, 127.1, 89.0, 83.4, 38.8, 27.6, 27.4 ppm; IR (neat): $\tilde{\nu} =$ 2978, 2932, 1755, 1721, 1279, 1152, 1107, 1094, 1069, 1026 912, 845, 733, 700 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{24}O_5$: *m*/*z* 391.1516 $[M+Na]^+$, found: *m*/*z* 391.1516 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-(4-fluorobenzyl)-3-oxobutanoate (4f)**: Prepared according to the general procedure with 4-fluorobenzyl bromide (30.0 μL, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 10 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4f** as a colorless oil [86% yield (66.2 mg), 92% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 23.6 min (major) and 24.8 min (minor)). $[\alpha]_D^{29} = -46.7$ ($c = 1.0$, $CHCl_3$; 92% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.99$ (2H, m, ArH), 7.62 (1H, app t, $J = 7.6$ Hz, ArH), 7.47 (2H, app t, $J = 8.0$ Hz, ArH), 7.08 (2H, dd, $J = 8.8$ Hz, $^4J(^1H, ^{19}F) = 5.6$ Hz, ArH), 6.90 (2H, app t, $J = 8.8$ Hz, ArH), 3.62 (2H, s, $ArCH_2$), 2.26 (3H, s, $COCH_3$), 1.40 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 202.1$, 165.2, 165.1, 162.0 (d, $^1J(^{13}C, ^{19}F) =$ 246.9 Hz), 133.7, 131.7 (d, $^3J(^{13}C, ^{19}F) = 8.2$ Hz), 130.2 (d, $^4J(^{13}C, ^{19}F) =$ 3.3 Hz), 129.8, 129.1, 128.6, 115.2 (d, $^2J(^{13}C, ^{19}F) = 21.4$ Hz), 88.9, 83.6, 37.8, 27.6, 27.4 ppm; IR (neat): $\tilde{\nu} = 2978$, 2934, 1755, 1721, 1510, 1279, 1223, 1153, 1099, 1069, 1026, 841, 708 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{23}FO_5$: *m*/*z* 409.1422 $[M+Na]^+$, found: *m*/*z* 409.1424 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-(4-bromobenzyl)-3-oxobutanoate (4g)**: Prepared according to the general procedure with 4-bromobenzyl bromide (60.0 mg, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 10 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4g** as a colorless oil [91% (81.8 mg), 91% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 29.4 min (major) and 33.0 min (minor)). $[\alpha]_D^{29} = -46.7$ ($c = 1.0$, $CHCl_3$; 91% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.99$ (2H, d, $J = 7.4$ Hz, ArH), 7.62 (1H, t, $J = 7.6$ Hz, ArH), 7.45 (2H, app t, $J = 7.8$ Hz, ArH), 7.34 (2H, d, $J = 8.3$ Hz, ArH), 6.98 (2H, d, $J = 8.3$ Hz, ArH), 3.61 (2H, s, $ArCH_2$), 2.27 (3H, s, $COCH_3$), 1.41 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.9$, 165.1, 165.0, 133.7, 133.5, 131.9, 131.4, 129.7, 129.1, 128.6, 121.3, 88.8, 83.7, 37.9, 27.6, 27.3 ppm; IR (neat): $\tilde{\nu} = 2978$, 1755, 1724, 1489, 1369, 1281, 1153, 1107, 1094, 1070, 843, 712 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{23}BrO_5$: *m*/*z* 469.0621 $[M+Na]^+$, found: *m*/*z* 469.0622 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-(4-methylbenzyl)-3-oxobutanoate (4h)**: Prepared according to the general procedure with 4-methylbenzyl bromide (44.4 mg, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 4 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4h** as a colorless oil [79% (60.5 mg), 89% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 24.1 min (major) and 28.2 min (minor)). $[\alpha]_D^{28} = -42.3$ ($c = 1.0$, $CHCl_3$; 89% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.00$ (2H, m, ArH), 7.60 (1H, tt, $J = 1.5$, 7.6 Hz, ArH), 7.46 (2H, app t, $J = 8.1$ Hz, ArH), 7.02 (2H, d, $J = 8.6$ Hz, ArH), 6.99 (2H, d, $J = 8.6$ Hz, ArH), 3.60 (2H, s, $ArCH_2$), 2.28 (3H, s, $COCH_3$), 2.24 (3H, s, $ArCH_3$), 1.41 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 202.2$, 165.4, 165.2, 136.7, 135.5, 131.2, 130.1, 129.8, 129.4, 129.0, 128.5, 89.1, 83.4, 38.4, 27.7, 27.5, 21.0 ppm; IR (neat): $\tilde{\nu} = 2978$, 2932, 1757, 1722, 1281, 1175, 1155, 1109, 1069, 1026, 841, 814, 712 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{23}H_{26}O_5$: *m*/*z* 405.1672 $[M+Na]^+$, found: *m*/*z* 405.1660 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-(4-methoxylbenzyl)-3-oxobutanoate (4i)**: Prepared according to the general procedure with 4-methoxybenzyl bromide (34.6 μL, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 7 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4i** as a colorless oil [92% (73.6 mg), 88% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 45.2 min (major) and 51.7 min (minor)). $[\alpha]_D^{30} = -43.1$ ($c = 1.0$, $CHCl_3$; 88% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.01$ (2H, m, ArH), 7.61 (1H, app t, $J = 7.4$ Hz, ArH), 7.47 (2H, app t, $J = 8.1$ Hz, ArH), 7.03 (2H, d, $J = 8.8$ Hz, ArH), 6.76 (2H, d, $J = 8.8$ Hz, ArH), 3.75 (3H, s, OCH_3), 3.58 (2H, s, $ArCH_2$), 2.25 (3H, s, $COCH_3$), 1.41 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 202.3$, 165.4, 165.1, 158.7, 133.5, 131.2, 129.8, 129.3, 128.5, 126.3, 113.7, 89.1, 83.3, 55.1, 38.0, 27.6, 27.5 ppm; IR (neat): $\tilde{\nu} = 2978$, 2934, 1755, 1514, 1281, 1248, 1177, 1153, 1111, 1096, 1069, 1026, 841, 731, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{23}H_{26}O_6$: *m*/*z* 421.1622 $[M+Na]^+$, found: *m*/*z* 421.1611 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-allyl-2-benzoyloxy-3-oxobutanoate (4j)**: Prepared according to the general procedure with allyl bromide (51.9 μL, 0.6 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 20 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4j** as a colorless oil [85% (53.9 mg), 91% *ee*]. Enantiomeric purity was determined after the reduction of the olefin moiety (see below). $[\alpha]_D^{27} = -29.2$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (2H, m, ArH), 7.56 (1H, tt, $J = 1.5$, 7.6 Hz, ArH), 7.47 (2H, app t, $J = 8.1$ Hz, ArH), 5.73 (1H, m, $CH{=}CH_2$), 5.10–5.18 (2H, m, $CH{=}CH_2$), 3.07 (2H, d, $J = 7.3$ Hz, $CH_2CH{=}CH_2$), 2.41 (3H, s, $COCH_3$), 1.46 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 200.8$, 165.4, 164.9, 133.5, 130.5, 129.8, 129.3, 128.5, 120.0, 88.2, 83.5, 37.8, 27.7, 26.9 ppm; IR (neat): $\tilde{\nu} = 3078$, 2980, 2934, 1755, 1721, 1315, 1281, 1242, 1157, 1138, 1107, 1096, 1069, 1026, 991, 924, 840, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{18}H_{22}O_5$: *m*/*z* 341.1359 $[M+Na]^+$, found: *m*/*z* 341.1366 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-propyl-3-oxobutanoate**: To a solution of 10% Pd/C (20 mg) in methanol (2 mL) was added **4j** (23.0 mg, 0.083 mmol), and the flask was charged with H_2. The reaction mixture was then stirred for 2 h at room temperature under hydrogen atmosphere (balloon) and filtered through celite. The filtrate was concentrated in vacuo and passed through short pad of silica gel (eluting with hexane/ethyl acetate = 10:1) to give *tert*-butyl (*R*)-2-benzoyloxy-2-propyl-3-oxobutanoate as a colorless oil [97% (22.5 mg), 91% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 300:1, flow rate = 0.5 mL min^{-1}, retention time; 30.3 min (major) and 32.2 min (minor)). $[\alpha]_D^{28} = -21.6$ ($c = 1.0$, $CHCl_3$; 91% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.09$ (2H, m, ArH), 7.60 (1H, tt, $J = 1.5$, 7.6 Hz, ArH), 7.47 (2H, app t, $J = 8.1$ Hz, ArH), 2.42 (3H, s, CH_3), 2.26 (2H, m, $CH_2CH_2CH_3$), 1.46 (9H, s, *t*Bu), 1.38 (2H, m, $CH_2CH_2CH_3$), 0.95 ppm (3H, t, $J = 7.3$ Hz, $CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.2$, 166.1, 165.0, 133.4, 129.9, 129.4, 128.5, 88.9, 83.3, 35.7, 27.7, 26.9, 17.0, 14.1 ppm; IR (neat): $\tilde{\nu} = 2972$, 2934, 2876, 1724, 1454, 1368, 1283, 1248, 1163, 1138, 1111, 1028, 845, 712 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{18}H_{24}O_5$: *m*/*z* 343.1516 $[M+Na]^+$, found: *m*/*z* 343.1529 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-*E*-crotyl-3-oxobutanoate (5:1 *E*/*Z* mixture) (4k)**: Prepared according to the general procedure with crotyl bromide (5:1 *E*/*Z* mixture) (29.0 μL, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 9 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4k** as a colorless oil [90% (60.1 mg, *E*/*Z* = 5:1), 92% *ee* (for *E* isomer)].

Enantiomeric purity was determined after the hydrolysis of the benzoyl group (see below). $[\alpha]_D^{31} = -25.2$ ($c = 1.0$, $CHCl_3$; $E/Z = 5:1$); ^{1}H NMR (400 MHz, $CDCl_3$) (major isomer): $\delta = 8.08$ (2H, m, ArH), 7.61 (1H, app t, $J = 7.3$ Hz, ArH), 7.47 (2H, app t, $J = 8.0$ Hz, ArH), 5.56 (1H, m, $CH_2CH{=}CH$), 5.36 (1H, m, $CH_2CH{=}CH_2$), 2.98 (2H, d, $J = 7.3$ Hz, $CH_2CH{=}CH_2$), 2.39 (3H, s, $COCH_3$), 1.46 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) (major isomer): $\delta = 201.0$, 165.6, 165.0, 133.4, 130.8, 129.8, 129.4, 128.5, 122.8, 88.4, 83.3, 36.9, 27.8, 27.0, 18.0 ppm; IR (neat): $\tilde{\nu} = 2978$, 2934, 1755, 1724, 1315, 1283, 1260, 1157, 1128, 1107, 968, 843, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{19}H_{24}O_5$: *m/z* 355.1516 $[M+Na]^+$, found: *m/z* 355.1528 $[M+Na]^+$.

***tert*-Butyl (*R*)-2 *E*-crotyl-2-hydroxy-3-oxobutanoate (5:1 *E*/*Z* mixture)**: To a solution of **4k** (5:1 *E*/*Z* mixture) (29.9 mg, 0.090 mmol) in CH_3OH (1.8 mL) was added 1 N aq. NaOH (180 μL, 0.18 mmol), and the mixture was stirred for 1 h at room temperature. The reaction solution was then diluted with water and extracted with hexane. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was passed through a short pad of silica gel (eluting with hexane/ethyl acetate = 5:1) to give *tert*-butyl (*R*)-2 *E*-crotyl-2-hydroxy-3-oxobutanoate as a colorless oil [84% (17.3 mg), 92% *ee* (for *E* isomer)]. Enantiomeric purity of *E* isomer was determined by GLC analysis (Astec Chiraldex B-DM (0.25 mm × 30 m) column, 100 °C isotherm, retention time; 35.9 min (minor) and 37.2 min (major)). $[\alpha]_D^{30} = -16.4$ ($c = 1.0$, $CHCl_3$; 92% *ee*, *E*/*Z* = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) (major isomer): $\delta = 5.58$ (1H, m, $CH_2CH{=}CH$), 5.33 (1H, m, $CH_2CH{=}CH_2$), 4.05 (1H, s, OH), 2.72 (1H, dd, $J = 7.3$, 14.4 Hz, $CHHCH{=}CH_2$), 2.54 (1H, dd, $J = 7.1$, 14.6 Hz, $CHHCH{=}CH_2$), 2.23 (3H, s, $COCH_3$), 1.47 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) (major isomer): $\delta = 204.3$, 169.8, 130.2, 123.5, 83.72, 83.68, 38.0, 27.8, 24.8, 18.0 ppm; IR (neat): $\tilde{\nu} = 3480$, 2980, 2936, 1719, 1369, 1287, 1260, 1225, 1155, 1140, 1109, 970, 843 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{12}H_{20}O_4$: *m/z* 251.1254 $[M+Na]^+$, found: *m/z* 251.1250 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2 *E*-cinnamyl-3-oxobutanoate (4l)**: Prepared according to the general procedure with cinnamyl bromide (47.3 mg, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 9 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4l** as a colorless oil [88% (69.8 mg), 90% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 30.1 min (major) and 36.3 min (minor)). $[\alpha]_D^{30} = -30.4$ ($c = 1.0$, $CHCl_3$; 90% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.08 (2H, m, ArH), 7.60 (1H, m, ArH), 7.46 (2H, app t, $J = 8.1$ Hz, ArH), 7.18–7.27 (5H, m, ArH), 6.47 (1H, d, $J = 15.9$ Hz, PhCH=CH), 6.09 (1H, dt, $J = 7.6$, 15.9 Hz, PhCH=CH), 3.22 (2H, d, $J = 7.6$ Hz, $PhCH{=}CHCH_2$), 2.42 (3H, s, $COCH_3$), 1.45 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 200.9$, 165.4, 165.0, 136.8, 134.9, 133.5, 129.9, 129.2, 128.53, 128.47, 127.5, 126.2, 121.9, 88.4, 83.6, 37.1, 27.8, 27.0 ppm; IR (neat): $\tilde{\nu} = 2978$, 2932, 1753, 1721, 1369, 1356, 1356, 1152, 1105, 1096, 1069, 1026, 966, 843, 743, 710, 692 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{24}H_{26}O_5$: *m/z* 417.1672 $[M+Na]^+$, found: *m/z* 417.1683 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-prenyl-3-oxobutanoate (4m)**: Prepared according to the general procedure with prenyl bromide (28.2 μL, 0.24 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 10 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4m** as a colorless oil [89% (61.9 mg), 87% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 15.7 min (major) and 16.8 min (minor)). $[\alpha]_D^{31} = -22.6$ ($c = 1.0$, $CHCl_3$; 87% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.08 (2H, m, ArH), 7.60 (1H, tt, $J = 1.5$, 7.4 Hz, ArH), 7.47 (2H, app t, $J = 7.8$ Hz, ArH), 5.09 (1H, app t, $J = 7.6$ Hz, $CH{=}C(CH_3)CH_3$), 3.06 (1H, dd, $J = 7.6$, 15.1 Hz, CHHCH=C), 2.98 (1H, dd, $J = 7.1$, 15.1 Hz, CHHCH=C), 2.40 (3H, s, $COCH_3$), 1.67 (3H, s, $CH{=}C(CH_3)CH_3$), 1.58 (3H, s, $CH{=}C(CH_3)CH_3$), 1.45 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.2$, 165.8, 165.1, 136.6, 133.4, 129.8, 129.4, 128.5, 115.9, 88.4, 83.2, 32.5, 27.7, 27.0, 25.9, 17.9 ppm; IR (neat): $\tilde{\nu} = 2978$, 2932, 1755, 1721, 1452, 1369, 1354, 1315, 1281, 1246, 1153, 1107, 1096, 1069, 1026, 843, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{20}H_{26}O_5$: *m/z* 369.1672 $[M+Na]^+$, found: *m/z* 369.1675 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-methallyl-3-oxobutanoate (4n)**: Prepared according to the general procedure with methallyl bromide (60.5 μL, 0.60 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 20 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4n** as a colorless oil [41% (27.5 mg), 83% *ee*]. Enantiomeric purity was determined after the hydrolysis of benzoyl group (see below). $[\alpha]_D^{29} = -24.9$ ($c = 1.0$, $CHCl_3$; 83% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (2H, m, ArH), 7.61 (1H, tt, $J = 1.5$, 7.6 Hz, ArH), 7.48 (2H, app t, $J = 8.1$ Hz, ArH), 4.84 (1H, t, $J = 1.4$ Hz, C=CHH), 4.79 (1H, s, C=CHH), 3.12 (1H, d, $J = 15.2$ Hz, $CHHC(CH_3){=}CH_2$), 3.08 (1H, d, $J = 15.2$ Hz, $CHHC(CH_3){=}CH_2$), 2.42 (3H, s, $COCH_3$), 1.74 (3H, s, $CH_2C(CH_3){=}CH_2$), 1.45 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.1$, 165.5, 164.9, 139.4, 133.5, 129.8, 129.3, 128.5, 116.2, 88.7, 83.5, 40.6, 27.7, 26.7, 23.4 ppm; IR (neat): $\tilde{\nu} = 2978$, 2934, 1757, 1722, 1452, 1369, 1356, 1315, 1281, 1153, 1107, 1096, 1070, 1026, 902, 845, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{19}H_{24}O_5$: *m/z* 355.1516 $[M+Na]^+$, found: *m/z* 355.1502 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-hydroxy-2-methallyl-3-oxobutanoate**: To a solution of **4n** (22.1 mg, 0.066 mmol) in CH_3OH (1.3 mL) was added 1 N aq. NaOH (140 μL, 0.14 mmol) and the mixture was stirred for 1 h at room temperature. The reaction solution was then diluted with water and extracted with hexane. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was passed through a short pad of silica gel (eluting with hexane/ethyl acetate = 5:1) to give *tert*-butyl (*R*)-2-hydroxy-2-methallyl-3-oxobutanoate as a colorless oil [66% (10.0 mg), 83% *ee*]. Enantiomeric purity was determined by GLC analysis (Astec Chiraldex B-DM (0.25 mm × 30 m) column, 80 °C isotherm, retention time; 81.1 min (major) and 83.5 min (minor)). $[\alpha]_D^{30} = -16.2$ ($c = 1.0$, $CHCl_3$; 83% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.87$ (1H, s, C=CHH), 4.79 (1H, s, C=CHH), 4.08 (1H, s, OH), 2.82 (1H, d, $J = 14.6$ Hz, $CHHC(CH_3){=}CH_2$), 2.62 (1H, d, $J = 14.6$ Hz, $CHHC(CH_3){=}CH_2$), 2.24 (3H, s, $COCH_3$), 1.76 (3H, s, $CH_2C(CH_3){=}CH_2$), 1.48 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 204.3$, 170.0, 140.4, 115.0, 87.0, 83.9, 41.7, 27.8, 24.7, 23.9 ppm; IR (neat): $\tilde{\nu} = 3482$, 2980, 2932, 1719, 1456, 1371, 1288, 1153, 1125, 1022, 897, 839, 772 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{12}H_{20}O_4$: *m/z* 251.1254 $[M+Na]^+$, found: *m/z* 251.1256 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-propargyl-3-oxobutanoate (4o)**: Prepared according to the general procedure with propargyl bromide (45.2 μL, 0.60 mmol) and **3a** (55.7 mg, 0.20 mmol) over the course of 24 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4o** as a colorless oil [29% (18.4 mg), 61% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 100:1, flow rate = 0.5 mL min^{-1}, retention time; 22.7 min (minor) and 26.6 min (major)). $[\alpha]_D^{30} = -32.9$ ($c = 1.0$, $CHCl_3$; 61% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.12 (2H, m, ArH), 7.63 (1H, app t, $J = 7.6$ Hz, ArH), 7.50 (2H, t, $J =$ 8.1 Hz, ArH), 3.36 (1H, dd, $J = 2.7$, 17.8 Hz, CHHCCH), 3.29 (1H, dd, $J = 2.7$, 17.6 Hz, CHHCCH), 2.49 (3H, s, $COCH_3$), 1.98 (1H, app t, $J =$ 2.7 Hz, CH_2CCH), 1.46 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 200.8$, 164.8, 164.3, 133.7, 129.9, 129.0, 128.6, 86.9, 84.0, 77.5, 71.6, 27.6, 26.9, 23.4 ppm;IR (neat): $\tilde{\nu} = 3287$, 2980, 2934, 1753, 1724, 1368, 1281, 1242, 1155, 1098, 1070, 839, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{18}H_{20}O_5$: *m/z* 339.1203 $[M+Na]^+$, found: *m/z* 399.1204 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-benzyl-3-oxopentanoate (4p)**: Prepared according to the general procedure with benzyl bromide (28.5 μL, 0.24 mmol) and **3f** (58.5 mg, 0.20 mmol) over the course of 4 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4p** as a colorless oil [88% (67.5 mg), 79% *ee*]. Enantiomeric purity was determined after the cleavage of the benzoyl group (see below). $[\alpha]_D^{32} = -37.3$ ($c = 1.0$, $CHCl_3$; 79% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.98$ (2H, m, ArH), 7.61 (1H, app t, $J = 7.6$ Hz, ArH), 7.46 (2H, app t, $J = 8.0$ Hz, ArH), 7.20 (3H, m, ArH), 7.07 (2H, m, ArH), 3.66 (2H, s, $PhCH_2$), 2.72 (1H, dq, $J = 7.1$, 18.8 Hz, $CHHCH_3$), 2.37 (1H, dq, $J = 7.3$, 19.0 Hz, $CHHCH_3$), 1.40 (9H, s, *t*Bu), 1.01 ppm (3H, t, $J = 7.1$ Hz, CH_2CH_3); ^{13}C NMR (100 MHz,

$CDCl_3$): δ = 205.2, 165.4, 165.1, 134.6, 133.5, 130.2, 129.8, 129.5, 128.5, 128.2, 127.1, 89.2, 83.3, 38.9, 33.0, 27.7, 7.3 ppm; IR (neat): $\tilde{\nu}$ = 2978, 2938, 1757, 1720, 1601, 1452, 1369, 1281, 1155, 1111, 1093, 1026, 953, 845, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{23}H_{26}O_5$: *m/z* 405.1672 $[M+Na]^+$, found: *m/z* 405.1666 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzyl-2-hydroxy-3-oxopentanoate**: To a solution of **4p** (57.3 mg, 0.15 mmol) in CH_3OH (2.0 mL) was added 1 N aq. NaOH (300 μL, 0.30 mmol), and the mixture was stirred for 1 h at 0 °C. The reaction solution was then diluted with water and extracted with hexane. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was passed through a short pad of silica gel (eluting with hexane/ethyl acetate = 5:1) to give *tert*-butyl (*R*)-2-benzyl-2-hydroxy-3-oxopentanoate as a colorless oil [94% (39.2 mg), 79% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 30:1, flow rate = 0.5 mL min^{-1}, retention time; 18.1 min (minor) and 21.7 min (major)). $[\alpha]_D^{31} = -54.8$ (c = 1.0, $CHCl_3$; 79% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.33 (5H, m, ArH), 4.01 (1H, s, OH), 3.36 (1H, d, J = 14.2 Hz, PhCHH), 3.14 (1H, d, J = 14.4 Hz, PhCHH), 2.72 (1H, dq, J = 7.3, 18.6 Hz, CH_3CHH), 2.48 (1H, dq, J = 7.3, 18.6 Hz, CH_3CHH), 1.42 (9H, s, *t*Bu), 1.05 ppm (3H, t, J = 7.1 Hz, CH_3CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.9, 169.9, 135.2, 130.4, 128.1, 127.0, 84.1, 84.0, 40.3, 30.6, 27.8, 7.8 ppm; IR (neat): $\tilde{\nu}$ = 3478, 2978, 1717, 1454, 1369, 1279, 1260, 1219, 1153, 1113, 839, 748, 700 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{16}H_{22}O_4$: *m/z* 301.1410 $[M+Na]^+$, found: *m/z* 301.1402 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-benzoyloxy-2-benzyl-3-oxohexanoate (4q)**: Prepared according to the general procedure with benzyl bromide (28.5 μL, 0.24 mmol) and **3g** (61.3 mg, 0.20 mmol) over the course of 12 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4q** as a colorless oil [40% (30.7 mg), 73% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 300:1, flow rate = 0.5 mL min^{-1}, retention time; 18.0 min (major) and 20.5 min (minor)). $[\alpha]_D^{28} = -34.5$ (c = 1.0, $CHCl_3$; 73% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (2H, m, ArH), 7.61 (1H, app t, J = 7.6 Hz, ArH), 7.46 (2H, app t, J = 7.8 Hz, ArH), 7.19 (3H, m, ArH), 7.07 (2H, m, ArH), 3.69 (1H, d, J = 14.6 Hz, PhCHH), 3.65 (1H, d, J = 14.7 Hz, PhCHH), 2.70 (1H, m, COCHH), 2.32 (1H, m, COCHH), 1.57 (2H, m, $CH_2CH_2CH_3$), 1.40 (9H, s, *t*Bu), 0.86 ppm (3H, t, J = 7.3 Hz, $CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.3, 165.3, 165.1, 134.6, 133.5, 130.3, 129.8, 129.5, 128.6, 128.2, 127.1, 89.3, 83.3, 41.3, 38.7, 27.7, 16.5, 13.5 ppm;IR (neat): $\tilde{\nu}$ = 2974, 1720, 1452, 1369, 1281, 1155, 1107, 1026, 845, 710 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{24}H_{28}O_5$: *m/z* 419.1829 $[M+Na]^+$, found: *m/z* 419.1845 $[M+Na]^+$.

***tert*-Butyl methyl (*R*)-2-(benzoyloxy)-2-benzylmalonate (4r)**: Prepared according to the general procedure with benzyl bromide (28.5 μL, 0.24 mmol) and **3h** (58.8 mg, 0.20 mmol) over the course of 3 h at 0 °C. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 10:1) to give **4r** as a colorless oil [94% (72.4 mg), 31% *ee*]. Enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak OD-H, hexane/isopropyl alcohol = 50:1, flow rate = 0.5 mL min^{-1}, retention time; 13.5 min (minor) and 16.0 min (major)). $[\alpha]_D^{23} = +1.9$ (c = 1.0, $CHCl_3$; 31% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (2H, m, ArH), 7.58 (1H, app t, J = 7.6 Hz, ArH), 7.44 (2H, t, J = 7.6 Hz, ArH), 7.26–7.20 (5H, m, ArH), 3.79 (3H, s, OCH_3), 3.66 (2H, s, $ArCH_2$), 1.42 ppm (9H, s,*t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.2, 165.0, 164.7, 134.2, 133.4, 130.3, 130.0, 129.3, 128.4, 128.2, 127.3, 83.6, 83.5, 52.9, 39.8, 27.7 ppm; IR (neat): $\tilde{\nu}$ = 1753, 1724, 1452, 1369, 1283, 1250, 1209, 1153, 1107, 1055, 843, 712, 702 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{24}O_6$: *m/z* 407.1465 $[M+Na]^+$, found: *m/z* 407.1474.

***tert*-Butyl (*R*)-2-benzyl-2-hydroxy-3-oxobutanoate (5a)**: To a solution of **4a** (32.0 mg, 0.088 mmol) in CH_3OH (2 mL) was added 1 N aq. NaOH (180 μL, 0.18 mmol), and the mixture was stirred for 2 h at 0 °C. The reaction solution was then diluted with water and extracted with hexane. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was passed through a short pad of silica gel (eluting with hexane/ethyl acetate = 5:1) to give **5a** as a colorless oil [80% (18.4 mg)]. $[\alpha]_D^{31} = -62.6$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–7.26 (5H, m, ArH), 4.02 (1H, s, OH), 3.36 (1H, d, J = 14.4 Hz, PhCHH), 3.13 (1H, d, J = 14.2 Hz, PhCHH), 2.24 (3H, s, CH_3), 1.43 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.0, 169.7, 135.1, 130.3, 128.1, 127.0, 84.2, 84.1, 40.0, 27.7, 24.9 ppm; IR (neat): $\tilde{\nu}$ = 3480, 2980, 1717, 1456, 1369, 1281, 1219, 1150, 1119, 837, 746, 700 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{15}H_{20}O_4$: *m/z* 287.1254 $[M+Na]^+$, found: *m/z* 287.1247 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-allyl-2-hydroxy-3-oxobutanoate (5j)**: $[\alpha]_D^{30} = -20.3$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.72 (1H, m, CH_2CH=CH_2), 5.12–5.19 (2H, m, CH_2CH=CH_2), 4.08 (1H, s, OH), 2.79 (1H, dd, J = 7.3, 14.4 Hz, CH_2CH=CHH), 2.62 (1H, dd, J = 7.1, 14.4 Hz, CH_2CH=CHH), 2.23 (3H, s, CH_3CO), 1.47 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.1, 169.7, 131.2, 119.4, 83.9, 83.4, 39.1, 27.8, 24.7 ppm; IR (neat): $\tilde{\nu}$ = 3483, 2980, 2928, 1721, 1369, 1287, 1244, 1150, 1016, 922, 841, 772, 673 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{11}H_{18}O_4$: *m/z* 237.1097 $[M+Na]^+$, found: *m/z* 237.1098 $[M+Na]^+$.

***tert*-Butyl (*R*)-2-(4-bromobenzyl)-2-hydroxy-3-oxobutanoate (5g)**: $[\alpha]_D^{25} = -64.0$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (2H, d, J = 8.8 Hz, ArH), 7.13 (2H, d, J = 8.8 Hz, ArH), 4.04 (1H, s, OH), 3.29 (1H, d, J = 14.4 Hz, ArCHH), 3.08 (1H, d, J = 14.4 Hz, ArCHH), 2.22 (3H, s, $COCH_3$), 1.43 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.7, 169.6, 134.1, 132.0, 131.2, 121.1, 84.5, 83.8, 39.4, 27.8, 24.8; IR (neat): $\tilde{\nu}$ = 3487, 2978, 1719, 1487, 1369, 1288, 1151, 1121, 1072, 1013, 841 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{15}H_{19}BrNaO_4$: *m/z* 365.0359 $[M+Na]^+$, found: *m/z* 365.0374 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*R*)-2-benzyl-2,3-dihydroxybutanoate (6a)**: To a solution of $ZnCl_2$ (27.2 mg, 0.2 mmol) in THF (1.0 mL) was added $NaBH_4$ (7.6 mg, 0.2 mmol), and the mixture was stirred at room temperature for 1 h. After cooling the mixture to −78 °C, THF (1.0 mL) solution of **5a** (26.4 mg, 0.1 mmol) was added dropwise. The reaction was stirred for 1 h at the same temperature. The reaction mixture was then poured into saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was passed through a short pad of silica gel (eluting with hexane/ethyl acetate = 4:1) to give **6a** as a colorless oil [89% (23.8 mg), d.r. > 20:1]. $[\alpha]_D^{28} = -12.1$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.27 (5H, m, ArH), 3.98 (1H, m, CHOH), 3.42 (1H, s, OH), 2.90 (2H, s, $PhCH_2$), 2.06 (1H, d, J = 10.5 Hz, CHOH), 1.39 (9H, s, *t*Bu), 1.31 ppm (3H, d, J = 6.6 Hz, CH_3CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.5, 135.8, 130.2, 128.0, 126.8, 83.4, 80.5, 71.9, 40.9, 27.9, 17.4 ppm; IR (neat): $\tilde{\nu}$ = 3480, 2978, 2934, 1722, 1395, 1369, 1279, 1258, 1221, 1155, 1128, 1053, 999, 895, 841, 739, 700 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{15}H_{22}O_4$: *m/z* 289.1410 $[M+Na]^+$, found: *m/z* 289.1389 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*R*)-2-allyl-2,3-dihydroxybutanoate (6j)**: $[\alpha]_D^{30} = +31.5$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.74 (1H, m, CH_2CH=CH_2), 5.10–5.16 (2H, m, CH_2CH=CH_2), 3.90 (1H, dq, J = 6.6, 10.2 Hz, $CH_3CH(OH)$), 3.49 (1H, s, OH), 2.31–2.41 (2H, m, CH_2CH=CH_2), 2.04 (1H, d, J = 10.3 Hz, $CH_3CH(OH)$), 1.49 (9H, s, *t*Bu), 1.23 ppm (3H, d, J = 6.6 Hz, $CH_3CH(OH)$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0, 131.9, 118.9, 83.2, 79.6, 71.4, 39.6, 23.0, 17.2 ppm; IR (neat): $\tilde{\nu}$ = 3495, 2980, 2936, 1724, 1641, 1393, 1371, 1283, 1238, 1152, 1109, 997, 918, 845, 756, 675 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{11}H_{20}O_4$: *m/z* 239.1254 $[M+Na]^+$, found: *m/z* 239.1255 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*R*)-2-allyl-2,3-dihydroxy-3-methylpentanoate (7a)**: To a 1.0 M solution (0.50 mL, 0.50 mmol) of ethylmagnesium bromide in diethyl ether was added *tert*-butyl (*R*)-2-allyl-2-hydroxy-3-oxobutanoate (21.4 mg, 0.10 mmol) at room temperature. The mixture was stirred for 2 h at the same temperature, and then the reaction was quenched with 1 N HCl and extracted with hexane. Organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was then purified by column chromatography on silica gel (eluding with hexane/ethyl acetate = 10:1) to give **7a** as a colorless oil [49% (12.0 mg), d.r. = 5.2:1]. $[\alpha]_D^{28} = +30.7$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) (major isomer): δ = 5.76 (1H, m, CH=CH_2), 5.09–5.15 (2H, m, CH=CH_2), 3.58 (1H, s, OH), 5.61 (2H, d, J = 7.1 Hz, CH_2CH=CH_2), 1.68 (2H, m, $CHHCH_3$), 1.49 (9H, s, *t*Bu), 1.27 (1H, m, $CHHCH_3$), 1.22 (3H, s, CH_3), 0.95 ppm (3H, t, J = 7.6 Hz, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) (major isomer): δ = 173.9, 132.9, 118.6, 83.6, 81.6, 75.4, 37.3, 28.6, 28.0,

20.0, 7.6 ppm; IR (neat): $\tilde{\nu}$ = 3493, 3076, 2978, 2932, 1713, 1460, 1395, 1369, 1271, 1236, 1144, 1090, 1047, 999, 916, 843 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{13}H_{24}O_4$: *m/z* 267.1567 $[M+Na]^+$, found: *m/z* 267.1558 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*R*)-2-allyl-2,3-dihydroxy-3-methylhex-5-enoate (7b)**: $[\alpha]_D^{29}$ = +55.3 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.93 (1H, m, CH=CH_2), 5.75 (1H, m, CH=CH_2), 5.04–5.16 (4H, m, CH=CH_2, CH=CH_2), 3.58 (1H, s, OH), 2.66 (1H, s, OH), 2.61 (2H, m, CH_2CH=CH_2), 2.46 (1H, dd, *J* = 6.6, 14.4 Hz, CHHCH=CH_2), 2.04 (1H, dd, *J* = 8.0, 13.9 Hz, CHHCH=CH_2), 1.51 (9H, s, *t*Bu), 1.24 ppm (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 134.0, 132.7, 118.8, 118.0, 83.8, 81.4, 75.1, 41.2, 37.3, 28.0, 21.4 ppm; IR (neat): $\tilde{\nu}$ = 3509, 3076, 2978, 2934, 1717, 1639, 1369, 1273, 1238, 1144, 1096, 1051, 999, 916, 843 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{14}H_{24}O_4$: *m/z* 279.1567 $[M+Na]^+$, found: *m/z* 279.1556 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*R*)-2-allyl-2,3-dihydroxy-3-methylpent-4-enoate (7c)**: $[\alpha]_D^{30}$ = +22.4 (*c* = 1.0, $CHCl_3$; 91% *ee*); ^1H NMR (400 MHz, $CDCl_3$) (major isomer): δ = 5.91 (1H, dd, *J* = 11.0, 17.3 Hz, CH=CH_2), 5.74 (1H, m, CH_2CH=CH_2), 5.36 (1H, dd, *J* = 1.4, 17.3 Hz, CH=CHH), 5.09–5.18 (3H, m, CH=CHH, CH_2CH=CH_2), 3.49 (1H, s, OH), 2.92 (1H, s, OH), 2.62 (1H, dd, *J* = 8.6, 14.2 Hz, CHHCH=CH_2), 2.52 (1H, m, CHHCH=CH_2), 1.50 (9H, s, *t*Bu), 1.35 ppm (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) (major isomer): δ = 173.5, 140.1, 132.6, 118.8, 114.4, 84.0, 80.8, 76.0, 37.4, 28.0, 23.1 ppm; IR (neat): $\tilde{\nu}$ = 3493, 3078, 2980, 2934, 1717, 1641, 1369, 1275, 1144, 1090, 997, 920, 845 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{13}H_{22}O_4$: *m/z* 265.1410 $[M+Na]^+$, found: *m/z* 265.1412 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*R*)-2-allyl-2,3-dihydroxy-3-phenylbutanoate (7d)**: $[\alpha]_D^{25}$ = +22.5 (*c* = 1.0, $CHCl_3$; 91% *ee*); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.52 (2H, m, ArH), 7.32 (2H, m, ArH), 7.26 (1H, m, ArH), 5.67 (1H, m, CH_2CH=CH_2), 5.05–5.10 (2H, m, CH_2CH=CH_2), 3.61 (1H, s, OH), 3.54 (1H, s, OH), 2.75 (1H, ddd, *J* = 0.7, 8.5, 14.0 Hz, CHHCH=CH_2), 2.31 (1H, ddt, *J* = 1.5, 5.8, 13.9 Hz, CHHCH=CH_2), 1.66 (3H, s, CH_3), 1.44 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 142.9, 132.4, 127.4, 127.1, 126.9, 118.9, 84.3, 81.5, 76.8, 38.2, 27.9, 25.0 ppm; IR (neat): $\tilde{\nu}$ = 1717, 1369, 1271, 1238, 1140, 1101, 997, 914, 841 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{17}H_{24}O_4$: *m/z* 315.1567 $[M+Na]^+$, found: *m/z* 315.1565 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*R*)-2-(4-bromobenzyl)-2,3-dihydroxy-3-(4-(trifluoromethyl)phenyl)butanoate (9)**: $[\alpha]_D^{24}$ = +3.5 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (2H, d, *J* = 8.2 Hz, ArH), 7.61 (2H, d, *J* = 8.2 Hz, ArH), 7.33 (2H, d, *J* = 8.2 Hz, ArH), 7.02 (2H, d, *J* = 8.5 Hz, ArH), 3.86 (1H, s, OH), 3.50 (1.0H, s, OH), 3.27 (1H, d, *J* = 13.5 Hz, ArCHH), 2.50 (1.0H, d, *J* = 13.8 Hz, ArCHH), 1.66 (3H, s, CH_3), 1.33 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9, 146.7, 134.7, 132.5, 131.0, 129.4 (q, $^2J_{C-F}$ = 32.2 Hz), 127.8, 124.4 (q, $^3J_{C-F}$ = 4.1 Hz), 124.3 (q, $^1J_{C-F}$ = 272.0 Hz), 120.9, 85.5, 81.7, 38.9, 27.8, 25.6 ppm (one peak overlaps with $CDCl_3$); IR (neat): $\tilde{\nu}$ = 1721, 1327, 1260, 1163, 1123, 1070, 1015, 851 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{22}H_{24}BrF_3O_4$: *m/z* 513.0685 $[M+Na]^+$, found: *m/z* 513.0675 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*S*)-2-allyl-2,3-dihydroxy-3-methylpent-4-enoate (8c)**: To a solution of $ZnCl_2$ (40.9 mg, 0.30 mmol) in THF (0.50 mL) was added a 1.0 M solution (0.60 mL, 0.60 mmol) of vinylmagnesium bromide in THF at room temperature, and the mixture was then stirred for 1 h. To the mixture was added *tert*-butyl (*R*)-2-allyl-2-hydroxy-3-oxobutanoate (21.4 mg, 0.10 mmol) at room temperature. The reaction mixture was stirred for 2 h at the same temperature, and then the reaction was quenched with 1 N HCl and extracted with hexane. Organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was then purified by column chromatography on silica gel (eluding with hexane/ethyl acetate = 10:1) to give **8c** as a colorless oil [84% (20.6 mg), d.r. > 20:1]. $[\alpha]_D^{32}$ = −3.8 (*c* = 1.0, $CHCl_3$; 91% *ee*); ^1H NMR (400 MHz, $CDCl_3$): δ = 6.12 (1H, dd, *J* = 11.0, 17.6 Hz, CH=CH_2), 5.73 (1H, m, CH_2CH=CH_2), 5.38 (1H, dd, *J* = 1.7, 17.6 Hz, CH=CHH), 5.14 (1H, dd, *J* = 1.7, 10.7 Hz, CH=CHH), 5.09–5.14 (2H, m, CH_2CH=CH_2), 3.55 (1H, s, OH), 2.94 (1H, s, OH), 2.62 (1H, dd, *J* = 8.3, 14.4 Hz, CHHCH=CH_2), 2.53 (1H, m, CHHCH=CH_2), 1.48 (9H, s, *t*Bu), 1.27 ppm (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6, 140.6, 132.5, 118.9, 113.6, 84.1, 80.4, 75.9, 37.6, 28.0, 22.6 ppm; IR (neat): $\tilde{\nu}$ = 3491, 2980, 2932, 1715, 1369, 1273, 1238, 1142, 1096, 1072, 999, 922, 843, 756, 671 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{13}H_{22}O_4$: *m/z* 265.1410 $[M+Na]^+$, found: *m/z* 265.1400 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*S*)-2-allyl-2,3-dihydroxy-3-phenylbutanoate (8d)**: $[\alpha]_D^{23}$ = +35.5 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.55 (2H, m, ArH), 7.22–7.32 (3H, m, ArH), 5.73 (1H, m, CH=CH_2), 5.08–5.14 (2H, m, CH=CH_2), 3.62 (1H, s, OH), 3.48 (1H, s, OH), 2.71 (1H, dd, *J* = 8.3, 13.9 Hz, CHHCH=CH_2), 2.63 (1H, app ddt, *J* = 1.4, 6.2, 13.9 Hz, CHHCH=CH_2), 1.60 (3H, s, CH_3), 1.27 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 144.3, 132.5, 127.5, 127.1, 126.3, 119.0, 84.3, 81.3, 76.9, 38.4, 27.7, 23.9 ppm; IR (neat): $\tilde{\nu}$ = 1731, 1387, 1371, 1283, 1229, 1144, 1096, 1007 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{17}H_{24}O_4$: *m/z* 315.1567 $[M+Na]^+$, found: *m/z* 315.1560 $[M+Na]^+$.

***tert*-Butyl (2*R*,3*S*)-2-(4-bromobenzyl)-2,3-dihydroxy-3-phenylbutanoate (10)**: $[\alpha]_D^{24}$ = −30.6 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.56 (2H, m, ArH), 7.22–7.37 (5H, m, ArH), 7.12 (2H, m, ArH), 3.90 (1H, s, OH), 3.28 (1H, d, *J* = 13.5 Hz, ArCHH), 3.28 (1H, s, OH), 3.09 (1H, d, *J* = 13.8 Hz, ArCHH), 1.67 (3H, s, CH_3), 1.07 ppm (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7, 144.2, 135.3, 132.4, 130.9, 127.6, 127.2, 126.4, 120.7, 84.6, 81.9, 77.3, 38.9, 27.5, 23.7 ppm; IR (neat): $\tilde{\nu}$ = 1732, 1487, 1373, 1285, 1269, 1207, 1144, 1072, 1013 cm^{-1}; HRMS (ESI) exact mass calcd for $C_{21}H_{25}BrO_4$: *m/z* 443.0828 $[M+Na]^+$, found: *m/z* 443.0844 $[M+Na]^+$.

Acknowledgements

This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

[1] For a general review, see: J. Christoffers, A. Baro, T. Werner, *Adv. Synth. Catal.* **2004**, *346*, 143.

[2] a) P. Y. Toullec, C. Bonaccorsi, A. Mezzetti, A. Togni, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5810; b) C. Bonaccorsi, M. Althaus, C. Becker, A. Togni, A. Mezzetti, *Pure Appl. Chem.* **2006**, *78*, 391; c) T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru, S. Kanemasa, *J. Am. Chem. Soc.* **2006**, *128*, 16488; d) A. M. R. Smith, D. Billen, K. K. Hii, *Chem. Commun.* **2009**, 3925.

[3] a) 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; b) M. R. Acocella, O. G. Mancheño, M. Bella, K. A. Jørgensen, *J. Org. Chem.* **2004**, *69*, 8165.

[4] M. Lu, D. Zhu, Y. Lu, X. Zeng, B. Tan, Z. Xu, G. Zhong, *J. Am. Chem. Soc.* **2009**, *131*, 4562.

[5] For recent review articles on phase-transfer catalysis, see: a) T. Ooi, K. Maruoka, *Angew. Chem.* **2007**, *119*, 4300; *Angew. Chem. Int. Ed.* **2007**, *46*, 4222; b) T. Hashimoto, K. Maruoka, *Chem. Rev.* **2007**, *107*, 5656.

[6] For a preliminary communication, see: T. Hashimoto, K. Sasaki, K. Fukumoto, Y. Murase, T. Ooi, K. Maruoka, *Synlett* **2009**, 661.

[7] G. Scheid, W. Kuit, E. Ruijter, R. V. A. Orru, E. Henke, U. Bornscheuer, L. A. Wessjohann, *Eur. J. Org. Chem.* **2004**, 1063; the authors describe the sodium hydride mediated alkylation of α-acyloxy-β-keto esters.

[8] a) T. Ooi, T. Miki, M. Taniguchi, M. Shiraishi, M. Takeuchi, K. Maruoka, *Angew. Chem.* **2003**, *115*, 3926; *Angew. Chem. Int. Ed.* **2003**, *42*, 3796; b) T. Ooi, T. Miki, K. Maruoka, *Org. Lett.* **2005**, *7*, 191; c) T. Ooi, T. Miki, K. Fukumoto, K. Maruoka, *Adv. Synth. Catal.* **2006**, *348*, 1539.

[9] a) M. Kitamura, S. Shirakawa, K. Maruoka, *Angew. Chem.* **2005**, *117*, 1573; *Angew. Chem. Int. Ed.* **2005**, *44*, 1549; b) M. Kitamura, S.

Shirakawa, Y. Arimura, X. Wang, K. Maruoka, *Chem. Asian J.* **2008**, *3*, 1702.
[10] a) D. S. Reddy, N. Shibata, J. Nagai, S. Nakamura, T. Toru, S. Kanemasa, *Angew. Chem.* **2008**, *120*, 170; *Angew. Chem. Int. Ed.* **2008**, *47*, 164; b) D. S. Reddy, N. Shibata, J. Nagai, S. Nakamura, T. Toru, *Angew. Chem.* **2009**, *121*, 817; *Angew. Chem. Int. Ed.* **2009**, *48*, 803.
[11] I. Drutu, E. S. Krygowski, J. L. Wood, *J. Org. Chem.* **2001**, *66*, 7025.
[12] Determined by ^{1}H NMR analysis of the crude material.
[13] M. Hatano, K. Ishihara, *Synthesis* **2008**, 1647.
[14] M. Hatano, S. Suzuki, K. Ishihara, *J. Am. Chem. Soc.* **2006**, *128*, 9998.
[15] CCDC 740881 (**9**) and CCDC 740880 (**10**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See Supporting Information for details.

Received: August 6, 2009
Published online: December 10, 2009

