Highly Enantioselective Addition of Mixed Diorganozincs to Aldehydes†

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Introduction

The enantioselective addition[1] of functionalized diorganozincs[2] to aldehydes catalyzed by (1*R*,2*R*)-bis(trifluoromethanesulfonamido)cyclohexane[3] **1** and titanium(IV) alkoxides constitutes an excellent method for the preparation of polyfunctional secondary alcohols.[4] A broad range of aldehydes and functionalized diorganozincs (FG-R)$_2$Zn can be used in this reaction, but an excess of diorganozinc (2−3 equiv, corresponding to 4−6 equiv of the FG-R group) is required in order to obtain high chemical yields and high enantioselectivities.[4] Recently, we have found that mixed diorganozincs of the type FG-R-ZnCH$_2$SiMe$_3$ (**2**) can be readily prepared and characterized by NMR spectroscopic methods.[5] The Me$_3$SiCH$_2$ group behaves as a nontransferable ligand[6,7] and preliminary results have shown that these new mixed zinc reagents are useful for Michael-additions to enones in NMP.[5,8]

Results and Discussion

Herein, we wish to report that various mixed diorganozincs of type **2** can be added to aldehydes with high enantioselectivity without using a large excess of the transferable FG-R group. Thus, the mixing of a diorganozinc (FG-R)$_2$Zn (**3**) (0.8−1.2 equiv), prepared either by a boron−zinc exchange or an iodine−zinc exchange,[2,4] and bis[(trimethylsilyl)methyl]zinc (**4**)[9] (0.9−1.3 equiv) led to the formation of the mixed diorganozinc reagent FG-R-ZnCH$_2$SiMe$_3$ (**2**). Usually, with nonfunctionalized dialkylzincs only 0.8 equiv was used, whereas with the less reactive functionalized dialkylzincs, 1.2 equiv is required. NMR-experiments show that less than 20% of (FG-R)$_2$Zn **3** remains at the equilibrium which is set up within a few minutes at rt.[5] The mixed diorganozincs **2** are less reactive than the zinc species **3**, decreasing significantly the addition rate to the aldehyde. The nonasymmetric catalysis induced by the addition of Ti(O*i*-Pr)$_4$ becomes more important. Thus, the addition of Pent(TMSM)Zn to benzaldehyde gives a moderate enantioselectivity (48% ee) in the presence of a large amount of Ti(O*i*-Pr)$_4$ (2.0 equiv). An improvement is obtained by reducing the quantity of Ti(O*i*-Pr)$_4$ to 1.6 equiv (88% ee) and further to 1.2 equiv (95% ee). In the general case, optimum enantioselectivities are obtained with 0.6 equiv of Ti(O*i*-Pr)$_4$ and 8 mol % of the chiral catalyst **1** (Scheme 1). The additions to aldehydes **5** are complete in ether at −20 °C after a reaction time of 14−26 h, and the alcohols **6** are obtained in 74−98% yield and 86−98% ee (Table 1).

Aromatic aldehydes such as benzaldehyde (entries 1−6) readily undergo the asymmetric addition leading to the benzylic alcohols **6a**−**f** in 74−93% yield. Unsaturated aldehydes such as cinnamaldehyde (entries 7 and 8) afford the corresponding allylic alcohols **6e**,**f** with 86−89% enantiomeric excess. Similarly, the addition to the functionalized unsaturated aldehyde (*E*)-4-(triisopropylsiloxy)-2-butenal[10] furnishes the desired selectively protected 1,4-diol **6i** (entry 9) in 95% ee. Compared to the previous procedure involving the use of an excess of the symmetrical diorganozinc reagent **3** similar yields and enantioselectivities are obtained (compare the yields and % ee in parentheses in Table 1). Aliphatic aldehydes require longer reaction times and lead to the secondary alcohols **6j**−l in good yields but somewhat lower enantiomeric excess (74−95% ee) compared to the reactions with functionalized diorganozincs (entries 10−12).

Interestingly, highly functionalized zinc reagents can be added to aldehydes by this method. Thus the hydroboration, boron−zinc exchange and addition of (TMSM)$_2$Zn of the dienic ethyl ester **7** furnishes the mixed zinc reagent **2**. Its reaction with benzaldehyde under typical reaction conditions (Ti(O-i-Pr)$_4$ (0.6 equiv), ether, −20 °C, 26 h) gives the chiral hydroxy ester **6m** in 81% yield and 93% ee (Scheme 2). We have also investigated the enantioselective transfer of the methyl group[11] and have prepared the mixed reagent Me(TMSM)Zn. Due to the small size of the methyl group, low enantioselectivity is usually observed with this diorganozinc reagent. Under regular reaction conditions (*S*)-phenylethanol **6n** is obtained with only 23% ee by the direct addition of Me$_2$Zn. Replacing Ti(O*i*-Pr)$_4$ by the more bulky titanium alkoxide[12] Ti(O*t*-Bu)$_4$ now affords **6n**, with 87% ee. By using the mixed reagent Me(TMSM)Zn with Ti(Oi-Pr)$_4$ comparable enantioselectivities are obtained (95% yield, 84% ee) showing that the CH$_2$SiMe$_3$ group is involved in the stereo-determining step of the addition.

In summary, we have shown that mixed diorganozincs of the type FG-R-Zn(TMSM) can be advantageously used for the enantioselective addition to aldehydes. The method avoids the use of a large excess of valuable diorganozinc reagents and provides an improvement of the enantioselectivity for the addition of small dialkylzincs such as Me$_2$Zn and Et$_2$Zn.

Experimental Section

Typical Procedure for the Enantioselective Addition of a Mixed Dialkylzinc to an Aldehyde. A dried and argon-flushed 50 mL Schlenk-flask was charged with (1*R*,2*R*)-1,2-bis-

† Dedicated to Professor Dieter Seebach on the occasion of his 60th birthday.

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(9) Moorhouse, W.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1974**, 2187−2190.

(10) Vettel, S.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 5849−5852.

(11) For the use of mixed methyl(alkyl)zincs in synthesis, see ref 7a.

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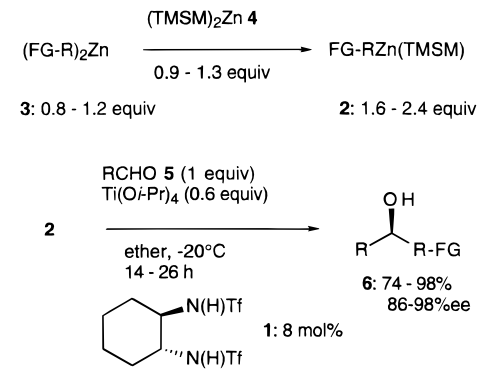
Scheme 1



(trifluoromethanesulfonamido)cyclohexane (**1**) (61 mg, 0.16 mmol, 8 mol %), Ti(O-*i*Pr)$_4$ (0.36 mL, 1.2 mmol, 0.6 equiv), and ether (3 mL). This catalyst solution was cooled to −20 °C. Meanwhile the dialkylzinc **3** (1.6 mmol, 0.8 equiv) and $(TMSCH_2)_2Zn$ **4** (0.43 g, 1.8 mmol, 0.9 equiv) were mixed at 25 °C in another Schlenk-flask. In the case of a functionalized dialkylzinc 1.2 equiv of $(FG\text{-}R)_2Zn$ and 1.3 equiv of $(TMSCH_2)_2Zn$ were used. The resulting mixed zinc reagent FG-R-$(TMSCH_2)$Zn was slowly added to the catalyst solution. After 10 min, the aldehyde (2.0 mmol, 1.0 equiv) was added. The reaction mixture was stirred at −20 °C for 14−26 h and worked up as usual. The crude product was purified by chromatography (hexanes:ether).

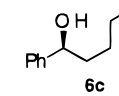
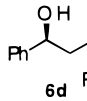
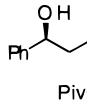
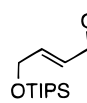
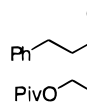
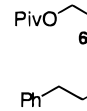
Analytical Data of Products of Table 1. (*S*)-1-Phenylpropanol (6a). Yield (295 mg, 92%, 98% ee) using diethylzinc (0.22 mL, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and benzaldehyde (250 mg, 2.36 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral gas chromatographic analysis; Chirasil CD; 120 °C isotherm; 100 kPa (H_2); 7.23 min minor, 7.43 min major isomer. $[\alpha]^{25}_D = -48.4$ (*c* 2.31, $CHCl_3$). IR (neat): 3360 (s), 2930 (s), 2870 (m), 1475 (m), 1031 (m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35 (m, 5H), 4.75 (t, J = 6.0 Hz, 1H), 2.48 (s, 1H), 1.81 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.0, 128.8, 127.9, 126.4, 76.4, 32.2, 10.6. The obtained analytical data is comparable to the literature.[13,14]

(*S*)-1-Phenylhexanol (6b). Yield (401 mg, 92%, 97% ee) using dipentylzinc (0.15 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and benzaldehyde (260 mg, 2.45 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral gas chromatographic analysis; Chirasil CD; 145 °C isotherm; 100 kPa (H_2); 7.53 min major, 7.95 min minor isomer. $[\alpha]^{25}_D = -36.8$ (*c* 3.18, $CHCl_3$). IR (neat): 3360 (s), 2930 (s), 2870 (m), 1475 (m), 1031 (m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33−7.25 (m, 5H), 4.61 (t, J = 7.1 Hz, 1H), 2.19 (s, 1H), 1.79−1.66 (m, 2H), 1.42−1.28 (m, 6H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.0, 128.3, 127.4, 125.9, 74.6, 39.0, 31.7, 25.4, 22.5, 13.9. The obtained analytical data is identical with the literature.[15]

(*S*)-5-Chloro-1-phenylpentanol (6c). Yield (336 mg, 86%, >94% ee) using bis(4-chlorobutyl)zinc (0.54 g, 2.2 mmol), **4** (0.57 g, 2.4 mmol), and benzaldehyde (209 mg, 1.97 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD, heptane/2-propanol = 95:5; flow = 0.6 mL/min; 27.05 min major, 28.42 min minor isomer. $[\alpha]^{25}_D = -14.7$ (*c* 2.36, benzene). IR (neat): 3370 (s), 2940 (s), 1454 (s), 1195 (m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30−7.02 (m, 5H), 4.58 (m, 1H), 3.48 (t, J = 6.7 Hz, 2H) 2.28 (s, 1H), 1.97−1.35 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.6, 129.1, 127.7, 126.1, 74.5, 44.9, 37.9, 33.5, 23.3. The obtained analytical data is identical with the literature.[16]

(*S*)-4-Hydroxy-4-phenylbutyl Pivalate (6d). Yield (379 mg, 81%, 96% ee) using bis(3-pivaloxypropyl)zinc (0.83 g, 2.2 mmol), **4** (0.43 g, 1.9 mmol), and benzaldehyde (0.199 g ,1.87 mmol). Purified by chromatrography (hexanes/ether = 2:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD, heptane/2-propanol = 90:10; flow 0.6 mL/min; 12.6 min major, 15.3 min minor isomer. $[\alpha]^{25}_D = -20.3$(*c* 2.87, benzene). IR (neat): 3540 (s), 2970 (m), 2930 (s), 1720 (s), 2480

Table 1. Secondary Alcohols 6 Obtained by the Catalytic Asymmetric Addition of the Mixed Diorganozincs FG-RZnCH_2TMS (2) to Aldehydes (5) in the Presence of the Chiral Catalyst

Zinc reagent **2** (FG-R)	Aldehyde **5** (R)	Alcohols **6**	Yield (%)[a,b]	%ee[c]
Et	Ph	 **6a**	98(98)	92(95)
Pent	Et	 **6b**	93(93)	97(98)
Cl$(CH_2)_4$	Et	 **6c**	86(93)	>94(95)
PivO$(CH_2)_3$	Et	 **6d**	81(92)	96(90)
PivO$(CH_2)_4$	Et	 **6e**	81	97
AcO$(CH_2)_5$	Ph	 **6f**	74(79)	90(93)
Et		 **6g**	95(93)	89(90)
Pent		 **6h**	89(87)	86(85)
Et		 **6i**	89(68)	95(88)
Et		 **6j**	87	>95
PivO$(CH_2)_4$		 **6k**	76	74
PivO$(CH_2)_5$		 **6l**	79	82

[a] Isolated yield of analytically pure products. [b] The yields in parenthesis refer to yields obtained using an excess of $(FG\text{-}R)_2Zn$ (2-3 equiv). [c] The enantiomeric excess in parenthesis refer to reactions performed with $(FG\text{-}R)_2Zn$ (**3**) instead of **2.**

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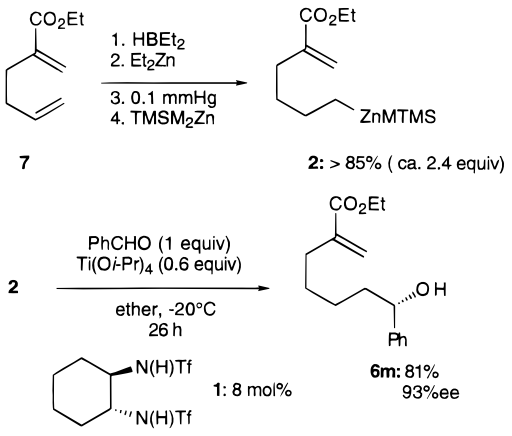
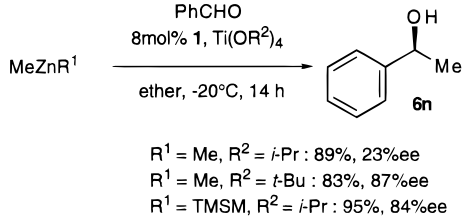
Scheme 2



Scheme 3



R^1 = Me, R^2 = *i*-Pr : 89%, 23%ee
R^1 = Me, R^2 = *t*-Bu : 83%, 87%ee
R^1 = TMSM, R^2 = *i*-Pr : 95%, 84%ee

(m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.36−7.28 (m, 5H), 4.72−4.70 (m, 1H), 4.10−4.06 (t, J = 6.0 Hz, 2H) 1.89−1.31 (m, 5H), 1.20 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 179.1, 144.9, 128.9, 128.0, 126.2, 74.4, 64.5, 39.1, 35.7, 27.6, 25.5. The obtained analytical data is identical with the literature.[16]

(*S*)-5-Hydroxy-5-phenylpentyl Pivalate (6e). Yield (438 mg, 81%, 97% ee) using bis(4-pivaloxybutyl)zinc (0.61 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and benzaldehyde (223 mg, 2.10 mmol). Purified by chromatrography (hexanes/ether = 2:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD, heptane/2-propanol = 95:5, flow 0.6 mL/min; 23.95 min major, 26.41 min minor isomer. $[\alpha]^{25}_D$ = −25.3 (*c* 1.50, $CHCl_3$). IR (neat): 3440 (s), 3090 (w), 3060 (s), 2940 (m), 1880 (s), 1550 (s). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35−7.27 (m, 5H), 4.65 (m, 1H), 4.03 (t, J = 6.5 Hz, 2H), 2.20 (br s, 1H), 1.82−1.22 (m, 6H), 1.75 (s, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 177.9, 143.9, 127.6, 126.7, 125.1, 73.6, 63.4, 37.9, 37.8, 27.7, 26.4, 21.4. MS (EI): 264 (0.6), 129 (25), 144 (26), 101 (100), 79 (25), 57 (75), 41 (25). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.53; H 9.07.

(*S*)-6-Hydroxy-6-phenylhexenyl Acetate (6f). Yield (388 mg, 74%, 90% ee) using bis(5-acetoxypentyl)zinc (0.65 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and benzaldehyde (236 mg, 2.22 mmol). Purified by chromatrography (hexanes/ether = 2:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD; heptane/2-propanol = 90:10; flow 0.6 mL/min; 17.50 min major, 19.42 min minor isomer. $[\alpha]^{25}_D$ = −22.1 (*c* 1.94, benzene). IR (neat): 3450 (s), 2940 (s), 1737 (s), 1464 (m), 1039 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27−7.18 (m, 5H), 4.56 (m, 1H), 3.95 (t, J = 6.7 Hz, 2H), 2.42 (s, 1H), 1.94 (s, 3H), 1.73−1.23 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.3, 144.9, 128.5, 127.5, 125.9, 74.4, 64.5, 38.9, 28.6, 25.5, 25.2, 20.9. The obtained analytical data is identical with the literature.[16]

(*E*)-(*S*)-5-Phenylpent-4-en-3-ol (6g). Yield (311 mg, 95%, 89% ee) using diethylzinc (0.22 mL, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and cinnamaldehyde (267 mg, 2.02 mmol). Purified by chromatrography (hexanes/ether = 2:1). The enantiomeric excess was determined by chiral gas chromatography analysis; Chirasil CD; 140 °C isotherm; 100 kPa (H_2); 8.57 min major, 8.67 min minor isomer. $[\alpha]^{25}_D$ = −5.6 (*c* 3.71, $CHCl_3$). IR (neat): 3360 (s), 2965 (s), 2930 (s), 1455 (m), 965 (s). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.24−7.09 (m, 5H), 6.40 (d, J = 16 Hz), 1H), 5.98 (dd, J = 16 Hz, J = 6.8 Hz, 1H), 4.05 ((dt, J = 6.8, J = 0.8 Hz, 1H), 1.83 (s, 1H), 1.57−1.45 (m, 2H), 0.79 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.2, 132.6, 130.9, 129.0, 128.1, 126.9, 74.9, 34.0, 30.6, 10.2. The obtained analytical data is comparable to the literature.[13,17]

(*E*)-(*S*)-1-Phenyloct-1-en-3-ol (6h). Yield (315 mg, 89%, 86% ee) using dipenthylzinc (0.15 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and cinnamaldehyde (230 mg, 1.74 mmol). Purified by chromatrography (hexanes/ether = 2:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD; heptane/2-propanol = 90:10; flow 0.6 mL/min; 13.09 min minor, 21.23 min major isomer. $[\alpha]^{25}_D$ = +1.6 (*c* 6.3, benzene). IR (neat): 3400 (s), 2920 (s), 2860 (s), 1700 (m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.27−7.11 (m, 5H), 6.43 (d, J = 16 Hz, 1H), 6.09 (dd, J = 16.0 Hz, 6.8 Hz, 1H), 4.20−4.05 (m, 1H), 2.24 (s, 1H), 1.54−1.44 (m, 2H), 1.33−1.20 (m, 6H), 0.79 (t, J = 6.3 Hz, 3H) . ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.1, 132.9, 130.7, 128.9, 128.0, 126.9, 73.6, 37.7, 32.2, 25.6, 23.0, 14.5. The analytical data obtained is identical with the literature.[18]

(*E*)-(*S*)-1-[(Triisopropylsilyl)oxy]hex-2-en-4-ol (6i). Yield (244 mg, 95%, 95% ee) using diethylzinc (0.15 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and 3-(triisopropylsiloxy)propanal (274 mg, 1.03 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral gas chromatographic analysis; Chirasil CD; 120 °C isotherm; 100 kPa (H_2); 21.40 min minor, 21.65 min major isomer. $[\alpha]^{25}_D$ = +2.3 (*c* 4.01, $CHCl_3$). IR (neat): 3370 (s), 2940 (s), 2870 (s), 1460 (s), 1130 (s), 1010 (m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.73 (m, 2H), 4.23 (m, 2GH), 4.08−3.98 (m, 1H), 3.87 (m, 1H), 1.80 (s, 1H), 1.63 (s, 1H), 1.58−1.48 (m, 21H), 0.86 (t, J = 7.3 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 131.31, 129.6, 73.0, 62.4, 29.23, 16.8, 10.6, 8.8. MS (EI): 272 (0.5), 254 (1), 229 (36), 131 (94), 103 (100), 89 (20), 75 (88), 61 (55). Anal. Calcd for $C_{15}H_{32}O_2Si$: C, 66.11; H, 11.84. Found: C, 66.06; H 11.81.

(*S*)-1-Phenylpentan-3-ol (6j). Yield (293 mg, 87%, >95% ee) using diethylzinc (0.15 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and hydrocinnamaldehyde (277 mg, 2.06 mmol). Purified by chromatrography (hexanes/ether = 2:1). The enantiomeric excess was determined by chiral gas chromatographic analysis; Chirasil CD; 120 °C isotherm; 100 kPa (H_2); 14.70 min major, 15.12 min minor isomer. $[\alpha]^{25}_D$ = +24.1 (*c* 1.08, EtOH). IR (neat): 3360 (s), 2930 (s), 2870 (m), 1475 (m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33−7.20 (m, 5H), 3.58 (m, 1H), 2.86−2.66 (m, 2H), 2.32 (s, 1H), 1.84−1.76 (m, 2H), 1.59−1.24 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 142.5, 128.6, 128.5, 125.9, 72.8, 38.7, 33.8, 30.4, 10.0. The obtained analytical data is comparable to the literature.[13,17]

(*S*)-7-Phenyl-5-hydroxyheptyl Pivalate (6k). Yield (446 mg, 76%, 74% ee) using bis(4-pivaloxybutyl)zinc (0.83 g, 2.2 mmol), **4** (0.57 g, 2.4 mmol), and hydrocinnamaldehyde (271 mg, 2.01 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD; heptane/2-propanol = 95:5; flow 0.6 mL/min; 17.57 min minor, 19.14 min major isomer. $[\alpha]^{25}_D$ = +10.7 (*c* 1.59, $CHCl_3$). IR (neat): 3680 (s), 3030 (w), 2940 (s), 1880 (s), 1540 (s), 1230 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28−7.10 (m, 5H), 4.05 (t, J = 6.6 Hz, 2H), 3.59 (m, 1H), 2.78−2.64 (m, 4H), 1.77−1.48 (m, 7H), 1.45 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.6, 142.0, 128.9, 126.0, 71.1, 64.2, 39.1, 38.7, 37.0, 32.3, 27.2, 22,0. MS (EI): 103 (43), 85 (16), 57 (100), 41 (23). Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.84; H 9.53.

(*S*)-8-Phenyl-6-hydroxyoctyl Pivalate (6l). Yield (475 mg, 79%, 82% ee) using bis(5-pivaloxypentyl)zinc (0.89 g, 2.2 mmol), **4** (0.57 g, 2.4 mmol), and hydrocinnamaldehyde (263 mg, 1.96 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD; heptane/2-propanol = 90:10; flow 0.6 mL/min; 14.04 min minor, 22.24 min major isomer. $[\alpha]^{25}_D$ = +41.8 (*c* 0.98, $CHCl_3$). IR (neat): 3680 (s), 3030 (w), 2940 (s), 1880 (s), 1540 (s), 1230 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28−7.10 (m, 5H), 4.02 (t, J = 6.6 Hz, 2H), 3.60 (m, 1H), 2.79−2.63 (m, 4H), 1.78−1.34 (m, 9H), 1.30 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5, 142.0, 128.6, 125.7, 71.1, 64.2, 39.0, 38.6, 37.3, 31.9, 28.5, 27.1, 25.9, 25.1. MS (EI): 288 (5), 186 (12), 117 (20), 104 (64), 91

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(62), 57 (100). Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.38; H 9.69.

Analytical Data of Products 6m and 6n. (*S*)-Ethyl 7-Phenyl-7-hydroxy-2-methyleneheptanoate (6m). Yield (428 mg, 81%, 93% ee) using **6m** (0.15 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and benzaldehyde (214 mg, 2.02 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral HPLC analysis; Chiracel OD, heptane/2-propanol = 95:5; flow 0.6 mL/min; 12.83 min major, 13.74 min minor isomer. $[\alpha]^{25}_D = -9.7$ (*c* 1.68, $CHCl_3$). IR (neat): 3480 (s), 2940 (vs), 1720 (vs), 1630 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34−7.21 (m, 5H), 6.08 (m, 1H), 5.46 (m, 1H), 4.60 (m, 1H), 4.15 (q, J = 8.0 Hz, 2H), 2.28 (t, J = 7.1 Hz, 2H), 1.96 (s, 1H), 1.84−1.42 (m, 6H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 144.8, 140.8, 128.4, 127.4, 125.8, 124.2, 74.4, 60.4, 38.8, 31.6, 28.2, 25.3, 14.1. MS (EI): 244 (7), 156 (100), 115 (43), 91 (40), 79 (54). Anal. Calcd for : C, 73.24; H, 8.45. Found: C, 73.01; H 8.61.

(S)-1-Phenylethanol (6n). Yield (262 mg, 95%, 84% ee) using dimethylzinc (0.15 g, 1.6 mmol), **4** (0.43 g, 1.9 mmol), and benzaldehyde (240 mg, 2.3 mmol). Purified by chromatrography (hexanes/ether = 4:1). The enantiomeric excess was determined by chiral gas chromatographic analysis; Chirasil CD; 120 °C isotherm; 100 kPa (H_2); 4.32 min major, 4.75 min minor isomer. $[\alpha]^{25}_D = -35.2$ (*c* 1.97, $CHCl_3$). IR (neat): 3360 (s), 2930 (s), 2870 (m), 1475 (m), 1031 (m). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30−7.32 (m, 5H), 4.78 (q, J = 8.0 Hz, 1H), 2.39 (s, 1H), 1.43 (d, J = 15.6 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 146.2, 128.9, 127.8, 125.8, 70.8, 25.6. The obtained analytical data is identical with the literature.[19,20]

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectras of compounds **6e**, **6i**, **6k**, **6l**, and **6m** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any masthead page for ordering information.

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