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A convenient method for the kinetic resolution of racemic 2-hydroxyalkanoates using diphenylacetic anhydride (DPHAA) and a chiral acyl-transfer catalyst

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ABSTRACT

Diphenylacetic anhydride (DPHAA) was found to be a useful reagent for the kinetic resolution of racemic 2-hydroxyalkanoates in the presence of a catalytic amount of (*R*)-benzotetramisole ((*R*)-BTM). The combined use of DPHAA and (*R*)-BTM effectively produced a variety of the optically active 2-hydroxyalkanoates and the corresponding 2-acyloxyalkanoates from racemic 2-hydroxyalkanoates (*s*-values = 42–177). A fairly broad substrate scope was demonstrated by this novel chiral induction system. We also revealed that the use of only 0.3 equiv of DPHAA is enough to provide the optically active 2-acyloxyalkanoates in good yields and with excellent ee's by the added use of 0.3 equiv of pivalic anhydride for the kinetic resolution of the racemic 2-hydroxyalkanoates.

1. Introduction

We have recently developed the first asymmetric esterification[1–5] of racemic secondary benzylic alcohols with free carboxylic acids using a carboxylic anhydride as a condensation reagent in the presence of chiral acyl-transfer catalysts, such as (*S*)-(−)-tetramisole and (*R*)-(+)-benzotetramisole [(*R*)-BTM], which were first introduced by Birman et al.[6,7] Because this protocol utilized the transacylation process to generate the mixed anhydride derived from free carboxylic acids and carboxylic anhydrides, not only racemic secondary alcohols, but also racemic carboxylic acids are applicable for asymmetric esterification in the same manner. In fact, we succeeded in developing a new method for the kinetic resolution of racemic α-arylpropanoic acids with achiral alcohols using chiral acyl-transfer catalysts.[8–12]

It is worth noting that free carboxylic acids could be employed as acyl donors in this reaction process; therefore, it is easy to optimize the best structure of the proper carboxylic acids for the kinetic resolution of racemic secondary alcohols.[1–4] Actually, we have also achieved the kinetic resolution of racemic 2-hydroxyalkanoates[13,14] using asymmetric esterification through the extensive modification of the structure of the acyl donors (Scheme 1, eq. (1)). Fortunately, it was proved that the diphenylacetyl moiety in the mixed anhydride, which was generated from diphenylacetic acid and pivalic anhydride in situ, is a very effective structure for the achievement of high enantioselectivities during the kinetic resolution. Based on these results, it is anticipated that diphenylacetic anhydride (DPHAA) might be an alternative and efficient acylating reagent for the kinetic resolution of racemic 2-hydroxyalkanoates. We now report a new method for the preparation of the optically active 2-hydroxy and 2-acyloxyalkanoates from the racemic compounds using DPHAA as an effective acyl donor in the presence of a chiral acyl-transfer catalyst (Scheme 1, eq. (2)).

2. Results and discussion

First, DPHAA[15] was conventionally prepared from diphenylacetic acid with acetic anhydride at 150 °C for 2 h in 86% yield (72% after recrystallization from dichloromethane/hexane = 1:4) according to a literature method (Scheme 2).

Next, we examined the kinetic resolution of a variety of racemic benzyl 2-hydroxyalkanoates using DPHAA and (*R*)-BTM under the standard reaction conditions established in a proceeding paper (in diethyl ether at room temperature for 12 h).[13] These results are summarized in Table 1. As expected, all the reactions smoothly proceeded to afford the corresponding diesters (*R*)-**2a–l** and the unreacted alcohols (*S*)-**1a–l** with good to excellent *s*-values[16] (*s* = 42–177). Very high enantioselectivities were observed (*s* = 125–152) when the reactions of **1a–c**, **1e** and **1h**, which possess the normal aliphatic alkyl chains [R = Me, Et, *n*-Pr, *n*-Bu, and $Ph(CH_2)_2$], were carried out (entries 1–3, 5, and 8). The reactions of **1d** and **1g** including the branched aliphatic alkyl chains (R = *i*-Pr and *c*-Hex) at the C-2 positions showed a slight decrease in both the reactivity and the selectivity (entries 4 and 7), while the reaction of **1f** (R = *i*-Bu) gave a good *s*-value (entry 6, *s* = 167).

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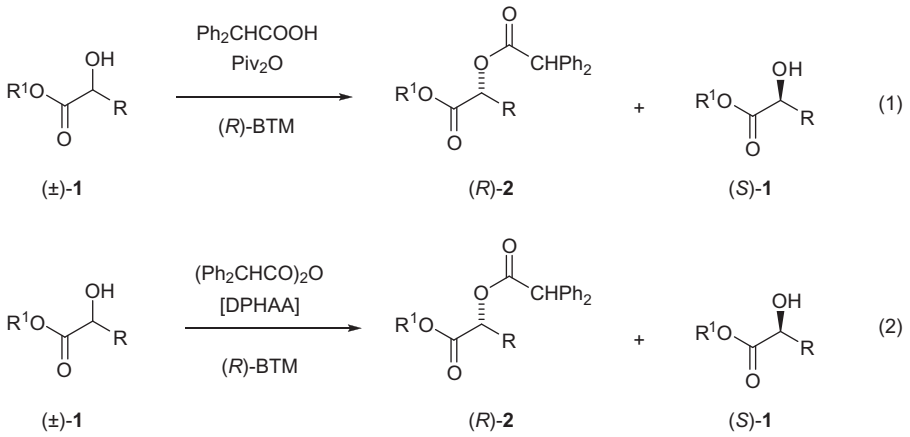
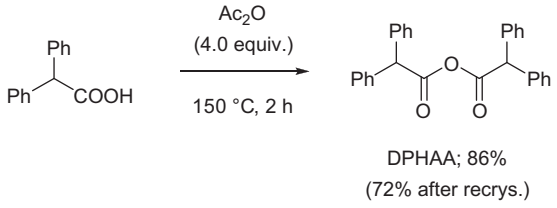


Scheme 1. Kinetic resolution of (±)-**1** using diphenylacetic acid and pivalic anhydride with (*R*)-BTM (eq. 1, our previous study); and an alternative method for the kinetic resolution of (±)-**1** using DPHAA with (*R*)-BTM (eq. 2, this study).



Scheme 2. Synthesis of diphenylacetic anhydride (DPHAA).[15]

We also tried to develop an asymmetric acyl-transfer reaction of several racemic ω-(*tert*-butyldimethylsiloxy)-2-hydroxyalkanoates **1i**–**l** having various methylene chains lengths as shown in entries 9–12. It was found that the selectivity of the kinetic resolution of **1i** was somewhat lowered by the influence of the siloxy group at the C-3 position in **1i** (entry 9, $s = 77$). Other reactions successfully produced the corresponding chiral diesters (93–95% ee) and the recovered chiral alcohols (91–97% ee) with excellent enantioselectivities irrespective of the length of the alkyl chains possessing *tert*-butyldimethylsiloxy groups (entries 10–12, $s = 100$, 177, and 119).

We further examined ways to reduce the required amount of DPHAA for achieving the effective kinetic resolution of racemic 2-hydroxyalkanoates; that is, the reaction using equimolar amounts of DPHAA (0.275–0.3 equiv) and pivalic anhydride (0.275–0.3 equiv) was carried out in the presence of (*R*)-BTM in diethyl ether at room temperature for 12 h as shown in Table 2. Except for entries 4 and 7, all the substrates were efficiently transformed into the corresponding chiral diesters in approximately 50% yield with excellent enantioselectivities ($s = 71$–208) similar to those listed in Table 1. Interestingly, a drastic decrease in both the reactivity and the selectivity was observed in the reactions of **1d** and **1g**, which have the branched aliphatic alkyl chains (R = *i*-Pr and *c*-Hex) at the C-2 positions (entries 4 and 7).

Determination of the transition state forming the optically active (*R*)-diester from methyl (*R*)-lactate with the zwitterionic intermediate (**z-int**), which was generated from DPHAA and (*R*)-BTM, was carried out using DFT calculations at the B3LYP/6-31G*//B3LYP/6-31G* level according to former report on the KR of the racemic 2-hydroxyalkanoates.[13,17] Among the several calculated transition states forming the desired (*R*)-diester from methyl (*R*)-lactate, the most stable structure (*R*)-**ts** is depicted in Scheme 3. The lactate moiety has a rigid structure in which the conformation is restricted by the attractive interaction between oxygen in the ester carbonyl group and the positive electronic charge on the face of the dihydroimidazolium salt (2.889 Å) as well as the coordination of oxygen in the acyl donor moiety onto hydrogen at the C-2 position in methyl (*R*)-lactate (2.339 Å). On the other hand, complexation of methyl (*S*)-lactate with **z-int** including (*R*)-BTM produced an unstable transition structure (*S*)-**ts** to afford the corresponding (*S*)-diester via a similar transacylation process. The coordination of oxygen in the acyl donor moiety onto hydrogen at the C-2 position in methyl (*S*)-lactate is not observed in the structure (*S*)-**ts**, therefore, the relative energy of the (*S*)-**ts** considerably increases ($E_{rel} = +3.82$ kcal/mol) compared with the value of the stable transition state (*R*)-**ts** ($E_{rel} = 0.00$ kcal/mol). These theoretical calculations using DFT rationalize the experimental results that the desired chiral (*R*)-diester was obtained selectively by the rapid transformation of methyl (*R*)-lactate through the transition state (*R*)-**ts**.[18,19]

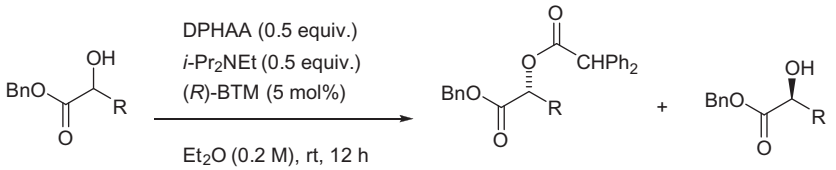
In the reactions of 2-hydroxyalkanoates **1d** and **1g** with DPHAA, the large branched aliphatic alkyl chains (R = *i*-Pr and *c*-Hex) should be very close to one of aromatic rings connected to the C-2 positions of the diphenylacetate anion in the transition state (*R*)-**ts**. This undesired steric effect considerably increases the structural energy of (*R*)-**ts**, therefore, the reactivity and the selectivity of the nucleophilic addition of **1d** and **1g** to **z-int** might be diminished as shown in entries 4 and 7 in Table 2.

(*S*)-Lactic acid is a common natural glycolic acid derivative, however, (*R*)-lactic acid is a synthetically valuable unnatural product. Therefore, we tried to produce a large amount of (*R*)-lactic acid ester (*R*)-**1a** as a rare chiral building block by the kinetic resolution of racemic lactic acid ester (±)-**1a** as shown in Scheme 4. From 10.0 g of (±)-**1a** and relatively large amounts of both reagents [DPHAA (0.6 equiv) and diisopropylethylamine (0.6 equiv)] in the presence of 5 mol % of (*S*)-BTM, the desired chiral ester (*R*)-**1a** was successfully obtained in good yield (4.4 g) with perfect purity (>99.9% ee) by this single operation.

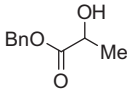
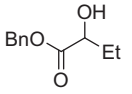
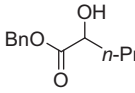
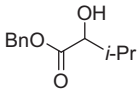
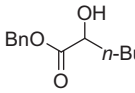
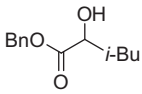
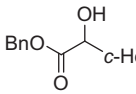
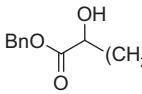
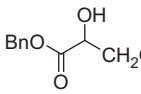
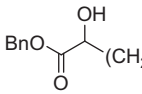
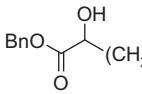
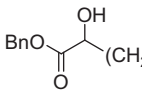
3. Conclusion

In summary, we have established a new and convenient process for the kinetic resolution of racemic 2-hydroxyalkanoate with DPHAA in the presence of (*R*)- or (*S*)-BTM. It was revealed that DPHAA could be utilized as an efficient acyl component to produce chiral 2-hydroxyalkanoates and the desired 2-acyloxyalkanoates from the racemic 2-hydroxyalkanoates. Further investigations of the present method to provide chiral materials and other applications of this novel protocol are now in progress in this laboratory.

Table 1
Kinetic resolution of racemic benzyl 2-hydroxyalkanoates (±)-**4a–l** using DPHAA with (*R*)-BTM



(±)-**1a-l** (*R*)-**2a-l** (*S*)-**1a-l**

Entry	Substrate		Yield (**2**;**1**) (%)	ee (**2**;**1**) (%)	*s*
1		**a**	51; 49	97; 74	140
2		**b**	48: 49	96: 86	152
3		**c**	45;55	97; 84	149
4		**d**	40; 60	92; 66	46
5		**e**	45; 55	96; 86	125
6		**f**	46; 52	97; 87	167
7		**g**	38; 53	91; 63	42
8		**h**	47; 53	96; 86	140
9		**i**	46; 54	94; 79	77
10		**j**	51; 49	93; 94	100
11		**k**	50; 43	95; 97	177
12		**l**	49; 49	95; 91	119

4. Experimental

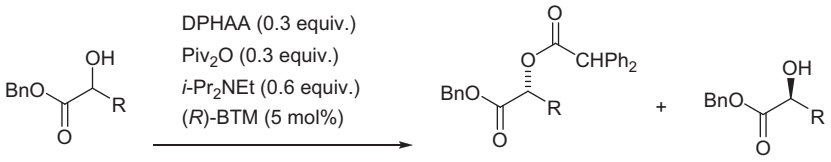
General. All melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with chloroform (in chloroform-*d*) as internal standard. Thin layer chromatography was performed on Wakogel B5F.

All reactions were carried out under argon atmosphere in dried glassware. Dichloromethane was distilled from diphosphorus pentoxide, then calcium hydride, and dried over MS 4 Å, benzene and toluene were distilled from diphosphorus pentoxide, and dried over MS 4 Å, and THF and diethyl ether were distilled from sodium/benzophenone immediately prior to use. All reagents were purchased from Tokyo Kasei Kogyo Co., Ltd, Kanto Chemical Co., Inc. or Aldrich Chemical Co., Inc., and used without further purification unless otherwise noted. Enantioselective acyl-transfer catalyst (*R*)-(+)-BTM was purchased from Tokyo Kasei Kogyo Co., Ltd (TCI).

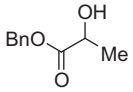
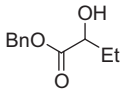
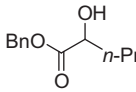
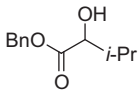
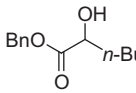
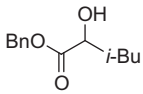
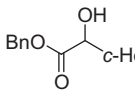
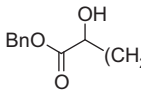
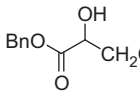
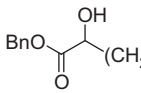
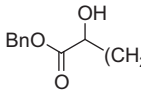
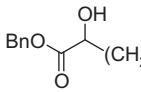
4.1. Typical procedure for the KR of racemic 2-hydroxyalkanoates

(For Table 1) Typical procedure for the asymmetric acylation of racemic 5-(*tert*-butyldimethylsiloxy)-2-hydroxypentanoate ((±)-**1k**) with DPHAA in the presence of (*R*)-BTM was described

Table 2
Kinetic resolution of racemic benzyl 2-hydroxyalkanoates (±)-**4a–l** using 0.3 equiv of DPHAA and 0.3 equiv of pivalic anhydride with (*R*)-BTM

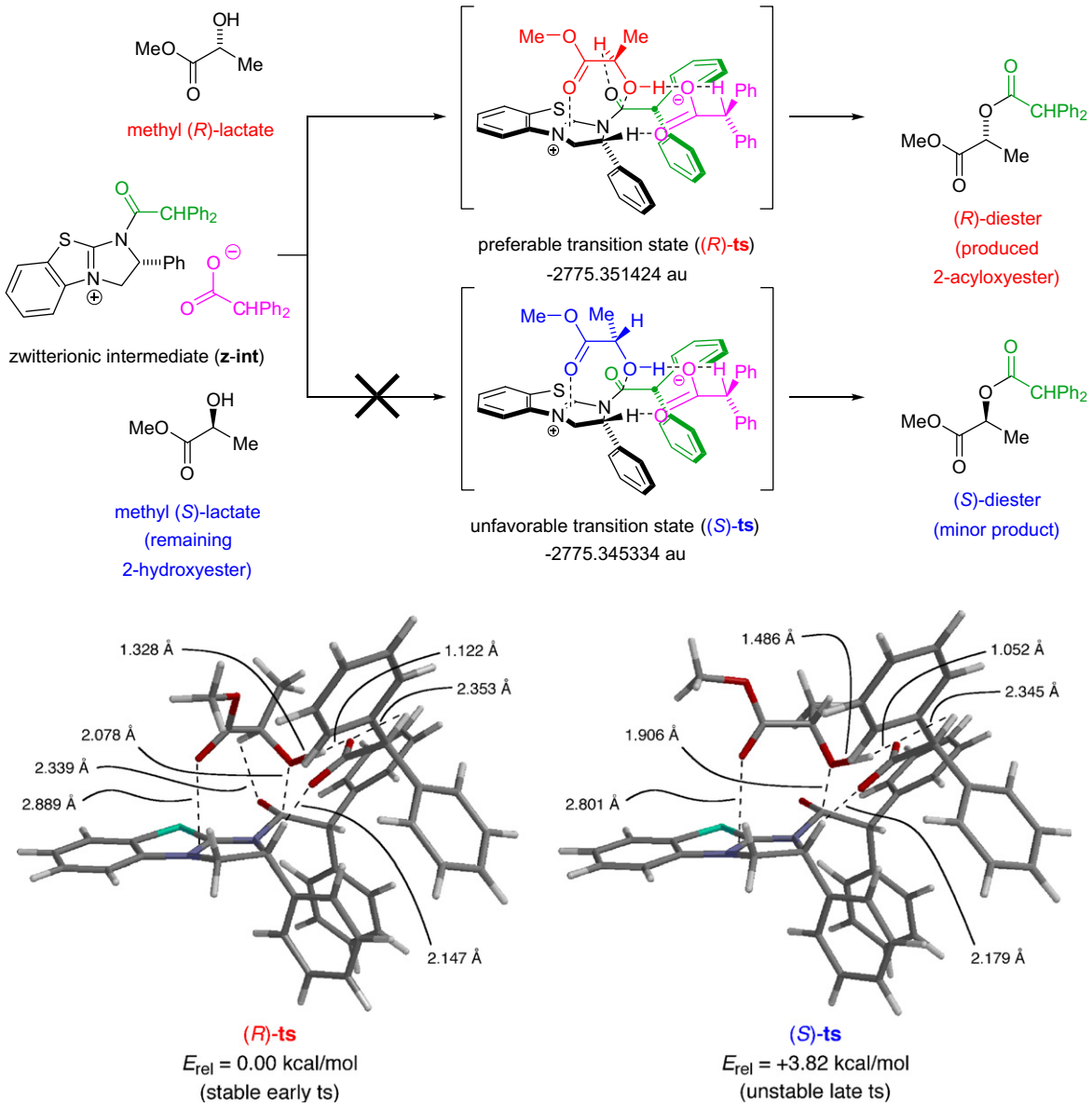


(±)-**1a-l** (*R*)-**2a-l** (*S*)-**1a-l**

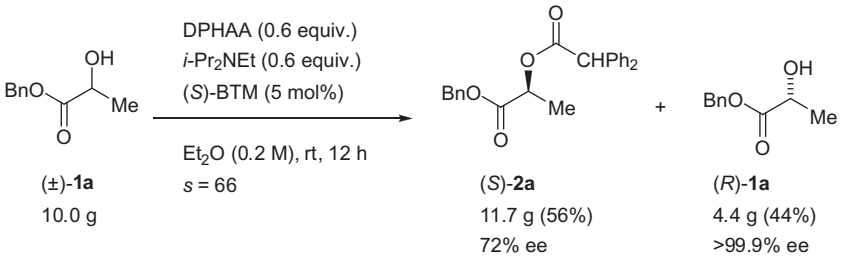
Entry	Substrate		Yield (**2**;**1**) (%)	ee (**2**;**1**) (%)	*s* (*s*[a] *s*[b])
1[c]		**a**	49; 48	96; 96	182 (146 140)
2		**b**	45; 45	96; 87	131 (126 152)
3		**c**	49; 47	94; 99	162 (171 149)
4		**d**	14; 84	68; 10	6 (53 46)
5		**e**	50; 50	94; 96	126 (128 125)
6		**f**	47; 48	92; 89	71 (140 167)
7		**g**	18; 82	52; 11	3 (47 42)
8		**h**	47; 45	96; 88	144 (202 140)
9		**i**	51; 49	91; 99	102 (80 77)
10		**j**	48; 50	95; 91	129 (146 100)
11		**k**	49; 51	97; 94	208 (186 177)
12		**l**	51; 48	93; 97	116 (155 119)

[a] The number in parentheses shows the *s*-value when using diphenylacetic acid and pivalic anhydride (Ref. 13).
[b] The number in parentheses shows the *s*-value when using DPHAA (Table 1).
[c] The reaction was carried out using DPHAA (0.275 equiv), pivalic anhydride (0.275 equiv), and diisopropylethylamine (0.55 equiv).

(Table 1, entry 11): To a solution of (±)-**1k** (75.2 mg, 0.222 mmol) in diethyl ether (1.1 mL) at room temperature were successively added (*R*)-BTM (2.8 mg, 0.0111 mmol), diisopropylethylamine (19.4 μL, 0.111 mmol), and DPHAA (45.2 mg, 0.111 mmol). After the reaction mixture had been stirred for 12 h at the same temperature, saturated aqueous $NaHCO_3$ was added. The organic layer was separated and the aqueous later was extracted with diethyl ether. The combined organic layer was dried over Na_2SO_4. After filtration of the mixture and evaporation of the solvent, the crude product was purified by preparative thin layer chromatography on silica to afford the corresponding optically active diester (*R*)-**2k** (59.4 mg, 50% yield, 95% ee) and the unreacted optically active 2-hydroxyester (*S*)-**1k** (32.6 mg, 43% yield, 97% ee), [*s* = 177].



Scheme 3. Optimized transition state geometries to form methyl 2-(diphenylacetoxy)propanoate from methyl lactate using DFT calculations at the B3LYP/6-31G*//B3LYP/6-31G* level.

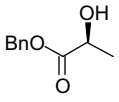


Scheme 4. Multi-gram scale synthesis of enantiomerically pure (*R*)-**1a** by the kinetic resolution of a large amount of (±)-**1a** using DPHAA with (*S*)-BTM.

(For Table 2) Typical procedure for the asymmetric acylation of racemic 5-(*tert*-butyldimethylsiloxy)-2-hydroxypentanoate ((±)-**1k**) with DPHAA and pivalic anhydride in the presence of (*R*)-BTM was described (Table 2, entry 11): To a solution of DPHAA (24.4 mg, 0.060 mmol) in diethyl ether (0.4 mL) at room temperature were successively added pivalic anhydride (12.2 μL, 0.060 mmol), diisopropylethylamine (20.9 μL, 0.120 mmol), (*R*)-BTM (2.5 mg, 0.0099 mmol), and (±)-**1k** (67.7 mg, 0.200 mmol) in diethyl ether (0.6 mL). After the reaction mixture had been stirred for 12 h at the same temperature, saturated aqueous $NaHCO_3$ was added. The organic layer was separated and the aqueous later was extracted with diethyl ether. The combined organic layer was

dried over Na_2SO_4. After filtration of the mixture and evaporation of the solvent, the crude product was purified by preparative thin layer chromatography on silica to afford the corresponding optically active diester (*R*)-**2k** (51.9 mg, 49% yield, 97% ee) and the unreacted optically active 2-hydroxyester (*S*)-**1k** (34.7 mg, 51% yield, 94% ee), [*s* = 208].

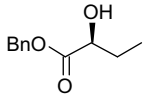
(Optically active 2-hydroxyesters).



(*S*)–**1a**

4.1.1. Benzyl (*S*)-lactate (*S*)-1a [Table 1, entry 1, 74% ee, *s* = 140]

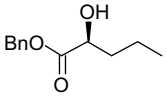
HPLC (CHIRALCEL OD-H, *i*-PrOH/hexane = 1:50, flow rate = 1.0 mL/min): t_R = 17.4 min (86.9%), t_R = 20.3 min (13.1%); IR (neat): 3457, 1738, 1498, 1456, 1045, 752, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.42–7.31 (m, 5H, Ph), 5.22 (s, 2H, Bn), 4.33 (dq, *J* = 5.4, 6.9 Hz, 1H, 2-H), 2.81 (d, *J* = 5.4 Hz, 1H, OH), 1.44 (d, *J* = 6.9 Hz, 3H, 3-H); ^{13}C NMR ($CDCl_3$): δ 175.5, 135.2, 128.6, 128.5, 128.2, 67.2, 66.8, 20.3; HR-MS: calcd for $C_{10}H_{12}O_3Na$ ($M+Na^+$) 203.0679, found 203.0673.



(*S*)–**1b**

4.1.2. Benzyl (*S*)-2-hydroxybutanoate (*S*)-1b [Table 1, entry 2, 86% ee, *s* = 152]

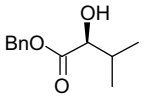
HPLC (CHIRALPAK AS-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 17.0 min (93.2%), t_R = 21.6 min (6.8%); IR (neat): 3477, 1737, 1498, 1456, 1061, 752, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.40–7.32 (m, 5H, Ph), 5.24 (d, *J* = 12.3 Hz, 1H, Bn), 5.20 (d, *J* = 12.3 Hz, 1H, Bn), 4.20 (ddd, *J* = 11.3, 7.3, 4.0 Hz, 1H, 2-H), 2.83 (d, *J* = 5.5 Hz, 1H, OH), 1.86 (ddq, *J* = 14.5, 4.0, 7.0 Hz, 1H, 3-H), 1.70 (ddq, *J* = 14.5, 7.3, 7.5 Hz, 1H, 3-H), 0.95 (dd, *J* = 7.5, 7.0 Hz, 3H, 4-H); ^{13}C NMR ($CDCl_3$): δ 175.0, 135.2, 128.6, 128.5, 128.3, 71.4, 67.2, 27.4, 8.8; HR-MS: calcd for $C_{11}H_{14}O_3Na$ ($M+Na^+$) 217.0835, found 217.0825.



(*S*)–**1c**

4.1.3. Benzyl (*S*)-2-hydroxypentanoate (*S*)-1c [Table 1, entry 3, 84% ee, *s* = 149]

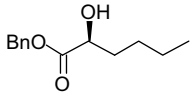
HPLC (CHIRALPAK AS-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 13.3 min (91.9%), t_R = 17.1 min (8.1%); IR (neat): 3479, 1737, 1456, 1136, 751, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.41–7.32 (m, 5H, Ph), 5.21 (s, 2H, Bn), 4.23 (ddd, *J* = 7.1, 5.0, 4.9 Hz, 1H, 2-H), 2.76 (d, *J* = 5.0 Hz, 1H, OH), 1.82–1.73 (m, 1H, 3-H), 1.70–1.60 (m, 1H, 3-H), 1.53–1.34 (m, 2H, 4-H), 0.92 (t, *J* = 7.5 Hz, 3H, 5-H); ^{13}C NMR ($CDCl_3$): δ 174.8, 135.2, 128.63, 128.55, 128.4, 75.0, 67.3, 32.1, 18.8, 15.8; HR-MS: calcd for $C_{12}H_{16}O_3Na$ ($M+Na^+$) 231.0992, found 231.0980.



(*S*)–**1d**

4.1.4. Benzyl (*S*)-2-hydroxy-3-methylbutanoate (*S*)-1d [Table 1, entry 4, 66% ee, *s* = 46]

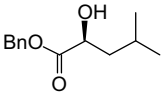
HPLC (CHIRALPAK AS-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 12.0 min (82.8%), t_R = 16.7 min (17.2%); IR (neat): 3508, 1735, 1498, 1456, 1030, 751, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.41–7.34 (m, 5H, Ph), 5.24 (d, *J* = 12.3 Hz, 1H, Bn), 5.20 (d, *J* = 12.3 Hz, 1H, Bn), 4.09 (dd, *J* = 6.3, 3.5 Hz, 1H, 2-H), 2.71 (d, *J* = 6.3 Hz, 1H, OH), 2.10 (dqq, *J* = 3.5, 7.0, 7.0 Hz, 1H, 3-H), 1.01 (d, *J* = 7.0 Hz, 3H, 4-H), 0.83 (d, *J* = 7.0 Hz, 3H, 4-H); ^{13}C NMR ($CDCl_3$): δ 175.3, 135.2, 128.6, 128.5, 128.3, 70.3, 67.2, 36.4, 18.0, 13.7; HR-MS: calcd for $C_{12}H_{16}O_3Na$ ($M+Na^+$) 231.0992, found 231.0985.



(*S*)–**1e**

4.1.5. Benzyl (*S*)-2-hydroxyhexanoate (*S*)-1e [Table 1, entry 5, 86% ee, *s* = 125]

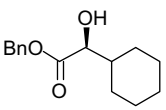
HPLC (CHIRALPAK AS-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 12.6 min (92.9%), t_R = 15.4 min (7.1%); IR (neat): 3478, 1738, 1498, 1456, 1137, 751, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.42–7.32 (m, 5H, Ph), 5.23 (d, *J* = 12.3 Hz, 1H, Bn), 5.20 (d, *J* = 12.3 Hz, 1H, Bn), 4.27–4.18 (m, 1H, 2-H), 2.87 (d, *J* = 5.5 Hz, 1H, OH), 1.87–1.74 (m, 1H, 3-H), 1.72–1.60 (m, 1H, 3-H), 1.48–1.25 (m, 4H, 4-H, 5-H), 0.88 (t, *J* = 7.0 Hz, 3H, 6-H); ^{13}C NMR ($CDCl_3$): δ 175.2, 135.2, 128.6, 128.5, 128.3, 70.5, 67.2, 34.0, 26.7, 22.3, 13.8; HR-MS: calcd for $C_{13}H_{18}O_3Na$ ($M+Na^+$) 245.1148, found 245.1155.



(*S*)–**1f**

4.1.6. Benzyl (*S*)-2-hydroxy-4-methylpentanoate (*S*)-1f [Table 1, entry 6, 87% ee, *s* = 167]

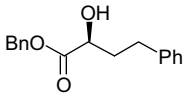
HPLC (CHIRALPAK AS-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 12.3 min (93.4%), t_R = 16.6 min (6.6%); IR (neat): 3474, 1737, 1498, 1456, 1090, 749, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.33–7.24 (m, 5H, Ph), 5.14 (d, *J* = 12.0 Hz, 1H, Bn), 5.11 (d, *J* = 12.0 Hz, 1H, Bn), 4.17 (ddd, *J* = 8.5, 5.5, 5.0 Hz, 1H, 2-H), 2.64 (d, *J* = 5.5 Hz, 1H, OH), 1.87–1.75 (m, 1H, 4-H), 1.55–1.46 (m, 2H, 3-H), 0.86 (d, *J* = 7.0 Hz, 3H, 5-H), 0.85 (d, *J* = 7.0 Hz, 3H, 5-H); ^{13}C NMR ($CDCl_3$): δ 175.7, 135.2, 128.6, 128.5, 128.3, 69.1, 67.2, 43.4, 24.4, 23.2, 21.5; HR-MS: calcd for $C_{13}H_{18}O_3Na$ ($M+Na^+$) 245.1148, found 245.1156.



(*S*)–**1g**

4.1.7. Benzyl (*S*)-2-cyclohexyl-2-hydroxyacetate (*S*)-1g [Table 1, entry 7, 63% ee, *s* = 42]

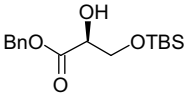
HPLC (CHIRALPAK AS-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 13.2 min (81.6%), t_R = 20.0 min (18.4%); IR (neat): 3504, 1735, 1498, 1452, 1114, 750, 697 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.41–7.32 (m, 5H, Ph), 5.24 (d, J = 12.0 Hz, 1H, Bn), 5.21 (d, J = 12.0 Hz, 1H, Bn), 4.06 (d, J = 3.5 Hz, 1H, 2-H), 2.69 (br s, 1H, OH), 1.81–1.57 (m, 5H, *c*-Hex), 1.43–1.03 (m, 6H, *c*-Hex); ^{13}C NMR ($CDCl_3$): δ 174.7, 135.2, 128.6, 128.5, 128.3, 74.8, 67.2, 42.0, 29.0, 26.23, 26.18, 25.94, 25.89; HR-MS: calcd for $C_{15}H_{20}O_3Na$ (M+Na^+) 271.1305, found 271.1306.



(*S*)–1h

4.1.8. Benzyl (*S*)-2-hydroxy-4-phenylbutanoate (*S*)-1h [Table 1, entry 8, 86% ee, *s* = 140]

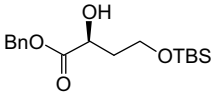
Mp: 58.9–59.6 °C (hexane); HPLC (CHIRALCEL OD-H, *i*-PrOH/hexane = 1:4, flow rate = 0.5 mL/min): t_R = 13.9 min (93.1%), t_R = 18.9 min (6.9%); IR (KBr): 3429, 1728, 1496, 1451, 1105, 752, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.32–7.23 (m, 5H, Ph), 7.22–7.16 (m, 2H, Ph), 7.13–7.05 (m, 3H, Ph), 5.11 (d, J = 12.0 Hz, 1H, Bn), 5.08 (d, J = 12.0 Hz, 1H, Bn), 4.16 (ddd, J = 7.5, 5.5, 4.0 Hz, 1H, 2-H), 2.78 (d, J = 5.5 Hz, 1H, OH), 2.72–2.56 (m, 2H, 4-H), 2.10–2.00 (m, 1H, 3-H), 1.93–1.83 (m, 1H, 3-H); ^{13}C NMR ($CDCl_3$): δ 175.0, 141.1, 135.1, 128.7, 128.6, 128.5, 128.39, 128.38, 126.0, 69.7, 67.4, 35.9, 30.9; HR-MS: calcd for $C_{17}H_{18}O_3Na$ (M+Na^+) 293.1148, found 293.1158.



(*S*)–1i

4.1.9. Benzyl (*S*)-3-(*tert*-butyldimethylsiloxy)-2-hydroxypropanoate (*S*)-1i [Table 1, entry 9, 79% ee, *s* = 77]

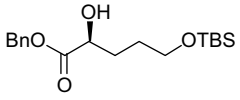
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:50, flow rate = 1.0 mL/min): t_R = 9.3 min (10.5%), t_R = 12.8 min (89.5%); IR (neat): 3506, 1748, 1462, 1123, 735, 697 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.39–7.31 (m, 5H, Ph), 5.22 (s, 2H, Bn), 4.26 (dt, J = 8.5, 3.0 Hz, 1H, 2-H), 3.96 (dd, J = 10.3, 3.0 Hz, 1H, 3-H), 3.87 (dd, J = 10.3, 3.0 Hz, 1H, 3-H), 3.07 (d, J = 8.5 Hz, 1H, OH), 0.86 (s, 9H, TBS), 0.04 (s, 3H, TBS), 0.02 (s, 3H, TBS); ^{13}C NMR ($CDCl_3$): δ 172.6, 135.3, 128.6, 128.4, 128.3, 72.0, 67.2, 65.0, 25.7, 18.2, −5.5, −5.6; HR-MS: calcd for $C_{16}H_{26}O_4SiNa$ (M+Na^+) 333.1493, found 333.1504.



(*S*)–1j

4.1.10. Benzyl (*S*)-4-(*tert*-butyldimethylsiloxy)-2-hydroxybutanoate (*S*)-1j [Table 1, entry 10, 94% ee, *s* = 100]

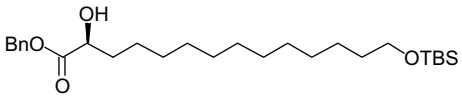
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:50, flow rate = 1.0 mL/min): t_R = 8.1 min (3.2%), t_R = 9.5 min (96.8%); IR (neat): 3489, 1733, 1471, 1111, 735, 697 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.39–7.31 (m, 5H, Ph), 5.23 (d, J = 12.3 Hz, 1H, Bn), 5.19 (d, J = 12.3 Hz, 1H, Bn), 4.40 (ddd, J = 7.6, 5.5, 4.0 Hz, 1H, 2-H), 3.84–3.76 (m, 2H, 4-H), 3.31 (d, J = 5.5 Hz, 1H, OH), 2.07 (dddd, J = 14.2, 7.0, 5.5, 4.0 Hz, 1H, 3-H), 1.89 (dddd, J = 14.2, 7.6, 6.0, 5.0 Hz, 1H, 3-H), 0.89 (s, 9H, TBS), 0.05 (s, 6H, TBS); ^{13}C NMR ($CDCl_3$): δ 174.7, 135.4, 128.6, 128.4, 128.3, 69.0, 67.0, 59.9, 36.2, 25.9, 18.2, −5.5, −5.6; HR-MS: calcd for $C_{17}H_{28}O_4SiNa$ (M+Na^+) 347.1649, found 347.1634.



(*S*)–1k

4.1.11. Benzyl (*S*)-5-(*tert*-butyldimethylsiloxy)-2-hydroxypentanoate (*S*)-1k [Table 1, entry 11, 97% ee, *s* = 177]

HPLC (CHIRALPAK AS-H, *i*-PrOH/hexane = 1:100, flow rate = 1.0 mL/min): t_R = 11.3 min (98.6%), t_R = 18.3 min (1.4%); IR (neat): 3466, 1735, 1470, 1094, 836, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.39–7.31 (m, 5H, Ph), 5.22 (d, J = 12.5 Hz, 1H, Bn), 5.19 (d, J = 12.5 Hz, 1H, Bn), 4.26 (dd, J = 7.5, 3.8 Hz, 1H, 2-H), 3.67–3.59 (m, 2H, 5-H), 3.25 (br s, 1H, OH), 1.96–1.88 (m, 1H, 3-H), 1.80–1.55 (m, 3H, 3-H, 4-H), 0.88 (s, 9H, TBS), 0.04 (s, 6H, TBS); ^{13}C NMR ($CDCl_3$): δ 174.9, 135.3, 128.6, 128.5, 128.2, 70.4, 67.1, 62.8, 31.4, 28.2, 25.9, 18.3, −5.4; HR-MS: calcd for $C_{18}H_{30}O_4SiNa$ (M+Na^+) 361.1806, found 361.1806.

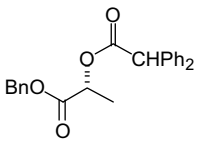


(*S*)–1l

4.1.12. Benzyl (*S*)-14-(*tert*-butyldimethylsiloxy)-2-hydroxytetradecanoate (*S*)-1l [Table 1, entry 12, 91% ee, *s* = 119]

HPLC (CHIRALPAK IC, *i*-PrOH/hexane = 1:50, flow rate = 0.5 mL/min): t_R = 19.6 min (4.5%), t_R = 21.4 min (95.5%); IR (neat): 3473, 1737, 1463, 1096, 836, 776 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.40–7.32 (m, 5H, Ph), 5.23 (d, J = 12.0 Hz, 1H, Bn), 5.19 (d, J = 12.0 Hz, 1H, Bn), 4.22 (dd, J = 7.0, 4.5 Hz, 1H, 2-H), 3.60 (t, J = 6.5 Hz, 2H, 14-H), 2.75 (br s, 1H, OH), 1.84–1.74 (m, 1H, 3-H), 1.72–1.60 (m, 1H, 3-H), 1.51 (tt, J = 7.0, 6.5 Hz, 2H, 13-H), 1.46–1.20 (m, 18H, 4-H, 5-H, 6-H, 7-H, 8-H, 9-H, 10-H, 11-H, 12-H), 0.90 (s, 9H, TBS), 0.05 (s, 6H, TBS); ^{13}C NMR ($CDCl_3$): δ 175.3, 135.2, 128.6, 128.5, 128.3, 70.5, 67.2, 63.3, 34.4, 32.9, 29.6, 29.58, 29.56, 29.50, 29.42, 29.42, 29.3, 26.0, 25.8, 24.6, 18.4, −5.3; HR-MS: calcd for $C_{27}H_{48}O_4SiNa$ (M+Na^+) 487.3214, found 487.3214.

(Optically active 2-acyloxyesters).

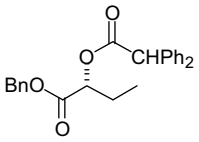


(*R*)–2a

4.1.13. Benzyl (*R*)-2-(diphenylacetyloxy)propanoate (*R*)-2a [Table 1, entry 1, 97% ee, *s* = 140]

HPLC (CHIRALCEL OJ-H, *i*-PrOH/hexane = 2:3, flow rate = 0.9 mL/min): t_R = 36.2 min (1.6%), t_R = 58.4 min (98.4%); IR (neat): 1496, 1454, 747, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.41–7.20 (m, 15H, Ph), 5.19 (q, J = 7.2 Hz, 1H, 2-H); 5.18 (d, J = 12.0 Hz, 1H,

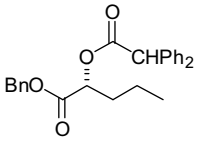
Bn); 5.13 (d, J = 12.0 Hz, 1H, Bn); 5.11 (s, 1H, 2′-H), 1.49 (d, J = 7.2 Hz, 3H, 3-H); ^{13}C NMR ($CDCl_3$): δ 171.9, 170.4, 138.3, 138.2, 135.2, 128.70, 128.66, 128.58, 128.56, 128.48, 128.3, 128.1, 127.3, 127.2, 69.3, 67.0, 56.6, 16.8; HR-MS: calcd for $C_{24}H_{22}O_4Na$ (M+Na$^+$) 397.1410, found 397.1427.



(*R*)–**2b**

4.1.14. Benzyl (*R*)-2-(diphenylacetyloxy)butanoate (*R*)-2b [Table 1, entry 2, 96% ee, *s* = 152]

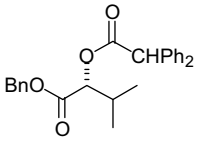
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 20.0 min (1.8%), t_R = 24.1 min (98.2%); IR (neat): 1736, 1496, 1454, 746, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.29–7.13 (m, 15H, Ph), 5.09 (d, J = 12.0 Hz, 1H, Bn), 5.05 (d, J = 12.0 Hz, 1H, Bn), 5.05 (s, 1H, 2′-H), 4.97 (dd, J = 7.5, 5.0 Hz, 1H, 2-H), 1.85–1.71 (m, 2H, 3-H), 0.77 (t, J = 7.5 Hz, 3H, 4-H); ^{13}C NMR ($CDCl_3$): δ 172.1, 169.8, 138.36, 138.27, 135.26, 128.71, 128.71, 128.57, 128.55, 128.4, 128.3, 128.2, 127.3, 127.2, 74.0, 66.9, 56.8, 24.5, 9.4; HR-MS: calcd for $C_{25}H_{24}O_4Na$ (M+Na$^+$) 411.1567, found 411.1559.



(*R*)–**2c**

4.1.15. Benzyl (*R*)-2-(diphenylacetyloxy)pentanoate (*R*)-2c [Table 1, entry 3, 97% ee, *s* = 149]

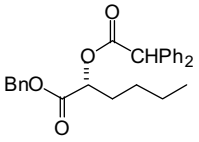
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 16.1 min (1.7%), t_R = 21.8 min (98.3%); IR (neat): 1742, 1496, 1454, 747, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.29–7.13 (m, 15H, Ph), 5.09 (d, J = 12.0 Hz, 1H, Bn), 5.05 (d, J = 12.0 Hz, 1H, Bn), 5.04 (s, 1H, 2′-H), 5.02 (dd, J = 7.0, 6.0 Hz, 1H, 2-H), 1.73–1.67 (m, 2H, 3-H), 1.21 (tq, J = 7.5, 7.5 Hz, 2H, 4-H), 0.75 (t, J = 7.5 Hz, 3H, 5-H); ^{13}C NMR ($CDCl_3$): δ 172.1, 170.0, 138.35, 138.26, 135.3, 128.71, 128.71, 128.57, 128.55, 128.4, 128.3, 128.2, 127.3, 127.2, 72.8, 66.9, 56.8, 33.0, 18.3, 13.4; HR-MS: calcd for $C_{26}H_{26}O_4Na$ (M+Na$^+$) 425.1723, found 475.1703.



(*R*)–**2d**

4.1.16. Benzyl (*R*)-2-(diphenylacetyloxy)-3-methylbutanoate (*R*)-2d [Table 1, entry 4, 92% ee, *s* = 46]

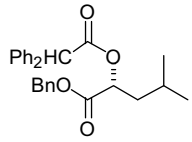
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 17.1 min (4.1%), t_R = 22.5 min (95.9%); IR (neat): 1739, 1496, 1454, 745, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.29–7.12 (m, 15H, Ph), 5.09 (d, J = 12.3 Hz, 1H, Bn), 5.06 (s, 1H, 2′-H), 5.05 (d, J = 12.3 Hz, 1H, Bn), 4.85 (d, J = 4.5 Hz, 1H, 2-H), 2.11 (dqq, J = 4.5, 7.0, 6.8 Hz, 1H, 3-H), 0.76 (d, J = 7.0 Hz, 3H, 4-H), 0.75 (d, J = 6.8 Hz, 3H, 4-H); ^{13}C NMR ($CDCl_3$): δ 172.1, 169.3, 138.4, 138.3, 135.3, 128.8, 128.7, 128.6, 128.5, 128.4, 128.33, 128.29, 127.26, 127.16, 77.4, 66.9, 56.9, 30.2, 18.6, 17.0; HR-MS: calcd for $C_{26}H_{26}O_4Na$ (M+Na$^+$) 425.1723, found 425.1732.



(*R*)–**2e**

4.1.17. Benzyl (*R*)-2-(diphenylacetyloxy)hexanoate (*R*)-2e [Table 1, entry 5, 96% ee, *s* = 125]

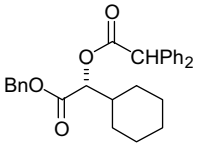
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:50, flow rate = 1.0 mL/min): t_R = 16.9 min (2.2%), t_R = 23.6 min (97.8%); IR (neat): 1739, 1496, 1455, 736, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.32–7.16 (m, 15H, Ph), 5.12 (d, J = 12.3 Hz, 1H, Bn), 5.08 (d, J = 12.3 Hz, 1H, Bn), 5.07 (s, 1H, 2′-H), 5.04 (dd, J = 7.0, 6.0 Hz, 1H, 2-H), 1.82–1.73 (m, 2H, 3-H), 1.23–1.10 (m, 4H, 4-H, 5-H), 0.78–0.71 (m, 3H, 6-H); ^{13}C NMR ($CDCl_3$): δ 172.1, 170.0, 138.3, 138.2, 135.3, 128.71, 128.71, 128.6, 128.5, 128.4, 128.3, 128.2, 127.3, 127.2, 72.9, 66.9, 56.8, 30.7, 27.0, 22.0, 13.7; HR-MS: calcd for $C_{27}H_{28}O_4Na$ (M+Na$^+$) 439.1880, found 439.1886.



(*R*)–**2f**

4.1.18. Benzyl (*R*)-2-(diphenylacetyloxy)-4-methylpentanoate (*R*)-2f [Table 1, entry 6, 97% ee, *s* = 167]

HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 14.4 min (1.7%), t_R = 25.3 min (98.3%); IR (neat): 1739, 1496, 1454, 739, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.29–7.13 (m, 15H, Ph), 5.10–5.00 (m, 4H, 2-H, 2′-H, Bn), 1.69 (ddd, J = 14.0, 9.8, 4.5 Hz, 1H, 3-H), 1.58–1.41 (m, 3H, 3-H, 4-H), 0.75 (d, J = 7.0 Hz, 3H, 5-H), 0.71 (d, J = 6.5 Hz, 3H, 5-H); ^{13}C NMR ($CDCl_3$): δ 172.1, 170.3, 138.3, 138.2, 135.2, 128.71, 128.69, 128.57, 128.54, 128.4, 128.3, 128.2, 127.3, 127.2, 71.7, 67.0, 56.8, 39.5, 24.5, 22.8, 21.3; HR-MS: calcd for $C_{27}H_{28}O_4Na$ (M+Na$^+$) 439.1880, found 439.1879.

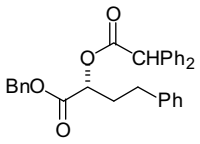


(*R*)–**2g**

4.1.19. Benzyl (*R*)-2-cyclohexyl-2-(diphenylacetyloxy)acetate (*R*)-2g [Table 1, entry 7, 91% ee, *s* = 42]

HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min): t_R = 18.8 min (4.4%), t_R = 34.6 min (95.6%); IR (neat): 1741, 1496, 1453, 747, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.27–7.13 (m, 15H, Ph), 5.09 (d, J = 12.5 Hz, 1H, Bn), 5.06 (d, J = 12.5 Hz, 1H, Bn), 5.05 (s, 1H, 2′-H), 4.84 (d, J = 5.0 Hz, 1H, 2-H), 1.85–1.74 (m, 1H, *c*-Hex), 1.63–1.37 (m, 6H, *c*-Hex), 1.10–0.80 (m, 4H, *c*-Hex); ^{13}C NMR ($CDCl_3$): δ 172.1, 169.3, 138.4, 138.3, 135.3, 128.78,

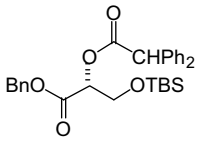
128.76, 128.54, 128.51, 128.4, 128.3, 128.2, 127.3, 127.1, 77.1, 66.8, 56.9, 39.5, 28.8, 27.3, 25.9, 25.8, 25.7; HR-MS: calcd for $C_{29}H_{30}O_4Na$ (M+Na$^+$) 465.2036, found 465.2031.



(*R*)–**2h**

4.1.20. Benzyl (*R*)-2-(diphenylacetyloxy)-4-phenylbutanoate (*R*)-2h [Table 1, entry 8, 96% ee, *s* = 140]

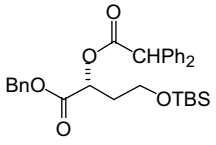
Mp: 75.3–76.0 °C (hexane); HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:9, flow rate = 1.0 mL/min): t_R = 11.4 min (2.0%), t_R = 12.2 min (98.0%); IR (KBr): 1734, 1496, 1455, 735, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.36–7.09 (m, 18H, Ph), 6.93–6.88 (m, 2H, Ph), 5.12 (d, *J* = 12.0 Hz, 1H, Bn), 5.11 (s, 1H, 2′-H), 5.07 (d, *J* = 12.0 Hz, 1H, Bn), 5.01 (dd, *J* = 7.0, 6.0 Hz, 1H, 2-H), 2.54–2.42 (m, 2H, 4-H), 2.12–2.05 (m, 2H, 3-H); ^{13}C NMR ($CDCl_3$): δ 171.9, 169.7, 140.1, 138.3, 138.2, 135.2, 128.77, 128.77, 128.66, 128.58, 128.48, 128.44, 128.41, 128.38, 128.3, 127.4, 127.3, 126.2, 72.1, 67.1, 56.8, 32.6, 31.0; HR-MS: calcd for $C_{31}H_{28}O_4Na$ (M+Na$^+$) 487.1880, found 487.1903.



(*R*)–**2i**

4.1.21. Benzyl (*R*)-3-(*tert*-butyldimethylsiloxy)-2-(diphenylacetyloxy)propanoate (*R*)-2i [Table 1, entry 9, 94% ee, *s* = 77]

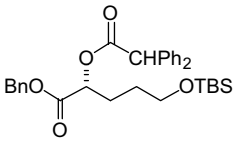
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:50, flow rate = 0.5 mL/min): t_R = 21.1 min (97.0%), t_R = 31.9 min (3.0%); IR (neat): 1743, 1496, 1455, 746, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.36–7.20 (m, 15H, Ph), 5.23 (dd, *J* = 5.0, 3.0 Hz, 1H, 2-H), 5.18 (d, *J* = 12.0 Hz, 1H, Bn), 5.14 (d, *J* = 12.0 Hz Hz, 1H, Bn), 5.13 (s, 1H, 2′-H), 4.03 (dd, *J* = 11.5, 5.0 Hz, 1H, 3-H), 3.91 (dd, *J* = 11.5, 3.0 Hz, 1H, 3-H), 0.80 (s, 9H, TBS), −0.05 (s, 3H, TBS), −0.06 (s, 3H, TBS); ^{13}C NMR ($CDCl_3$): δ 172.0, 167.8, 138.3, 138.1, 135.2, 128.8, 128.7, 128.6, 128.53, 128.46, 128.3, 128.2, 127.3, 127.2, 74.4, 67.1, 62.6, 56.8, 25.6, 18.1, −5.58, −5.58; HR-MS: calcd for $C_{30}H_{36}O_5SiNa$ (M+Na$^+$) 527.2224, found 527.2245.



(*R*)–**2j**

4.1.22. Benzyl (*R*)-4-(*tert*-butyldimethylsiloxy)-2-(diphenylacetyloxy)butanoate (*R*)-2j [Table 1, entry 10, 93% ee, *s* = 100]

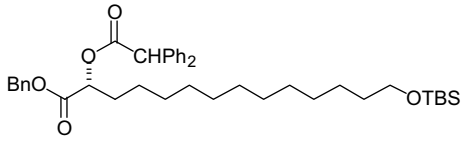
HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:50, flow rate = 1.0 mL/min): t_R = 6.3 min (96.6%), t_R = 9.6 min (3.4%); IR (neat): 1740, 1497, 1455, 747, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.46–7.31 (m, 15H, Ph), 5.36 (dd, *J* = 9.0, 4.0 Hz, 1H, 2-H), 5.28 (d, *J* = 12.3 Hz, 1H, Bn), 5.23 (d, *J* = 12.3 Hz, 1H, Bn), 5.21 (s, 1H, 2′-H), 3.67 (ddd, *J* = 10.3, 6.0, 4.5 Hz Hz, 1H, 4-H), 3.60 (ddd, *J* = 10.3, 8.0, 5.0 Hz, 1H, 4-H), 2.18 (dddd, *J* = 14.1, 8.0, 6.0, 4.0 Hz, 1H, 3-H), 2.08 (dddd, *J* = 14.1, 9.0, 5.0, 4.5 Hz, 1H, 3-H), 0.93 (s, 9H, TBS), 0.05 (s, 3H, TBS), 0.03 (s, 3H, TBS); ^{13}C NMR ($CDCl_3$): δ 171.8, 170.1, 138.4, 138.2, 135.3, 128.74, 128.71, 128.6, 128.5, 128.4, 128.3, 128.1, 127.3, 127.2, 69.8, 66.9, 58.2, 56.8, 34.0, 25.8, 18.2, −5.5, −5.6; HR-MS: calcd for $C_{31}H_{38}O_5SiNa$ (M+Na$^+$) 541.2381, found 541.2391.



(*R*)–**2k**

4.1.23. Benzyl (*R*)-5-(*tert*-butyldimethylsiloxy)-2-(diphenylacetyloxy)pentanoate (*R*)-2k [Table 1, entry 11, 95% ee, *s* = 177]

HPLC (CHIRALPAK IC, *i*-PrOH/hexane = 1:50, flow rate = 1.0 mL/min): t_R = 9.5 min (2.4%), t_R = 11.3 min (97.6%); IR (neat): 1601, 1496, 1454, 839, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.35–7.20 (m, 15H, Ph), 5.16 (d, *J* = 12.0 Hz Hz, 1H, Bn), 5.12 (d, *J* = 12.0 Hz, 1H, Bn), 5.11 (s, 1H, 2′-H), 5.11 (dd, *J* = 8.5, 5.0 Hz, 2H, 2-H), 3.51 (t, *J* = 6.0 Hz Hz, 2H, 5-H), 1.97–1.81 (m, 2H, 3-H), 1.50–1.41 (m, 2H, 4-H), 0.85 (s, 9H, TBS), −0.02 (s, 6H, TBS); ^{13}C NMR ($CDCl_3$): δ 172.0, 169.8, 138.3, 138.2, 135.2, 128.7, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.3, 127.2, 72.8, 66.9, 62.0, 56.8, 28.1, 27.7, 25.9, 18.2, −5.4; HR-MS: calcd for $C_{32}H_{40}O_5SiNa$ (M+Na$^+$) 555.2537, found 555.2536.



(*R*)–**2l**

4.1.24. Benzyl (*R*)-14-(*tert*-butyldimethylsiloxy)-2-(diphenylacetyloxy)tetradecanoate (*R*)-2l [Table 1, entry 12, 95% ee, *s* = 119]

HPLC (CHIRALPAK AD-H, *i*-PrOH/hexane = 1:100, flow rate = 1.0 mL/min): t_R = 13.6 min (2.6%), t_R = 19.5 min (97.4%); IR (neat): 1745, 1496, 1457, 837, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.24–7.09 (m, 15H, Ph), 5.05 (d, *J* = 12.3 Hz, 1H, Bn), 5.01 (d, *J* = 12.3 Hz, 1H, Bn), 5.00 (s, 1H, 2′-H), 4.97 (t, *J* = 6.5 Hz, 1H, 2-H), 3.49 (t, *J* = 6.5 Hz, 2H, 14-H), 1.69 (td, *J* = 7.0, 6.5 Hz Hz, 2H, 3-H), 1.40 (tt, *J* = 7.3, 6.5 Hz, 2H, 13-H), 1.24–0.09 (m, 18H, 4-H, 5-H, 6-H, 7-H, 8-H, 9-H, 10-H, 11-H, 12-H), 0.78 (s, 9H, TBS), −0.07 (s, 6H, TBS); ^{13}C NMR ($CDCl_3$): δ 172.1, 170.0, 138.3, 138.2, 135.3, 128.71, 128.70, 128.6, 128.5, 128.4, 128.3, 128.2, 127.3, 127.2, 72.9, 66.9, 63.3, 56.8, 32.9, 31.0, 29.62, 29.56, 29.56, 29.43, 29.39, 29.26, 28.9, 26.0, 25.8, 24.9, 18.4, −5.3; HR-MS: calcd for $C_{41}H_{58}O_5SiNa$ (M+Na$^+$) 681.3946, found 681.3947.

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