Article

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Desymmetrization of *meso*-1,2-Diols by a Chiral *N*,*N*-4-Dimethylaminopyridine Derivative Containing a 1,1′-Binaphthyl Unit: Importance of the Hydroxy Groups

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This work is dedicated to Prof. Teruaki Mukaiyama on the occasion of his 90th birthday.

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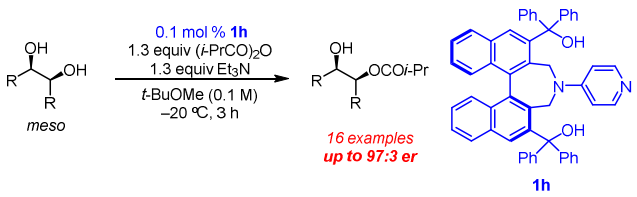


Abstract

We developed an acylative desymmetrization of *meso*-1,2-diols using a binaphthyl-based *N*,*N*-4-dimethylaminopyridine (DMAP) derivative **1h** with *tert*-alcohol substituents. The reaction proceeds with a wide range of acyclic *meso*-1,2-diols and six-membered-ring *meso*-1,2-diols to provide a monoacylate selectively with a high enantiomeric ratio (er). Only 0.1 mol % of the catalyst facilitated the reaction within a short reaction time (3 h) to afford enantio-enriched monoacylated products in moderate to good yield. Several control experiments

revealed that the *tert*-alcohol units of catalyst **1h** play a significant role in achieving high catalytic activity, chemoselectivity of monoacylation, and enantioselectivity.

Introduction

N,*N*-4-Dimethylaminopyridine (DMAP) and 4-pyrrolidinopyridine (PPY) are powerful catalysts for acylation and have been used in organic synthesis for many decades.[1] Enantiomerically pure variants of these catalysts[2] have also been well explored since the pioneering works reported by Vedejs[3] and Fu[4], and have been used in the kinetic resolution of secondary alcohols and other important enantioselective acyl transfer processes.[5] However, only a limited number of catalysts can be applied to a wide range of substrates and/or reactions with high efficiency and enantioselectivity. Furthermore, methods to obtain such enantiomerically pure catalysts often require a cumbersome procedure involving the optical resolution[6] of a racemic intermediate. Thus, precise modification of the catalyst (e.g., the introduction of electronically and sterically demanding substituents) is not always easy, and this has limited further expansion of the catalyst library. Very recently, we reported two classes of chiral nucleophilic catalysts prepared from L-amino acid[7] or (*S*)-1,1′-bi-2-naphthol as a chiral source.[8] Notably, binaphthyl-based catalysts with *tert*-alcohol units (Ar = Ph or 4-*t*-BuC_6H_4, Figure 1a) showed extremely high catalytic activity and enantioselectivity in Steglich rearrangements,[8a] the kinetic resolution of benzylic carbinols[8b] and *d,l*-1,2-diols,[8a,c] and the desymmetrization of *meso*-1,2-hydrobenzoin[8a] (Figure 1b–e).

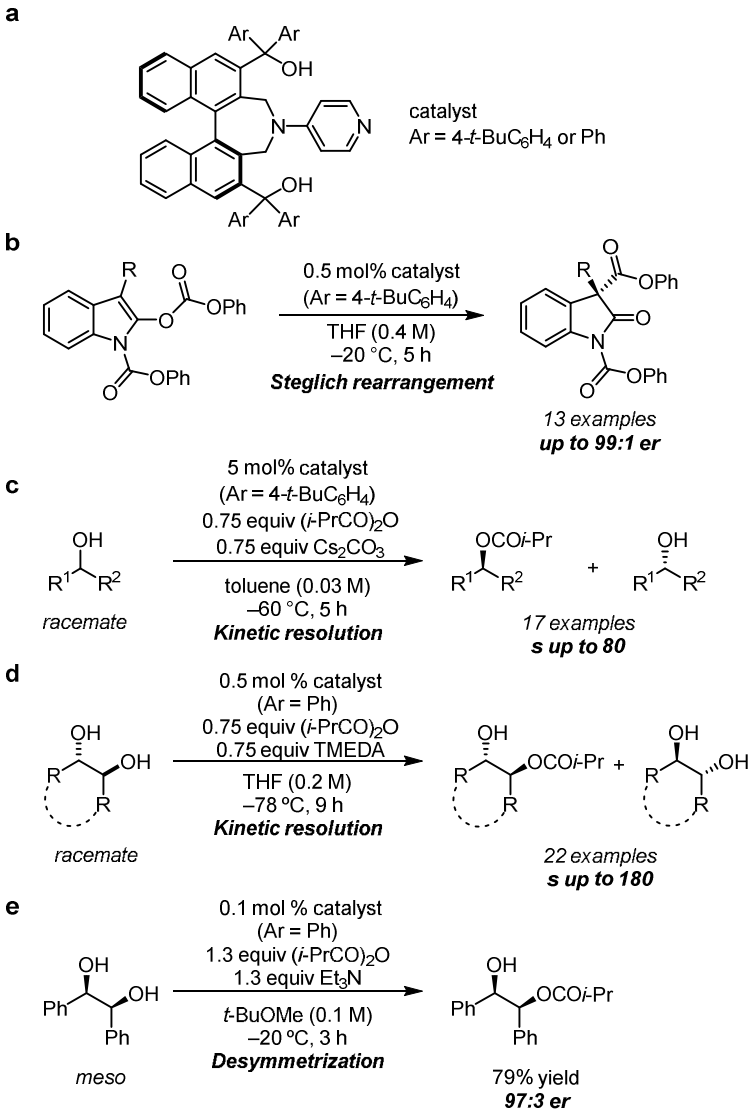
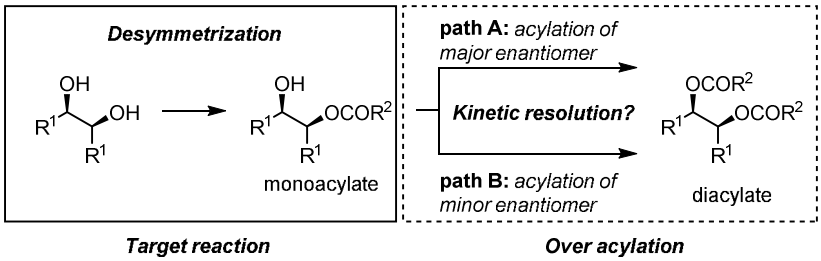


Figure 1. Various acyl transfer reactions catalyzed by binaphthyl-based chiral DMAP derivatives.

If we wish to produce valuable chiral building blocks[9] having two continuous hydroxy groups, the desymmetrization of *meso*-1,2-diols is a straightforward method for obtaining enantiomerically pure 1,2-diol derivatives[5b,10] because, in principle, the desymmetrization of a *meso*-compound provides an enantiomer-enriched product in a theoretical yield of up to 100% and seems to be more efficient than kinetic resolution of a racemate (up to 50% theoretical

yield). Many different synthetic methods for the desymmetrization of 1,2-diols using enzymatic[11] or non-enzymatic approaches (metal catalysis[12] or organocatalysis[13]) have been reported. However, only a few methods[13a,b,e,i] can be applied to a wide range of substrates (acyclic- and cyclic *meso*-1,2-diol) with high yield and high enantioselectivity (>95:5 enantiomeric ratio [er]). Furthermore, an ideal method for the acylative enantioselective desymmetrization of *meso*-1,2-diols would need to provide a high chemoselectivity of monoacylation and the production of only a minimum amount of an undesired diacylated product (over-acylation). If the second acylation step involves kinetic resolution, the enantiomeric ratio of the monoacylated product would be seriously affected (Scheme 1, path A or B)[14]: when the major enantiomer of the monoacylate undergoes a second acylation, the enantioselectivity of the monoacylate will decrease (Path A). In contrast, when the minor enantiomer of the monoacylate undergoes a second acylation, the enantioselectivity of the monoacylate will increase (Path B). To prevent this undesirable over-reaction, a chiral nucleophilic catalyst would need to exhibit extremely high catalytic activity for the acylation of a diol rather than a monofunctional alcohol.[8c,15]



Scheme 1. General scheme for the acylative desymmetrization of *meso*-1,2-diol.

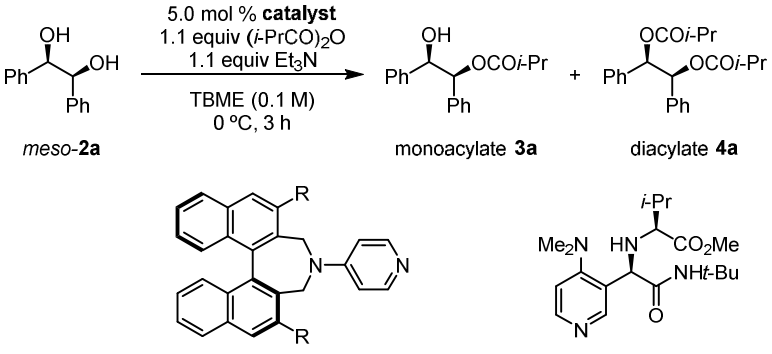
In this paper, we describe the details of the desymmetrization of an array of *meso*-1,2-diols, including acyclic and cyclic substrates, with moderate to high enantioselectivity by binaphthyl-based catalyst **1h**, which is known to be a highly active and enantioselective

chiral DMAP derivative that uses positive interactions (hydrogen-bonding) between the catalyst and substrate.[8a] Several key experiments were also carried out to better understand the mechanism of the reaction.

Results and Discussion

We began by seeking to identify an optimal catalyst for the acylative desymmetrization of acyclic *meso*-1,2-diol **2a** (*meso*-hydrobenzoin) as a model substrate. The reaction was carried out in the presence of 5 mol % of chiral DMAP derivatives, 1.1 equiv. of isobutyric anhydride, and 1.1 equiv. of triethylamine in *tert*-butyl methyl ether (TBME) at 0 ºC for 3 h (Table 1).

Table 1. Catalyst screening for the desymmetrization of *meso*-**2a**[a)]



1a: R = H
1b: R = OMe
1c: R = Ph
1d: R = 2-Naph
1e: R = CO_2Et
1f : R = CONHPh
1g: R = COOH (HCl salt)
1h: R = $C(OH)Ph_2$
1i: R = $C(OH)(4\text{-}Ph\text{-}C_6H_4)_2$
1j: R = $C(OH)(4\text{-}t\text{-}Bu\text{-}C_6H_4)_2$
1k: R = $C(OH)(4\text{-}TIPS\text{-}C_6H_4)_2$
1l: R = $C(OH)(3,5\text{-}(MeO)_2\text{-}C_6H_3)_2$
1m: R = $C(OH)Me_2$

Entry	Catalyst	**3a** [%][b)]	**4a** [%][b)]	**2a** [%][b)]	**3a**/**4a**	ER of **3a**[c)]
1	**1a**	32	29	35	1.1	49:51
2	**1b**	34	38	32	0.89	43:57
3	**1c**	47	29	31	1.6	42:58
4	**1d**	4	0	94	-	-
5	**1e**	40	28	39	1.4	40:60
6	**1f**	38	23	43	1.7	51:49
7	**1g**	34	20	43	1.7	40:60

8	**1h**	86	10	8	8.6	94:6
9	**1i**	78	16	14	4.9	77:23
10	**1j**	65	13	25	5.0	84:16
11	**1k**	73	21	10	3.5	82:18
12	**1l**	29	39	32	0.74	55:45
13	**1m**	49	20	33	2.5	60:40
14	**5**	36	23	39	1.6	43:57
15[d]	**1h**	23	0	77	-	52:48

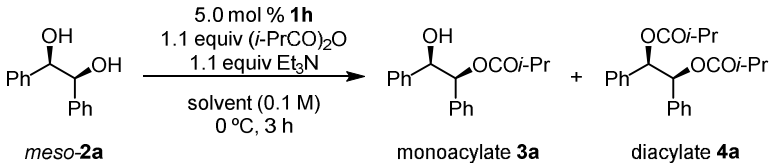
[a] Reactions were performed on a 0.1 mmol scale in TBME (0.1 M) under an argon atmosphere. [b] NMR yields were determined by ^{1}H NMR analysis using 2-methoxynaphthalene as an internal standard. [c] Enantiomer ratios were determined by HPLC analysis using CHIRALCEL OJ-H. [d] Isobutyryl chloride was used instead of isobutyric anhydride.

Catalyst **1a** without any substituents at the 3,3′-positions of the binaphthyl unit afforded a racemic monoacylate **3a** along with a significant amount of diacylate **4a** and the recovery of **2a** (**3a**/**4a** = 1.1; 32% NMR yield of **3a**; 49:51 er; entry 1). Further screening of catalysts **1b**–**g** did not improve either the enantiomeric ratio of **3a** or the chemoselectivity of monoacylation (**3a**/**4a** = 0.89–1.7; 4–47% NMR yield; up to 40:60 er; entries 2–7). In contrast, catalyst **1h**, which has two *tert*-alcohol units (R = $C(OH)Ph_2$) within a chiral binaphthyl unit, was effective in producing **3a** with high enantioselectivity (86% NMR yield of **3a**; 94:6 er; entry 8), and formation of the diacylate **4a** was significantly suppressed (**3a**/**4a** = 8.6). Subsequent precise tuning of the aryl moiety of the *tert*-alcohol revealed that catalysts with 4- or 3,5-substituted aryls **1i**–**l** or dimethyl moieties **1m** were less effective than catalyst **1h** with regard to both the enantioselectivity of **3a** and the chemoselectivity of monoacylation (**3a**/**4a** = 0.74–5.0; 29–78% NMR yield; up to 84:14 er; entries 9–13). On the other hand, α-amino acid-based C_1-symmetric catalyst **5** developed by our group[7] was also ineffective in this reaction (**3a**/**4a** = 1.6; 36% NMR yield; 43:57 er; entry 14). Furthermore, the results clearly indicated that the leaving group of acylation reagents ($^-$OCO*i*-Pr vs $^-$Cl), which consist of the counteranion of *N*-acylpyridinium

ion generated from catalyst **1h** and the acylation reagent, strongly affected the enantioselectivity of **3a** (52:48 er, entry 15), and the low yield of **3a** (23% NMR yield) and the high chemoselectivity of monoacylation with isobutyryl chloride may be explained by the low solubility and reactivity of *N*-acylpyridinium chloride.[16] Accordingly, catalyst **1h** and isobutyric anhydride were selected as the optimal combination for further optimization of the reaction conditions (entry 8).

Next, we screened various solvents in the desymmetrization of **2a** with the optimal catalyst **1h** and isobutyric anhydride at 0 °C for 3 h (Table 2). The reactions in ethereal solvents, involving *t*-BuOMe (TBME), Et_2O, THF, and cyclopentyl methyl ether (CPME), afforded **3a** in high yield and with high chemoselectivity of monoacylation (**3a**/**4a** = 8.0–14; 80–86% NMR yield of **3a**; 88:12 to 94:6 er; entries 1–4). A series of other common organic solvents, except hexane, could also be used in the reaction while maintaining an acceptable chemoselectivity of monoacylation and enantioselectivity (**3a**/**4a** = 0.83–31; 81–92% NMR yield; up to 92:8 er; entries 5–9). With aprotic or protic polar solvents (DMF, acetonitrile, and *t*-amyl alcohol) as reaction media, the enantiomeric ratios of **3a** and in some cases the chemoselectivity of monoacylation were decreased (**3a**/**4a** = 2.8–21; 56–84% yield; up to 87:13 er; entries 10–12). A similar tendency was observed in our previous studies,[8a,b] and such solvents might inhibit efficient hydrogen-bonding between catalyst **1h** and substrate **2a**. After taking into account these results and extensive screening of the reaction conditions involving effects of bases, reaction temperature, concentration of substrate (see the Supporting Information for details), we selected the reaction in the presence of catalyst **1h** and triethylamine in TBME (0.1 M) at -20 °C for further optimizations (**3a**/**4a** = 14, 85% NMR yield of **3a**; 98:2 er; entry 13).

Table 2. Solvent screening for the desymmetrization of *meso*-**2a**[a)]



meso-**2a** monoacylate **3a** diacylate **4a**

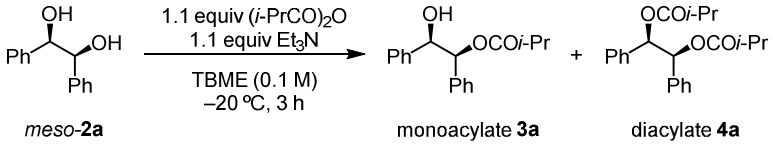
Entry	Solvent	**3a** [%][b]	**4a** [%][b]	**2a** [%][b]	**3a**/**4a**	ER of **3a**[c]
1	TBME	86	10	8	8.6	94:6
2	Et_2O	80	10	11	8.0	88:12
3	THF	83	7	10	12	91:9
4	CPME	82	6	16	14	93:7
5	hexane	19	23	57	0.83	87:13
6	toluene	82	8	21	10	89:11
7	CH_2Cl_2	92	3	6	31	88:12
8	EtOAc	81	6	16	14	90:10
9	acetone	82	7	12	12	92:8
10	DMF	56	15	21	3.7	54:46
11	MeCN	84	4	15	21	87:13
12	*t*-amyl alcohol	56	20	24	2.8	71.5:28.5
13[d]	TBME	85	6	9	14	98:2

[a] Reactions were performed on a 0.1 mmol scale in solvent (0.1 M) under an argon atmosphere. [b] NMR yields were determined by ^{1}H NMR analysis using 2-methoxynaphthalene as an internal standard. [c] Enantiomer ratios were determined by HPLC analysis using CHIRALCEL OJ-H. [d] The reaction was carried out at –20 °C for 3 h.

We next sought to reduce the catalyst loading of **1h** because 5 mol % of **1h** still gave a high chemoselectivity of monoacylation and high enantioselectivity (Table 3). We found that as little as 0.1 mol % of catalyst **1h** was sufficient to facilitate the reaction without a loss of chemoselectivity or enantioselectivity (**3a**/**4a** = 12–21; 83–86% NMR yield; 97:3 er; entries 2–4 vs 1). While the use of 0.05 mol % of **1h** showed an acceptable level of efficiency, a fair amount of *meso*-**2a** remained after 3 h (**3a**/**4a** = 26; 77% NMR yield; 97:3 er; 22% NMR yield of recovery **2a**; entry 5). After further adjusting the amounts of isobutyric anhydride and

triethylamine (1.3 or 1.5 equivalents, respectively, entries 7 and 8), we identified the optimal reaction conditions (0.1 mol % of **1h**, 1.3 equiv of isobutyric anhydride, and triethylamine in TBME (0.2 M) at –20 ºC for 3 h) (**3a**/**4a** = 14; 86% NMR yield of **3a**; 98:2 er; entry 7).

Table 3. Effects of catalyst loading in the desymmetrization of *meso*-**2a**[a)]



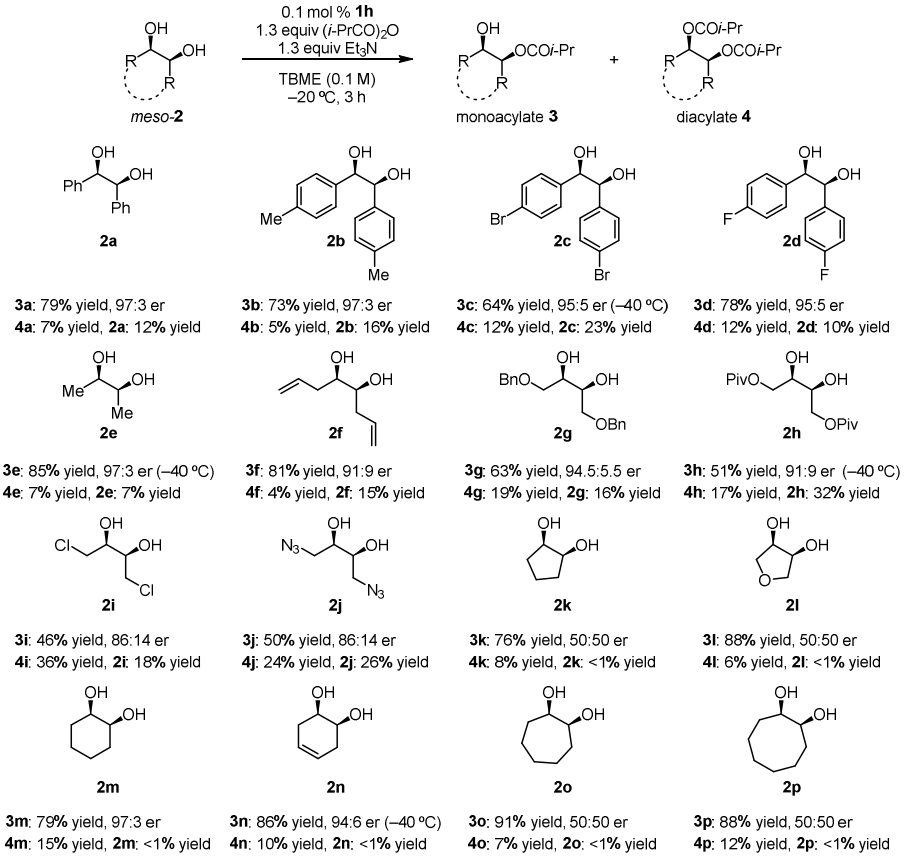
Entry	X [mol %]	**3a** [%][b)]	**4a** [%][b)]	**2a** [%][b)]	**3a**:**4a**	ER of **3a**[c)]
1[d)]	5.0	85	6	9	14	98:2
2[e)]	1.0	86	7	8	12	97:3
3	0.5	83	5	14	17	97:3
4	0.1	83	4	12	21	97:3
5	0.05	77	3	22	26	97:3
7[f)]	0.1	86	6	5	14	98:2
8[g)]	0.1	83	14	<1	5.9	97:3

[a)] Reactions were performed on a 0.1 mmol scale in TBME (0.1 M) under an argon atmosphere. [b)] NMR yields were determined by ^{1}H NMR analysis using 2-methoxynaphthalene as an internal standard. [c)] Enantiomer ratio was determined by HPLC analysis using CHIRALCEL OJ-H. [d)] The same result as shown in entry 13 in Table 2. [e)] Reaction was performed on a 0.2 mmol scale. [f)] 1.3 equiv of isobutyric anhydride and triethylamine were used. [g)] 1.5 equiv of isobutyric anhydride and triethylamine were used.

Next, the desymmetrization reactions of various *meso*-1,2-diols including acyclic and cyclic variants were examined under the optimal conditions (Figure 2). The reactions with *meso*-hydrobenzoin derivatives **2a**–**d** gave the products in good yields with excellent enantioselectivities (64–79% isolated yields of **3a**–**d** with 95:5 to 97:3 er), and the chemoselectivities of these monoacylates were synthetically useful (**3**/**4** = 5.3–14.6). Acyclic diols with alkyl-, allyl-, and hetero atom-functionalized alkyl substituents **2e**–**j** could be subjected to this catalytic system to afford monoacylates **3e**–**j** in moderate to good yields with high enantioselectivities (46–85% isolated yields of **3e**–**j** with 86:14 to 97:3 er). Among them, substrates **2i** and **2j** with electron-withdrawing groups gave significant amounts of diacylates **4i** and **4j** : the reason for this formation of undesirable diacylates is not yet clear. Next, we tested

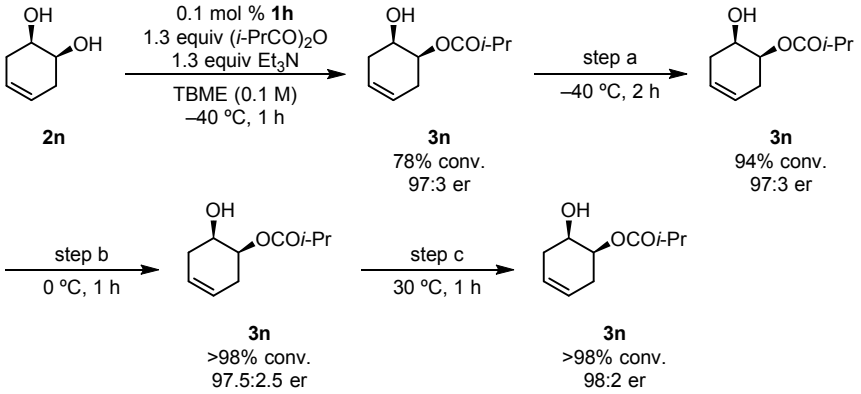
cyclic substrates **2k**–**2p**. The enantioselective desymmetrization only proceeded with six-membered-ring 1,2-diols **2m** and **2n** (79% isolated yield of **3m** with 97:3 er, and 86% isolated yield of **3n** with 94:6 er), and the reactions of other cyclic substrates **2k**, **2l**, **2o**, and **2p** under the optimal conditions only afforded racemate of monoacylates, albeit with high chemoselectivity (**3**/**4** = 7.3–14.7). A possible explanation for this result may be intramolecular acyl migration (racemization) during the reaction (3 h).

Figure 2. Desymmetrization of various *meso*-1,2-diols promoted by catalyst **1h**



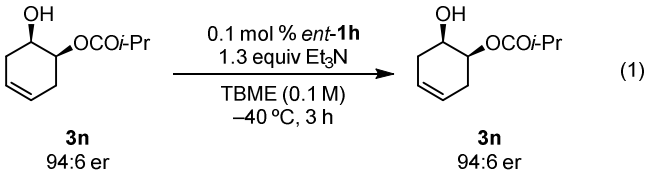
To validate this assumption, the reaction of **2p** in the initial stage (3 or 30 min) under otherwise identical conditions was examined. The reaction also gave **3p** with a 50:50 er.[17] This suggests that enantioselective acylation might not occur with catalyst **1h** even in the initial stage of the

reaction. As shown in Scheme 2, we also check the racemization during the course of the reaction of **2n**. No racemization of enantio-enriched six-membered monoacylate **3n** was observed even with a different reaction time (step a) and higher reaction temperatures [0 °C (step b) and 30 °C (step c)].



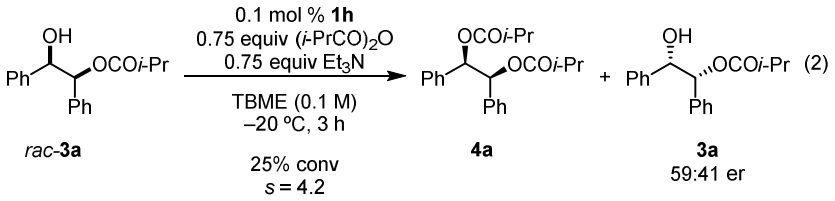
Scheme 2. Racemization studies of the acylative desymmetrization of *meso*-1,2-diol **2n**.

Subsequently, the enantio-enriched six-membered monoacylate **3n** (94:6 er) was subjected to the reaction conditions in the presence of enantiomer of **1h** (*ent*-**1h**) as depicted in eq. 1. Such control experiments strongly suggested that intramolecular acyl transfer (racemization) of **3n** under this catalytic system is rather difficult, although further investigation is required to clarify the reason for the lack of enantioselectivity with cyclic substrates except **2m** and **2n**.



(1)

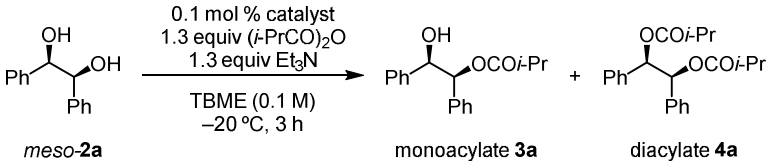
Furthermore, to evaluate the possibility of kinetic resolution in the second acylation step (see also Scheme 1), *rac*-**3a** was subjected to the optimal conditions to afford **4a** in 25% conversion with $s = 4.2$ along with recovered **3a** (eq. 2).

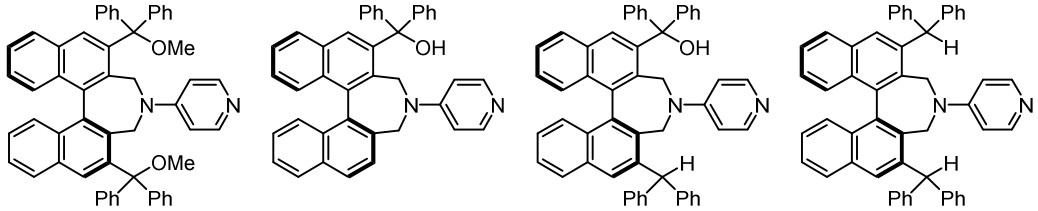


An analysis of the enantiomeric ratio of **3a** in this control experiment pointed out that the second acylation step consumes the major enantiomer of monoacylate **3a** in the enantioselective desymmetrization of *meso*-**2a** with catalyst **1h** (e.g., Path A, Scheme 1). This indicates that the enantiomeric ratio of monoacylate decreases when a significant amount of diacylate **4a** is generated (e.g., **3i** and **3j** in Figure 2).

To gain further insight into the role of the tertiary hydroxy units on the catalyst **1h**, we conducted additional experiments (Table 4). The desymmetrization of *meso*-**2a** was carried out using bis-methyl ether catalyst **1h′**, C_1-symmetric catalyst **1h″**, pseudo C_2-symmetric catalyst **1h‴** (lack of one hydroxy group), and C_2-symmetric catalyst **1h⁗** (lack of two hydroxy group) under the optimal conditions (entries 2–5). The catalysts **1h′** and **1h″** were significantly less effective than catalyst **1h** with respect to both conversion and enantioselectivity (38% NMR yield of **3a** with 58:42 er, and 35% NMR yield of **3a** with 52:48 er, respectively, entries 2 and 3 vs entry 1). On the other hand, the catalyst **1h″**nearly maintained enantiomeric ratio of **3a** (95:5 er), but catalyst **1h⁗** was less efficient in both the conversion and enantiomeric ratio of **3a** (10% NMR yield of **3a**;69:31 er; entry 5 vs entry 1). These results clearly indicated that C_2-symmetric catalyst **1h** with the two *tert*-alcohol units are essential to achieve high catalytic activity and high enantioselectivity.

Table 4. Effects of the *tert*-alcohol unit(s) of the catalyst in the desymmetrization of *meso*-**2a**[a)]





1h′ **1h″** **1h‴** **1h⁗**

Entry	Catalyst	**3a** [%][b)]	**4a** [%][b)]	**2a** [%][b)]	**3a**/**4a**	ER of **3a**[c)]
1[d]	**1h**	79	7	12	11	97:3
2	**1h′**	38	6	52	6.3	58:42
3	**1h″**	35	16	48	2.2	52:48
4	**1h‴**	56	3	41	17	95:5
5	**1h⁗**	10	1	89	10	69:31

[a)] Reactions were performed on a 0.1 mmol scale in TBME (0.1 M) under an argon atmosphere. [b)] NMR yields were determined by ^{1}H NMR analysis using 2-methoxynaphthalene as an internal standard. [c)] Enantiomer ratio was determined by HPLC analysis using CHIRALCEL OJ-H. [d)] The same result as shown in Figure 2.

Conclusion

We have developed an acylative desymmetrization of *meso*-1,2-diols using a binaphthyl-based DMAP derivative **1h** with *tert*-alcohol units. The reaction proceeds with a wide range of acyclic *meso*-1,2-diols, *meso*-cyclohexane 1,2-diol, and *meso*-cyclohexene 1,2-diol. Notably, as little as 0.1 mol % of the catalyst facilitates the reaction within a short reaction time (3 h) to afford enantio-enriched monoacylated products in moderate to good yields (up to 85% yield) with high enantioselectivities (up to 97:3 er). To the best of our knowledge, this is the first example of an organocatalytic acylative desymmetrization reaction with extremely low catalyst loading and suppression of the diacylate to a lower level than in previous organocatalytic approaches.[13] Control experiments revealed that the *tert*-alcohol units of catalyst **1h** play a significant role in achieving high catalytic activity, chemoselectivity of monoacylation, and enantioselectivity. To clarify the detailed reaction mechanism and the role of the *tert*-alcohol units, computational studies are now underway.

Experimental Section

General

Nuclear Magnetic Resonance (NMR) spectra were recorded on JEOL ECS-400 (^{1}H 400 MHz, ^{13}C 100 MHz) spectrometers. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm) relative to residual $CHCl_3$ in $CDCl_3$ (δ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin =quintet, sext = sextet, sep = septet, b = broad, m = multiplet), coupling constants, and integration. Chemical shifts for ^{13}C NMR are reported in parts per million (ppm) relative to $CDCl_3$ (δ 77.16 ppm) with complete proton decoupling. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 spectrophotometer, with Vmax in cm^{-1}. High-resolution mass spectrometry was performed on a JEOL JMS-700 MStation (FAB-MS) or an Agilent 6520 Accurate Mass QTOF LC/MS (ESI-MS). Optical rotations were measured on a JASCO DIP-1000. Melting points were

recorded on a SANSYO SMP-300. Enantiomeric ratios were determined by analytical liquid chromatography (HPLC), with a Shimadzu chromatograph (DAICEL CHIRALPAK® IA-3 (4.6 × 150 mm), DAICEL CHIRALPAK® AS-3 (4.6 × 150 mm), and DICEL CHIRALCEL OJ-H (4.6 × 250 mm), in comparison with authentic racemic samples. Chiral GC analysis was performed on a gas chromatograph (SHIMADZU GC-14B) equipped with a flame ionization detector using a fused silica capillary. Column chromatography was performed with silica gel 60 N (spherical, neutral, 40–50 μm) purchased from KANTO CHEMICAL CO., INC. All experiments were carried out under an argon atmosphere unless otherwise noted.

Materials

All reagents were obtained from commercial sources and used as received unless otherwise noted. Dry tetrahydrofuran [THF], dry diethyl ether [Et_2O], diethyl ether [Et_2O], *t*-amyl alcohol, triethylamine [Et_3N], *N*-ethyldiisopropylamine [*i*-Pr_2NEt], pyridine, 1-methylimidazole [NMI], *N*,*N*,*N*′,*N*′-tetramethylethylenediamine [TMEDA], tripotassium phosphate [K_3PO_4], cycloheptene, *meso*-erythritol and 2,2-dimethoxypropane were purchased from Wako Pure Chemical Industries, Ltd. Dry diisopropyl ether [*i*-Pr_2O], 1,8-bis(dimethylamino)naphthalene [proton-sponge], sodium hydroxide [NaOH], cyclohexa-1,4-diene, 4,4'-difluorobenzil, 4,4'-dimethylbenzil, *meso*-2,3-butanediol, *cis*-cyclopentanediol, *cis*-cyclohexanediol and *cis*-1,2-cyclooctanediol were purchased from Sigma-ALDRICH Japan. Ethyl acetate [EtOAc], methanol [MeOH], dichloromethane [CH_2Cl_2], toluene, benzene, cesium carbonate [Cs_2CO_3], potassium carbonate [K_2CO_3], hydrochloric acid aqueous solution [HCl], magnesium sulfate [$MgSO_4$], ammonium chloride [NH_4Cl], copper(I) bromide [CuBr], benzyl bromide [BnBr], sodium bicarbonate [$NaHCO_3$], iodine [I_2], potassium iodate [KIO_3], *p*-nitrobenzoyl chloride and molecular sieve 4A [MS4A] were purchased from NAKALAI TESQUE, INC. Hexane, dimethylformamide [DMF], chloroform [$CHCl_3$], and *n*-butyl lithium [*n*-BuLi] were purchased from KANTO CHEMICAL CO., INC. Isobutyric

anhydride [$(i\text{-PrCO})_2O$], isobutyryl chloride [*i*-PrCOCl], cyclopentyl methyl ether [CPME], *t*-butyl methyl ether [*t*-BuOMe], 1,8-diazabicyclo[5,4,0]-7-undecene [DBU], *meso*-1,4-dichloro-2,3-butanediol, *cis*-3,4-tetrahydrofurandiol, 4,4′-dibromobenzil, erythritol anhydride, sodium borohydride [$NaBH_4$], sodium hydride [NaH], methylmagnesium bromide [MeMgBr] and potassium acetate [KOAc] were purchased from Tokyo Chemical Industry Co., Ltd. Acetone was purchased from Japan Alcohol Trading CO., LTD. Hexane, DMF, EtOAc, CPME, *t*-BuOMe, and *t*-amyl alcohol were used after dehydration with MS4A. CH_2Cl_2, $(i\text{-PrCO})_2O$, Et_3N, $i\text{-Pr}_2NEt$, pyridine and TMEDA were distilled over CaH_2. Toluene was distilled over CaH_2 and stored in the presence of MS4A. MS4A was used after drying with a heat gun under reduced pressure. All catalysts were synthesized according to the respective literature[8a,c] except for catalyst **1m, 1h‴,** and **1h⁗**. *meso*-**2b**–**d**,[18] **2j**[19] and **2n**[20] were synthesized according to the literature. *meso*-**2f**, **2g**, **2h** and **2o** were synthesized by a slight modification of the procedures in the literature. *meso*-**2a**, **2e**, **2i**, **2k**, **2l**, **2m**, and **2p** were purchased from commercial suppliers. Racemic samples of monoacylate and diacylate were synthesized by a general acylation method with 5 mol % of DMAP, 1.5 equiv of $(i\text{-PrCO})_2O$, and 1.5 equiv of Et_3N in CH_2Cl_2. Benzoate was synthesized by a general benzoylation method with 1.5 equiv of TMEDA and 1.5 equiv of benzoyl chloride [BzCl] in CH_2Cl_2.[13a] *p*-Nitrobenzoate was synthesized by a general *p*-nitrobenzoylation method with 1.5 equiv of TMEDA and 1.5 equiv of *p*-nitrobenzoyl chloride in CH_2Cl_2.

Syntheses of catalysts 1m, 1h‴, and **1h⁗**

(*S*)-2,6-bis(hydroxydimethylmethyl)-4-(pyridin-4-yl)-4,5-dihydro-3*H*-dinaphtho[2,1-c:1′,2′-e]azepine (1m). To a solution of **1e** (50.5 mg, 97.8 μmol) in THF (1.00 mL) was added methyl lithium (3.0 M in diethoxymethane, 666 μL, 2.0 mmol) at 0 °C. The reaction solution was stirred for 1 h at 0 °C. After stirring for 1 h, water (2 mL) was added to reaction vessel. The resulting solution was extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated *in vacuo*. The Purification of the crude product by flash column chromatography on silica gel (eluent:

$CHCl_3$/MeOH = 5/1, v/v) gave **1m** (22.8 mg, 46.7 μmol, 48% yield) as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$ in 0.03% TMS) δ 8.19–8.08 (m, 2H), 8.00 (s, 2H), 7.90 (d, *J* = 8.2 Hz, 2H), 7.50–7.42 (m, 2H), 7.32–7.13 (m, 10H), 6.73 (d, *J* = 6.0 Hz, 2H), 6.16 (d, *J* = 13.0 Hz, 2H), 3.68 (d, *J* = 13.0 Hz, 2H), 1.84 (s, 6H), 1.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 148.2, 143.4, 138.4, 132.3, 131.4, 130.8, 128.5, 128.5 (2), 127.5, 126.2, 125.6, 109.3, 73.4, 45.1, 32.8, 31.8; IR (KBr) 3333, 2976, 1595, 1508, 1234 cm^{-1}; HRMS (ESI^+) calculated for $C_{33}H_{32}N_2O_2$ $[M+H]^+$ 489.2537, found 489.2540; mp 169.5–170.2 °C; $[\alpha]^{22}_D$ –161.4 (*c* 0.20, $CHCl_3$, *S*-configuration).

(*S*)-(6-benzhydryl-4-(pyridin-4-yl)-4,5-dihydro-3*H*-dinaphtho[2,1-c:1′,2′-e]azepin-2-yl)diphenylmethanol (1h″′). To a solution **1h** (0.173 g, 0.23 mmol), triethylsilane (37.0 μL, 0.23 mmol) in CH_2Cl_2 (2.2 mL) was added trifluoroacetic acid (0.123 mL, 1.61 mmol) for 1 min at 0 °C. The reaction mixture was warm up to room temperature and stirred 2 h. Then, water (10 mL) and $NaHCO_3$aq (10 mL) were added to the reaction mixture and extracted with CH_2Cl_2 (20 mL × 3). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The purification of the crude product by flash column chromatography on silica gel (eluent: EtOAc/MeOH = 15/1, v/v) gave **1h″′** (64.2 mg, 0.09 mmol, 38% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (bs, 2H), 7.67 (t, *J* = 7.3 Hz, 2H), 7.46–7.15 (m, 22H), 7.13–6.95 (m, 8H), 6.72 (d, *J* = 7.3 Hz, 2H), 6.16 (bs, 2H), 5.69 (s, 1H), 5.27 (d, *J* = 12.1 Hz, 1H), 4.80 (d, *J* = 13.5 Hz, 1H), 3.55 (d, *J* = 13.5 Hz, 1H), 3.28 (d, *J* = 12.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 147.7, 146.7, 145.9, 143.5, 143.1, 142.4, 139.2, 138.7, 136.4, 132.7, 132.2, 131.8, 131.0, 130.6, 130.5, 130.3, 129.6, 128.9, 128.8, 128.5, 128.4, 128.3, 127.9, 127.8, 127.6, 127.5, 127.3, 126.9 (2), 126.6, 126.4, 126.2, 126.0, 108.5, 83.1, 54.6, 45.5, 45.2, 29.8; IR (KBr) 3057, 3024, 2360, 1595, 1508, 1242, 993, 750, 698 cm^{-1}; HRMS (FAB^+) calculated for $C_{53}H_{41}N_2O$ $[M+H]^+$ 721.3213, found 721.3221; mp 220 ºC dec.; $[\alpha]^{22}_D$ –324.1 (*c* 1.00, $CHCl_3$, (*S*)-configuration).

(*S*)-2,6-dibenzhydryl-4-(pyridin-4-yl)-4,5-dihydro-3*H*-dinaphtho[2,1-c:1′,2′-e]azepine (1h″′′). To a solution **1h** (0.197 g, 0.27 mmol), triethylsilane (0.41 mL, 2.7 mmol) in CH_2Cl_2

(2.2 mL)was added trifluoroacetic acid (0.145 mL, 1.89 mmol) for 1 min at 0 °C. The reaction mixture was warm up to room temperature and stirred for 2 h. Then, water (10 mL) and $NaHCO_3$ aq (10 mL) were added to the reaction mixture and extracted with CH_2Cl_2 (20 mL × 3). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The purification of the crude product by short pad of silica gel (eluent: EtOAc) gave **1h‴′** (0.196 g, 0.27 mmol, >98% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 4.6 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.48–7.39 (m, 4H), 7.37–7.23 (m, 10H), 7.18–7.02 (m, 10H), 6.83 (d, *J* = 6.9 Hz, 4H), 6.35 (d, *J* = 5.0 Hz, 2H), 5.79 (s, 2H), 4.75 (d, *J* = 13.4 Hz, 2H), 3.40 (d, *J* = 13.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 149.5, 143.4, 142.6, 139.7, 136.7, 132.7, 132.2, 130.3, 129.6, 129.5, 128.8, 128.5, 128.4, 127.6, 126.8, 126.7, 126.2, 126.0, 108.5, 54.7, 44.9; IR (KBr) 3059, 3024, 2360, 1593, 1508, 750, 700 cm^{-1}; HRMS (FAB$^+$) calculated for $C_{53}H_{41}N_2$ $[M+H]^+$ 705.3264, found 705.3259; mp >280 ºC; $[\alpha]^{22}_D$ –370.7 (*c* 1.00, $CHCl_3$, (*S*)-configuration).

Synthesis of *meso*-2f, **2g**, **2h** and **2o**

Synthesis of (4*R*,5*S*)-octa-1,7-diene-4,5-diol (*meso*-2f). To a suspension of CuBr (2.75 g, 19.2 mmol) in THF (5.9 mL) at –40 °C is added vinyl magnesium bromide (1.0 M in THF, 28.8 mL, 28.8 mmol) dropwise. After 0.5 h, a solution of erythritol anhydride (1.05 g, 12.2 mmol) in THF (6.6 mL) is added dropwise. After 4 h, the mixture was allowed to slowly warm to 0 °C and saturated aqueous $NaHCO_3$ (15 mL) was added. The precipitates were filtered off, and the filtrate was separated and the aqueous layer was extracted with EtOAc. The organic extracts were combined, dried $MgSO_4$, concentrated under reduced pressure and purified by Gel Permeation Chromatography (elution: toluene) to give the a colorless solid **2f** (123 mg, 0.865 mmol, 7% yield). The spectroscopic data of **2f** was in good agreement with previously reported data.[21] Colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90–5.76 (m, 2H), 5.21–5.05 (m, 4H), 3.65 (dd, *J* = 7.3, 3.2 Hz, 2H), 2.53–2.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 118.3, 72.9, 36.4; IR (KBr) 3310, 3076, 2899, 1645, 989 cm^{-1}

Synthesis of (2*R*,3*S*)-1,4-bis(benzyloxy)butane-2,3-diol (*meso*-2g). This compound was prepared through four-step telescoped reactions as follows:

(1) ((4*R*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene) bis(2,2-dimethylpropanoate). 2h (8.69 g, 29.9 mmol), 2,2-dimethoxypropane (20 mL, 162.7 mmol), and *p*-toluenesulfonic acid (576 mg, 3.03 mmol) were stirred in anhydrous toluene (300 mL) under argon. After stirring for 30 min at 50 °C, the reaction mixture was further stirred at 40 °C for 6 h. A saturated aqueous solution of $NaHCO_3$ was added and the mixture was stirred for 30 min. The aqueous layer was extracted with ethyl acetate. The organic layers were combined and washed with brine. After drying over $MgSO_4$, solvent was concentrated *in vacuo* and the residue was passed through a short pad of silica gel (eluent: Et_2O) to give yellow oil **5** (9.70 g, 29.4 mmol, 98% yield). This crude product was used for next reaction without further purification and characterization.

(2) ((4*R*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)dimethanol. The crude product from previous reaction (9.20 g, 27.9 mmol) was stirred in methanol (70 mL) at room temperature. KOH aq (6 M, 70 mL, 420 mmol) was added, then the reaction mixture was stirred for 4 h at 60 °C. After methanol was removed *in vacuo*, the aqueous layer was extracted with THF. The organic layers were combined and washed with brine. After drying over $MgSO_4$, solvent was concentrated *in vacuo* and the residue was passed through a pad of silica gel (eluent: EtOAc) to give yellow oil (2.64 g, 16.26 mmol, 58% yield). The spectroscopic data was in good agreement with previously reported data.[22] This crude product was used for next reaction without further purification.

(3) (4*R*,5*S*)-4,5-bis((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolane. To a suspension of NaH (60% dispersion in paraffin liquid, 487 mg, 12.2 mmol) in THF (60 mL) was added dropwise the crude product from previous reaction (629.7 mg, 0.22 M in THF, 18.2 mL, 3.88 mmol) at room temperature. The resulting mixture was stirred for 10 min, and then BnBr (1.05 mL, 8.8 mmol) was added to reaction vessel at room temperature. The reaction mixture was stirred for

24 h, and then saturated aqueous NH_4Cl was added to reaction vessel. The resulting solution was extracted with EtOAc, dried over $MgSO_4$, and concentrated *in vacuo* to give the crude product (939 mg, 2.74 mmol, 71% yield). The crude product was directly used next reaction without further purification and characterization.

(4) To a solution of the crude product from previous reaction (825.1 mg, 2.49 mmol) in MeOH (25 mL) was added aqueous HCl (6.0 M, 5 mL, 30 mmol) at 0 °C. The reaction mixture was heated up to room temperature and stirred for 24 h. After stirring for 24 h, saturated aqueous $NaHCO_3$ was added to reaction vessel. The resulting solution was concentrated *in vacuo*. The residue was dissolved EtOAc and water. The resulting solution was extracted with EtOAc, dried over $MgSO_4$, and concentrated *in vacuo* to give the crude product. The purification of the crude product by recrystallization from Et_2O-hexane gave colorless solid **2g** (438.2 mg, 1.45 mmol, 58% yield, first crop). The spectroscopic data of **2g** was in good agreement with previously reported data.[18] Colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.27 (m, 10H), 4.55 (s, 4H), 3.90–3.79 (m, 2H), 3.71–3.60 (m, 4H), 2.67 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 128.6, 128.0 (2), 73.7, 71.5, 71.2; IR (KBr) 3462, 3277, 2903, 1456, 1213, 752 cm^{-1}

Synthesis of (2*R*,3*S*)-2,3-dihydroxybutane-1,4-diyl-bis(2,2-dimethylpropanoate) (*meso*-2h)

Meso-erythritol (10.0 g, 81.9 mmol) was stirred in pyridine (400 mL) at room temperature. The solution was cooled to 0 °C and then pivaloyl chloride (20.2 mL, 164 mmol) was added. The reaction mixture was stirred for 2 h at room temperature. Then the resulting mixture was concentrated *in vacuo*. The purification of the crude product by recrystallization from Et_2O-hexane gave colorless solid **2h** (11.5 g, 39.7 mmol, 48% yield). Colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40–4.29 (m, 4H), 3.79–3.73 (m, 2H), 1.23 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6, 70.7, 65.6, 39.1, 27.3; IR (KBr) 3499, 2986, 2972, 1705, 1180 cm^{-1}; HRMS (FAB$^+$) $[M+H]^+$ calculated for $C_{14}H_{27}O_6$ 291.1802, found 291.1774; mp 82.7–83.0 °C

(1*R*,2*S*)-cycloheptane-1,2-diol (*meso*-2o). This compound was prepared through two-step reactions as follows:

(1) *cis*-2-hydroxycycloheptyl acetate. Cycloheptene (4.23 g, 43.9 mmol) was added to a stirred solution of KIO_3 (2.36 g, 11.0 mmol) and I_2 (5.59 g, 22.0 mmol) in AcOH (73.3 mL) at room temperature under argon. The resulting mixture was stirred at 60 °C for 4 h. After cooling, KOAc (4.33 g, 44.1 mmol) was added and the mixture was heated at reflux for 4 h. After cooling, water (2 mL) was added and the solvent was evaporated under reduced pressure over a period of 1 h. Et_2O (100 mL) was added and the organic layer was washed with saturated aqueous Na_2SO_3 until the brown color was removed, dried $MgSO_4$ and evaporated under reduced pressure to give a crude mixture of mono and diacetate. Then, the purification of the crude product by flash column chromatography on a silica gel (eluent: hexane/Et_2O = 5/1 to 3/1 to 1/1 to Et_2O, v/v) gave the monoacetate (3.54 g, 20.6 mmol, 47% yield). The spectroscopic data of monoacetate was in good agreement with previously reported data.[23]

(2) K_2CO_3 (6.09 g, 44.1 mmol) was added to a stirred solution of monoacetate (3.44 g, 20.0 mmol) from previous reaction in 10% aqueous methanol (78.5 mL) at room temperature. After stirring vigorously for 2 h, methanol was removed under reduced pressure. Then, a minimum of saturated aqueous NH_4Cl, followed by solid brine were added to the mixture and the water layer was extracted six times with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The purification of the crude product by recrystallization from Et_2O-hexane gave colorless solid **2o** (591 mg, 4.54 mmol, 23% yield). The spectroscopic data of **2o** was in good agreement with previously reported data.[24] Colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89–3.79 (m, 2H), 2.62 (brs, 2H), 1.87–1.26 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.8, 30.8, 27.8, 22.1; IR (KBr) 3354, 2928, 1458, 1074, 930 cm^{-1}.

General procedure for the desymmetrization of *meso*-1,2-diol with catalyst 1h

When 0.1 mol % of the catalyst was used in the reaction, a solution of the catalyst in chloroform (10.0 mM) was prepared in advance. This stock solution was added to a test tube, and the solvent was removed. The resulting catalyst was used for the following reaction.

Catalyst **1h**, *meso*-diol **2a**–**p**, and Et_3N were stirred in *t*-BuOMe (TBME) at room temperature. The mixture was cooled to −20 °C, and then isobutyric anhydride was added. The reaction mixture was stirred for 3 h. Methanol was added to quench the reaction and the mixture was stirred for 1 h at room temperature. After the mixture was concentrated *in vacuo*, the catalyst was separated from the crude product by flash column chromatography on a short pad of silica gel (eluent: Et_2O). Purification of the crude product by flash column chromatography on ~~a~~ silica gel (eluent: hexane/Et_2O = 5/1 to 3/1 to1/1 to Et_2O, v/v) gave the monoacylate **3a–p**, diacylate **4a–p**, and recovered substrate **2a–p**. The enantiomeric ratios of **3a–d** and **3f–p** were determined by chiral HPLC analysis, and that of **3e** was determined by chiral GC analysis. The analytical data for **3a**, **4a** and **2a** have been reported previously.[8a]

Analytical data for products 3b–p and 4b–p

(1*S*,2*R*)-2-hydroxy-1,2-di-*p*-tolylethyl isobutyrate (3b). According to the general procedure, substrate **2b** (72.3 mg, 0.298 mmol) with catalyst **1h** (0.3 μmol), Et_3N (54.2 μL, 0.390 mmol), and isobutyric anhydride (64.6 μL, 0.390 mmol) in TBME (3 mL) at −20 °C gave monoacylate **3b** (68.3 mg, 0.219 mmol, 73% yield, 97:3 er), diacylate **4b** (6.0 mg, 0.0157 mmol, 5% yield), and recovered **2b** (11.4 mg, 0.0470 mmol, 16% yield). Colorless solid. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 95/5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 254 nm), T_R = 10.5 min (minor) and T_R = 12.7 min (major), 97:3 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.08 (m, 8H), 5.84 (d, *J* = 6.7 Hz 1H), 4.90 (d, *J* = 6.7 Hz, 1H), 2.45 (sep, *J* = 7.0 Hz, 1H), 2.34 (s, 3H), 2.34 (s, 3H), 2.07 (s, 1H), 1.04 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 137.9, 137.5, 137.0, 134.2, 128.9, 128.7, 127.5, 127.0, 78.3, 76.3, 34.0, 21.2, 21.1, 18.7; IR (KBr) 3536, 2974, 2866, 1717, 1452, 1389, 1152, 970, 748, 706 cm^{-1}; HRMS (FAB$^+$) $[M+Na]^+$ calculated for $C_{20}H_{24}O_3Na$ 335.1617, found 335.1625; mp 83.6–84.2 °C; $[\alpha]^{24}_D$ +14.9 (*c* 1.00, $CHCl_3$, 97:3 er)

(1*R*,2*S*)-1,2-di-*p*-tolylethane-1,2-diyl bis(2-methylpropanoate) (4b). Colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.05 (m, 8H), 6.02 (s, 2H), 2.47 (sep, *J* = 7.2 Hz, 2H), 2.32 (s, 6H), 1.57 (s, 1H), 1.05 (d, *J* = 7.2 Hz, 6H), 1.03 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 138.0, 133.7, 128.8, 127.7, 76.2, 34.2, 21.3, 18.9, 18.8; IR (KBr) 2974, 1736, 1516, 1354, 1182, 762 cm^{-1}; HRMS (FAB$^+$) $[M+Na]^+$ calculated for $C_{24}H_{30}O_4Na$ 405.2036, found 405.2029; mp 108.8–109.9 °C

(1*S*,2*R*)-1,2-bis(4-bromophenyl)-2-hydroxyethyl isobutyrate (3c). According to the general procedure, substrate **2c** (111.7 mg, 0.300 mmol) with catalyst **1h** (0.3 μmol), Et_3N (54.2 μL, 0.390 mmol), and isobutyric anhydride (64.6 μL, 0.390 mmol) in TBME (3 mL) at −40 °C gave monoacylate **3c** (85.4 mg, 0.193 mmol, 64% yield, 95:5 er), diacylate **4c** (19.0 mg, 0.0371 mmol, 12% yield), and recovered **2c** (25.2 mg, 0.0677 mmol, 23% yield). Colorless solid. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 254 nm), T_R = 44.9 min (minor) and T_R = 53.5 min (major), 95:5 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.41 (m, 4H), 7.12–7.06 (m, 4H), 5.80 (d, *J* = 5.6 Hz, 1H), 4.93 (q, *J* = 5.6, 3.1 Hz, 1H), 2.52 (sept, *J* = 6.9 Hz, 1H), 2.15 (d, *J* = 3.1 Hz, 1H), 1.09 (d, *J* = 6.9 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 138.4, 135.6, 131.6, 131.4, 129.3, 128.8, 122.7, 122.3, 77.8, 75.9, 34.1, 18.9; IR (KBr) 3524, 3503, 2976, 1728, 1489, 745 cm^{-1}; HRMS (FAB$^+$) calculated for $C_{18}H_{18}{}^{79}Br^{81}BrO_3Na$ $[M+Na]^+$ 464.9494, found 464.9470; mp 110.0–111.1 °C; $[\alpha]^{22}_D$ +7.2 (*c* 1.0, $CHCl_3$, 94:6 er).

(1*R*,2*S*)-1,2-bis(4-bromophenyl)ethane-1,2-diyl bis(2-methylpropanoate) (4c). Colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.39 (m, 4H), 7.10-7.03 (m, 4H), 5.98 (s, 2H), 2.51 (sep, *J* = 7.0 Hz, 2H), 1.08 (d, *J* = 7.0 Hz, 6H), 1.07 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 135.2, 131.5, 129.3, 122.7, 75.5, 34.1, 18.9, 18.8; IR (KBr) 2974, 1728, 1558, 1489, 1153, 808 cm^{-1}; HRMS (FAB$^+$) calculated for $C_{22}H_{24}{}^{79}Br^{81}BrO_4Na$ $[M+Na]^+$ 534.9913, found 534.9938; mp 151.4–152.5 °C

(1*S*,2*R*)-1,2-bis(4-bromophenyl)-2-hydroxyethyl isobutyrate (3d). According to the general procedure, substrate **2d** (75.0 mg, 0.300 mmol) with a catalyst **1h** (0.3 μmol), Et_3N (54.2 μL, 0.390 mmol), and isobutyric anhydride (64.6 μL, 0.390 mmol) in TBME (3 mL) at −20 °C gave monoacylate **3d** (74.9 mg, 0.234 mmol, 78% yield, 95:5 er), diacylate **4d** (13.5 mg, 0.0346 mmol, 12% yield), and recovered **2d** (7.4 mg, 0.0296 mmol, 10% yield). Colorless solid. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 254 nm), T_R = 29.4 min (minor) and T_R = 31.4 min (major), 95:5 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.15 (m, 4H), 7.05–6.91 (m, 4H), 5.82 (d, *J* = 6.2 Hz, 1H), 4.91 (dd, *J* = 6.2, 2.7 Hz, 1H), 2.49 (sept, *J* = 7.0 Hz, 1H), 2.31 (bs, 1H), 1.06 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 162.8 (d, *J* = 247.3 Hz), 162.6 (d, *J* = 246.3 Hz), 135.3 (d, *J* = 2.8 Hz), 132.6 (d, *J* = 2.9 Hz), 129.4 (d, *J* = 7.7 Hz), 128.8 (d, *J* = 8.6 Hz), 115.4 (d, *J* = 22.0 Hz), 115.2 (d, *J* = 22.0 Hz) 77.8, 75.9, 34.1, 18.8; IR (KBr) 3516, 2974, 1717, 1609, 1512, 1236, 797 cm^{-1}; HRMS (FAB$^+$) calculated for $C_{18}H_{18}F_2O_3Na$ $[M+Na]^+$ 343.1116, found 343.1131; mp 104.1–104.6 °C; $[\alpha]^{22}_D$ +7.1 (*c* 1.00, $CHCl_3$, 95:5 er).

(1*R*,2*S*)-1,2-bis(4-fluorophenyl)ethane-1,2-diyl bis(2-methylpropanoate) (4d). Colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.14 (m, 4H), 6.99 (t, *J* = 8.5 Hz, 4H), 6.02 (s, 2H), 2.49 (sep, *J* = 6.9 Hz, 2H), 1.10–0.97 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 175.5, 162.8 (d, *J* = 247.3 Hz), 132.3 (d, *J* = 2.9 Hz), 129.4 (d, *J* = 8.6 Hz), 115.3 (d, *J* = 22.0 Hz), 75.5, 34.2, 18.9, 18.8; IR (KBr) 2976, 1728, 1605, 1514, 123.1, 773 cm^{-1}; HRMS (FAB$^+$) calculated for $C_{22}H_{24}F_2O_4Na$ $[M+Na]^+$ 413.1514, found 413.1518; mp 118.7–119.5 °C.

(2*S*,3*R*)-3-hydroxybutan-2-yl isobutyrate (3e).[25] According to the general procedure, substrate **2e** (56.6 mg, 0.628 mmol) with a catalyst **1h** (0.6 μmol), Et_3N (108 μL, 0.780 mmol), and isobutyric anhydride (129 μL, 0.778 mmol) in TBME (6 mL) at −40 °C gave monoacylate **3e** (85.5 mg, 0.534 mmol, 85% yield, 97:3 er), diacylate **4e** (10.5 mg, 0.0456 mmol, 7% yield), and recovered **2e** (3.8 mg, 0.0422 mmol, 7% yield). Pale yellow oil. Enantiomeric ratio was

determined by chiral GC with CP-Cyclodextrin-B-2,3,6-M-19 (65 °C hold), T_R = 46.7 min (major) and T_R = 51.4 min (minor), 97:3 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.85 (dq, *J* = 6.4, 3.2 Hz, 1H), 3.87 (dq, *J* = 6.4, 3.2 Hz, 1H), 2.55 (sep, *J* = 6.9 Hz, 1H), 1.92 (s, 1H), 1.23–1.11 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 74.2, 69.8, 34.2, 19.1 (2), 18.0, 14.4; IR (neat) 3447, 2978, 1734, 1716, 1206, 1082 cm^{-1}; $[\alpha]^{21}_D$ -0.49 (*c* 1.00, $CHCl_3$, 97:3 er).

(2*R*,3*S*)-butane-2,3-diyl bis(2-methylpropanoate) (4e).[13h] Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 0.03% TMS) δ 5.03–4.95 (m, 2H), 2.53 (sep, *J* = 6.9, 1H), 1.21 (d, *J* = 6.4 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 6H), 1.15 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 71.0, 34.2, 19.0, 18.4, 15.1; IR (neat) 2965, 2924, 1738, 1096, 1016, 800 cm^{-1}

(4*S*,5*R*)-5-hydroxyocta-1,7-dien-4-yl isobutyrate (3f). According to the general procedure, substrate **2f** (40.7 mg, 0.286 mmol) with a catalyst **1h** (0.286 μmol), Et_3N (51.6 μL, 0.371 mmol), and isobutyric anhydride (61.6 μL, 0.372 mmol) in TBME (2.86 mL) at −20 °C gave monoacylate **3f** (49.0 mg, 0.231 mmol, 81% yield, 91:9 er), diacylate **4f** (3.1 mg, 0.0110 mmol, 4% yield), and recovered **2f** (6.2 mg, 0.0436 mmol, 15% yield). Colorless oil. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 205 nm), T_R = 8.4 min (major) and T_R = 9.0 min (minor), 91:9 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87–5.66 (m, 2H), 5.15 (d, *J* = 3.7 Hz, 1H), 5.13–5.08 (m, 3H), 4.89 (dt, *J* = 8.5, 4.6 Hz, 1H), 3.74 (dt, *J* = 8.5, 4.6 Hz, 1H), 2.54 (sep, *J* = 6.9 Hz, 1H), 2.48–2.24 (m, 3H), 2.23–2.05 (m, 1H), 1.15 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 134.2, 133.8, 118.6, 117.9, 75.1, 71.6, 37.3, 34.5, 34.3, 19.2, 19.0; IR (neat) 3464, 3078, 2976, 1732, 1472, 914 cm^{-1}; HRMS (FAB$^+$) calculated for $C_{12}H_{21}O_3$ $[M+H]^+$ 213.1485, found 213.1476; $[\alpha]^{23}_D$ +17.5 (*c* 1.00, $CHCl_3$, 91:9 er).

(4*R*,5*S*)-octa-1,7-diene-4,5-diyl bis(2-methylpropanoate) (4f). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79–5.65 (m, 2H), 5.14–5.01 (m, 6H), 2.53 (sep, *J* = 7.0 Hz, 2H), 2.44–2.25 (m, 4H), 1.16 (d, *J* = 7.0 Hz, 6H), 1.15 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 0.03%

TMS) δ 176.3, 133.3, 118.2, 72.4, 34.6, 34.3, 19.1 (2); IR (neat) 2976, 1732, 1470, 1258, 918 cm^{-1}; HRMS (FAB^+) calculated for $C_{16}H_{26}O_4Na$ $[M+Na]^+$ 305.1723, found 305.1710.

(2*S*,3*R*)-1,4-bis(benzyloxy)-3-hydroxybutan-2-yl isobutyrate (3g). According to the general procedure, substrate **2g** (90.8 mg, 0.300 mmol) with a catalyst **1h** (0.300 μmol), Et_3N (54.2 μL, 0.390 mmol), and isobutyric anhydride (64.6 μL, 0.390 mmol) in TBME (3 mL) at −20 °C gave monoacylate **3g** (70.7 mg, 0.190 mmol, 63% yield, 94.5:5.5 er), diacylate **4g** (25.2 mg, 0.0569 mmol, 19% yield), and recovered **2g** (14.8 mg, 0.0489 mmol, 16% yield). Colorless oil. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 254 nm), T_R = 31.6 min (minor) and T_R = 34.3 min (major), 94.5:4.5 er; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.23 (m, 10H), 5.07 (ddd, *J* = 6.6, 4.6, 3.7 Hz, 1H), 4.54 (d, *J* = 2.7 Hz, 2H), 4.53 (d, *J* = 3.7 Hz, 2H), 4.12–4.01 (m, 1H), 3.77 (dd, *J* =11.0, 4.8 Hz, 1H), 3.71 (dd, *J* = 10.5, 3.4 Hz, 1H), 3.56 (dd, *J* = 9.6, 3.7 Hz, 1H), 3.49 (dd, *J* = 10.1, 6.2 Hz, 1H) 2.74 (bd, *J* = 5.5 Hz, 1H), 2.55 (sep, *J* = 7.0 Hz, 1H), 1.14 (d, *J* = 4.1 Hz, 3H), 1.12 (d, *J* = 3.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 137.9, 137.8, 128.5, 128.4, 127.9, 127.8, 127.7, 73.5, 73.4, 72.1, 70.7, 69.8, 68.9, 34.0, 19.0, 18.9; IR (KBr) 3468, 3446, 2974, 1732, 1454, 1194, 739 cm^{-1}; HRMS (FAB^+) calculated for $C_{22}H_{28}O_5Na$ $[M+Na]^+$ 395.1828, found 395.1838; $[\alpha]^{23}_D$ +18.1 (*c* 1.0, $CHCl_3$, 94.5:5.5 er)

(2*R*,3*S*)-1,4-bis(benzyloxy)butane-2,3-diyl bis(2-methylpropanoate) (4g). Colorless solid. δ 7.35–7.24 (m, 13H), 5.38–5.32 (m, 2H), 4.50 (d, *J* = 11.9 Hz, 2H), 4.45 (d, *J* = 11.9 Hz, 2H), 3.64 (dd, *J* = 10.7, 3.4 Hz 2H), 3.57 (dd, *J* = 10.7, 5.7 Hz, 2H), 2.50 (sep, *J* = 7.1 Hz, 1H), 1.11 (d, *J* = 7.1 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 138.0, 128.5, 127.8, 127.7, 73.2, 70.6, 68.2, 34.1, 19.1, 18.9; IR (KBr) 2972, 1730, 1356, 1188, 746 cm^{-1}; HRMS (FAB^+) calculated for $C_{26}H_{34}O_6Na$ $[M+Na]^+$ 465.2247, found 465.2228; mp 57.4–58.2 °C

(2*R*,3*S*)-2-hydroxy-3-(isobutyryloxy)butane-1,4-diyl bis(2,2-dimethylpropanoate) (3h). According to the general procedure, substrate **2h** (87.2 mg, 0.300 mmol) with a catalyst **1h** (0.3 μmol), Et_3N (54.2 μL, 0.390 mmol), and isobutyric anhydride (64.6 μL, 0.390 mmol) in TBME

(3 mL) at −40 °C gave monoacylate **3h** (55.1 mg, 0.153 mmol, 51% yield, 91:9 er), diacylate **4h** (21.8 mg, 0.0506 mmol, 17% yield), and recovered **2h** (27.8 mg, 0.0957 mmol, 32% yield). Colorless oil. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 205 nm), T_R = 17.6 min (major) and T_R = 18.9 min (minor), 91:9 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (ddd, *J* = 4.6, 5.1, 3.2 Hz, 1H), 4.44 (dd, *J* = 12.3, 2.7 Hz, 1H), 4.32 (dd, *J* = 12.3, 5.0 Hz, 1H), 4.24 (dd, *J* = 11.9, 2.7 Hz, 1H), 4.16 (dd, *J* = 11.9, 5.6 Hz, 1H), 4.02–3.91 (m, 1H), 2.80 (bs, 1H), 2.56 (sep, *J* = 7.0 Hz, 1H), 1.20 (s, 9 H), 1.18 (s, 9H), 1.17 (d, *J* = 7.0 Hz, 3H), 1.17 (d, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.0, 178.6, 175.9, 70.9, 68.7, 65.1, 62.4, 39.0 (2), 34.1, 27.2, 19.0, 18.9; IR (KBr) 3501, 2978, 1732, 1157, 767 cm^{-1}; HRMS (FAB^+) calculated for $C_{18}H_{32}O_7Na$ $[M+Na]^+$ 383.2045, found 383.2048; $[\alpha]^{24}_D$ +15.0 (*c* 1.030, $CHCl_3$, 91:9 er)

(2*R*,3*S*)-2,3-bis(isobutyryloxy)butane-1,4-diyl bis(2,2-dimethylpropanoate) (4h). Pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.22–5.16 (m, 2H), 4.36 (dd, *J* = 12.1, 2.5 Hz, 2H), 4.13 (dd, *J* = 12.1, 5.7 Hz, 2H), 2.55 (sep, *J* = 6.9 Hz, 2H), 1.23–1.13 (m, 30H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 175.7, 69.0, 61.9, 39.0, 34.1, 27.2, 19.0, 18.9; IR (KBr) 2978, 2941, 1734, 1140, 768 cm^{-1}; HRMS (FAB^+) calculated for $C_{22}H_{38}O_8Na$ $[M+Na]^+$ 453.2458, found 453.2455; mp 47.1–47.9 °C

(2*R*,3*S*)-1,4-dichloro-3-hydroxybutan-2-yl isobutyrate (3i). According to the general procedure, substrate **2i** (79.2 mg, 0.498 mmol) with a catalyst **1h** (0.5 μmol), Et_3N (90.2 μL, 0.649 mmol), and isobutyric anhydride (108 μL, 0.651 mmol) in TBME (5 mL) at −20 °C gave monoacylate **3i** (52.2 mg, 0.228 mmol, 46% yield, 86:14 er), diacylate **4i** (53.0 mg, 0.177 mmol, 36% yield), and recovered **2i** (14.2 mg, 0.0893 mmol, 18% yield). Colorless oil. Enantiomeric ratio was determined with 4-nitro benzoate by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 254 nm), T_R = 13.4 min (minor) and T_R = 21.9 min (major), 86:14 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.99 (dt, *J* = 8.4, 3.7 Hz, 1H), 4.16 (ddd, *J* = 8.4, 6.0, 2.7 Hz, 1H), 3.90 (d, *J* = 3.7 Hz, 2H), 3.75 (dd, *J* = 11.6, 2.7

Hz, 1H), 3.63 (dd, *J* = 11.6, 6.0 Hz, 1H), 2.68–2.55 (m, 1H), 2.52–2.32 (bs, 1H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.20 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 70.2, 42.8, 34.1, 19.0, 18.9; IR (neat) 3335, 2974, 1740, 1153, 1070, 708 cm^{-1}; HRMS (ESI^+) calculated for $C_8H_{14}Cl_2O_3Na$ $[M+Na]^+$ 251.0212, found 251.0218; $[\alpha]^{22}_D$ +5.3 (*c* 0.6, $CHCl_3$, 86:14 er)

(2*R*,3*S*)-1,4-dichlorobutane-2,3-diyl bis(2-methylpropanoate) (4i). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35–5.28 (m, 2H), 3.85–3.82 (m, 1H), 3.81–3.77 (m, 1H), 3.67 (d, *J* = 2.9, 1.4 Hz, 1H), 3.64 (d, *J* = 2.9, 1.8 Hz, 1H), 2.61 (sep, *J* = 7.0 Hz, 2H), 1.20 (d, *J* = 7.0 Hz, 6H), 1.20 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 70.2, 42.8, 34.1, 19.0, 18.9; IR (neat) 2976, 2938, 1746, 1470, 1144 cm^{-1}; HRMS (ESI^+) calculated for $C_{12}H_{20}Cl_2O_4Na$ $[M+Na]^+$ 321.0632, found 321.0621

(2*S*,3*R*)-1,4-diazido-3-hydroxybutan-2-yl isobutyrate (3j). According to the general procedure, substrate **2j** (68.4 mg, 0.397 mmol) with a catalyst **1h** (0.4 μmol), Et_3N (72.2 μL, 0.519 mmol), and isobutyric anhydride (86.2 μL, 0.520 mmol) in TBME (4 mL) at −20 °C gave monoacylate **3j** (48.6 mg, 0.201 mmol, 50% yield, 86:14 er), diacylate **4j** (29.4 mg, 0.0941 mmol, 24% yield), and recovered **2j** (17.6 mg, 0.102 mmol, 26% yield). Colorless oil. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 205 nm), T_R = 21.5 min (major) and T_R = 24.3 min (minor), 86:14 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.93 (ddd, *J* = 7.6, 4.5, 3.2 Hz, 1H), 4.04–3.95 (m, 1H), 3.62 (dd, *J* = 13.4, 3.2 Hz, 1H), 3.58 (*J* = 13.4, 4.5 Hz, 1H), 3.48 (dd, *J* = 12.6, 3.2 Hz, 1H), 3.37 (dd, *J* = 12.6, 6.4 Hz, 1H), 2.62 (sep, *J* = 6.9 Hz, 1H), 2.45 (d, *J* = 6.0 Hz, 1H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.21 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 72.5, 69.4, 53.7, 50.8, 34.1, 18.9, 18.8; IR (neat) 3564, 2976, 2104, 1732, 1472 cm^{-1}; HRMS (ESI^+) calculated for $C_8H_{14}N_6O_3Na$ $[M+Na]^+$ 265.102, found 265.1011; $[\alpha]^{22}_D$ +8.6 (*c* 1.0, $CHCl_3$, 86:14 er).

(2*R*,3*S*)-1,4-diazidobutane-2,3-diyl bis(2-methylpropanoate) (4j). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23–5.17 (m, 2H), 3.57 (dd, *J* = 13.4, 3.2 Hz, 2H), 3.41 (dd, *J* = 13.4, 5.5

Hz, 2H), 2.16 (sep, J = 7.2 Hz, 2H), 1.20 (d, J = 7.2 Hz, 6H), 1.20 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 70.4, 50.5, 34.0, 18.8, 18.7; IR (neat) 2978, 2104, 1748, 1748, 1472, 1389 cm^{-1}; HRMS (FAB$^+$) calculated for $C_{12}H_{20}N_6O_4Na$ $[M+Na]^+$ 335.1438, found 335.1464.

(1*S*,2*R*)-2-hydroxycyclopentyl isobutyrate (3k).[25] According to the general procedure, substrate **2k** (62.4 mg, 0.611 mmol) with a catalyst **1h** (0.6 μmol), Et_3N (108 μL, 0.780 mmol), and isobutyric anhydride (130 μL, 0.784 mmol) in TBME (6 mL) at −20 °C gave monoacylate **3k** (79.6 mg, 0.462 mmol, 76% yield, 50:50 er) and diacylate **4k** (12.5 mg, 0.0516 mmol, 8% yield). Colorless oil. Enantiomeric ratio was determined with benzoate by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 78.4/1.6, v/v, flow rate = 0.8 mL/min, 30 °C, UV = 254 nm), T_R = 8.8 min and T_R = 11.9 min, 50:50 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97 (q, J = 5.4 Hz, 1H), 4.18 (q, J = 5.4 Hz 1H), 2.59 (sep, J = 7.0 Hz, 1H), 2.09–1.49 (m, 7H), 1.19 (d, J = 7.0 Hz, 3H), 1.19 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 76.6, 73.4, 34.2, 30.9, 28.3, 19.6, 19.2; IR (neat) 3458, 2972, 1732, 1472, 1204, 1036 cm^{-1}

(1*R*,2*S*)-cyclopentane-1,2-diyl bis(2-methylpropanoate) (4k).[13h] Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17–5.10 (m, 2H), 2.51 (sep, J = 6.9 Hz, 1H), 2.04–1.55 (m, 6H), 1.16 (d, J = 6.9 Hz, 6H), 1.15 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 74.1, 34.2, 28.4, 19.3, 19.1, 19.0; IR (neat) 2974, 1732, 1470, 1387, 1263 cm^{-1}

(3*S*,4*R*)-4-hydroxytetrahydrofuran-3-yl isobutyrate (3l).[26] According to the general procedure, substrate **2l** (65.8 mg, 0.632 mmol) with a catalyst **1h** (60 μmol), Et_3N (108 μL, 0.78 mmol), and isobutyric anhydride (130 μL, 0.784 mmol) in TBME (6 mL) at −20 °C gave monoacylate **3l** (97.2 mg, 0.558 mmol, 88% yield) and diacylate **4l** (9.6 mg, 0.0393 mmol, 6% yield). Colorless oil. Enantiomeric ratio was determined with benzoate by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 78.4/1.6, v/v, flow rate = 0.8 mL/min, 30 °C, UV = 254 nm), T_R = 12.4 min and T_R = 16.7 min, 50:50 er; ^{1}H NMR (400 MHz, $CDCl_3$, 0.03% TMS) δ 5.17–5.10 (m, 1H), 4.50–4.43 (m, 1H), 4.09 (dd, J = 10.1, 6.0 Hz, 1H), 3.98 (dd, J = 9.3, 5.5 Hz, 1H), 3.83 (dd, J = 10.1, 4.1 Hz, 1H), 3.72 (dd, J = 9.3, 5.5 Hz, 1H), 2.65 (sep, J = 7.0 Hz, 1H),

1.22 (d, J = 7.0 Hz, 3H), 1.21 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 73.6, 72.4, 71.1, 70.9, 34.1, 19.2, 19.1; IR (neat) 3462, 2937, 1732, 1204, 988 cm^{-1}.

(3*R*,4*S*)-tetrahydrofuran-3,4-diyl bis(2-methylpropanoate) (4l). Colorless oil.. ^{1}H NMR (400 MHz, $CDCl_3$) 5.35–5.29 (m, 2H), 4.14–4.06 (m, 2H), 3.83–3.76 (m, 2H), 2.57 (sep, J = 6.9 Hz, 2H), 1.18 (d, J = 6.9 Hz, 6H), 1.18 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 71.4, 70.5, 33.9, 19.0, 18.9; IR (neat) 2976, 2940, 1738, 1470, 1198 cm^{-1}; HRMS (FAB^+) calculated for $C_{12}H_{21}O_5$ $[M+H]^+$ 245.1383, found 245.1403.

(1*S*,2*R*)-2-hydroxycyclohexyl isobutyrate (3m).[13h] According to the general procedure, substrate **2m** (69.3 mg, 0.597 mmol) with a catalyst **1h** (0.6 μmol), Et_3N (108 μL, 0.780 mmol), and isobutyric anhydride (129 μL, 0.778 mmol) in TBME (6 mL) at −20 °C gave monoacylate **3m** (87.6 mg, 0.470 mmol, 79% yield, 97:3 er) and diacylate **4m** (22.4 mg, 0.0874 mmol, 15% yield). Colorless oil. Enantiomeric ratio was determined with 4-nitro benzoate by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 254 nm), T_R = 9.8 min (minor) and T_R = 10.5 min (major), 97:3 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97–4.89 (m, 1H), 3.88–3.81 (m, 1H), 2.59 (sep, J = 6.9 Hz, 1H), 2.11–1.52 (m, 7H), 1.44–1.31 (m, 2H), 1.19 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 73.7, 69.6, 34.3, 30.3, 27.2, 21.8, 21.5, 19.2, 19.1; IR (neat) 3462, 2937, 1732, 1204, 988 cm^{-1}; $[\alpha]^{22}_D$ +5.6 (*c* 1.4, $CHCl_3$, 97:3 er, (1*S*, 2*R*)) [lit[27]. $[\alpha]^{20}_D$ -5.6 [*c* 1.4, $CHCl_3$, 88:12 er, (1*R*, 2*S*)]

(1*R*,2*S*)-cyclohexane-1,2-diyl bis(2-methylpropanoate) (4m).[13h] Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.01 (d, J = 8.2 Hz, 2H), 2.52 (sep, J = 6.9, 1H), 1.90–1.73 (m, 2H), 1.71–1.55 (m, 4H), 1.52–1.35 (m, 2H), 1.16 (d, J = 6.9 Hz, 6H), 1.15 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 70.7, 34.3, 27.8, 21.8, 19.1, 19.0; IR (neat) 2974, 2941, 1734, 1196, 984 cm^{-1}.

(1*S*,6*R*)-6-hydroxycyclohex-3-en-1-yl isobutyrate (3n).[25] According to the general procedure, substrate **2n** (68.6 mg, 0.601 mmol) with a catalyst **1h** (0.600 μmol), Et_3N (108 μL, 0.780 mmol), and isobutyric anhydride (129 μL, 0.778 mmol) in TBME (6 mL) at −40 °C gave

monoacylate **3n** (95.7 mg, 0.519 mmol, 86% yield, 94:6 er) and diacylate **4n** (15.0 mg, 0.0590 mmol, 10% yield). Colorless oil. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® AS-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 205 nm), T_R = 11.6 min (minor) and T_R = 12.2 min (major), 94:6 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65–5.54 (m, 2H), 5.07 (ddd, *J* = 6.1, 6.4, 2.3, 1H), 4.08–4.01 (m, 1H), 2.59 (sep, *J* = 6.9 Hz, 1H), 2.46–2.19 (m, 4H), 2.03 (bs, 1H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 123.9, 123.3, 71.7, 67.3, 34.2, 31.3, 28.2, 19.0; IR (neat) 3478, 3032, 2974, 1732, 1202, 671 cm^{-1}

(1*R*,2*S*)-cyclohex-4-ene-1,2-diyl bis(2-methylpropanoate) (4n). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 (dd, *J* = 1.8, 1.6 Hz 2H), 5.19–5.13 (m, 2H), 2.52 (sep, *J* = 7.0 Hz, 1H), 2.44–2.24 (m, 4H), 1.15 (d, *J* = 7.0 Hz, 6H), 1.13 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 123.7, 68.8, 34.2, 28.7, 19.1, 18.9; IR (neat) 3036, 2974, 1732, 1261, 671 cm^{-1}; HRMS (FAB^+) calculated for $C_{14}H_{22}O_4Na$ $[M+Na]^+$ 277.1410, found 277.1393.

(1*S*,2*R*)-2-hydroxycycloheptyl isobutyrate (3o). According to the general procedure, substrate **2o** (52.2 mg, 0.400 mmol) with a catalyst **1h** (0.4 μmol), Et_3N (72.2 μL, 0.519 mmol), and isobutyric anhydride (86.2 μL, 0.520 mmol) in TBME (4 mL) at −20 °C gave monoacylate **3o** (73.3 mg, 0.366 mmol, 91% yield, 50:50 er) and diacylate **4o** (7.3 mg, 0.0270 mmol, 7% yield). Colorless oil. Enantiomeric ratio was determined by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 205 nm), T_R = 21.5 min and T_R = 24.3 min, 50:50 er; ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97 (dt, *J* = 8.2, 2.7 Hz, 1H), 3.96 (td, *J* = 6.0, 2.3 Hz, 1H), 2.59 (sep, *J* = 7.1 Hz, 2H), 2.39–2.11 (bs, 1H), 2.03–1.87 (m, 1H), 1.83–1.37 (m, 9H), 1.19 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 77.7, 72.7, 34.3, 31.7, 27.9, 27.1, 22.8, 22.1, 19.1 (2); IR (neat) 3480, 2934, 1732, 1456, 1159 cm^{-1}; HRMS (FAB^+) calculated for $C_{11}H_{20}O_3Na$ $[M+Na]^+$ 223.1304, found 223.1283

(1*R*,2*S*)-cycloheptane-1,2-diyl bis(2-methylpropanoate) (4o). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 0.03% TMS) δ 5.08 (dd, *J* = 6.9, 2.7 Hz, 2H), 2.55 (sep, *J* = 6.9 Hz, 2H), 1.98–1.85 (m, 2H), 1.78–1.47 (m, 8H), 1.17 (d, *J* = 6.9 Hz, 6H), 1.16 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 74.3, 34.3, 28.8, 26.7, 22.6, 19.1 (2); IR (neat) 2972, 1732, 1470, 1263, 1067 cm^{-1}; HRMS (FAB $^+$) calculated for $C_{15}H_{26}O_4Na$ $[M+Na]^+$ 293.1723, found 293.1739.

(1*R*,2*S*)-cyclooctane-1,2-diyl bis(2-methylpropanoate) (3p). According to the general procedure, substrate **2p** (86.4 mg, 0.599 mmol) with a catalyst **1h** (0.600 μmol), Et_3N (108 μL, 0.780 mmol), and isobutyric anhydride (129 μL, 0.778 mmol) in TBME (6 mL) at −20 °C gave monoacylate **3p** (113.3 mg, 0.529 mmol, 88% yield, 50:50 er) and diacylate **4p** (19.8 mg, 0.0696 mmol, 12% yield). Colorless oil. Enantiomeric ratio was determined with benzoate by HPLC with DAICEL CHIRALPAK® IA-3 (hexane/*i*-PrOH = 98.5/1.5, v/v, flow rate = 1.0 mL/min, 30 °C, UV = 254 nm), T_R = 5.5 min and T_R = 9.1 min, 50:50 er. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (dt, *J* = 9.2, 2.7 Hz, 1H), 3.99–3.90 (m, 1H), 2.57 (sep, *J* = 6.9 Hz, 1H), 2.13–1.97 (m, 1H), 1.87–1.39 (m, 11H), 1.20–1.15 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 72.0, 34.3, 30.3, 27.9, 27.0, 25.6, 24.5, 22.0, 19.1; IR (neat) 3460, 2972, 1732, 1472, 1200 cm^{-1}; HRMS (FAB^+) calculated for $C_{12}H_{22}O_3Na$ $[M+Na]^+$ 237.1461, found 237.1436.

(1*S*,2*R*)-2-hydroxycyclooctyl isobutyrate (4p). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17–5.10 (m, 2H), 2.52 (sep, *J* = 7.0 Hz, 2H), 2.05–1.92 (m, 2H), 1.76–1.51 (m, 10H), 1.16 (d, *J* = 7.0 Hz, 6H), 1.15 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 73.4, 34.3, 28.5, 26.4, 23.0, 19.1, 19.0; IR (neat) 2974, 2936, 1732, 1472, 1261, 1069, 964 cm^{-1}; HRMS (FAB^+) calculated for $C_{16}H_{28}O_4Na$ $[M+Na]^+$ 307.1879, found 307.1850.

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Supporting Information

^{1}H and ^{13}C spectra of the substrates and products, and HPLC analysis of racemic and chiral products

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