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Desymmetrization of *meso*-1,2-Diols via the Dynamic Kinetic Resolution of Its Monodichloroacetates

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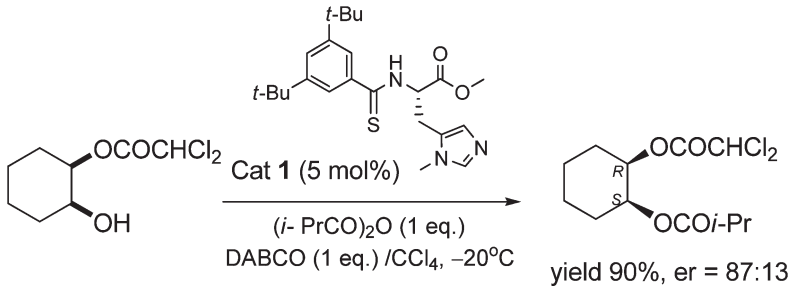

Enantioselective acylation catalyzed by the thioamide modified 1-methylhistidine methyl ester **1** in combination with DABCO-mediated racemization of the substrate led to the efficient dynamic kinetic resolution of *meso*-1,2-diol monodichloroacetates. In this way, cyclic and acyclic *meso*-1,2-diol monodichloroacetates can be transformed to the enantiomerically enriched (1*S*,2*R*)-heterosubstituted diol diesters which are stable in enantiomerically pure form and can be readily used for further organic transformations.

Introduction

The nonenzymatic desymmetrization of *meso*-1,2-diols via direct asymmetric monoacylation is an important methodology for the synthesis of chiral building blocks. Previous organocatalytic desymmetrizations of *meso*-1,2-diols such as *cis*-1,2-cyclohexanediol with alkyl anhydrides as the electrophile gave moderate ee values and moderate conversions.[1] In 2009, Schreiner's research group reported a desymmetrization of *meso*-1,2-diols employing a 1-methylhistidine-containing oligopeptide. By using this method, (1*S*,2*R*)-1,2-cyclohexanediol monoacetate could be formed with an er value of 94:6 by GC analysis of the reaction mixture. But the er value of the isolated product decreased to 80:20 due to partial racemization during the workup process.[2] Organocatalytic desymmetrizations of *cis*-1,2-cyclohexanediol with more reactive benzoyl chloride as the electrophile provided higher enantioselectivities at low temperature with the highest ee value of 97%.[3] The desymmetrization of *cis*-1,2-cyclohexanediol can also be achieved by monoprotecting one of the hydroxy groups to the corresponding silyl ether (er 96:4, 82% yield), but 20% catalyst loading is required.[4]

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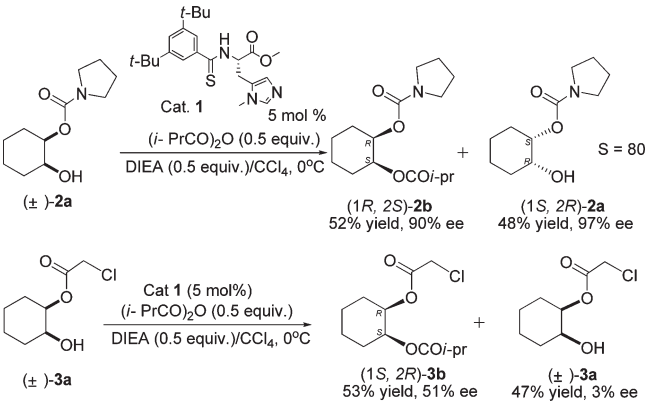
SCHEME 1. KR of Monoprotected Secondary Alcohols by Catalyst 1

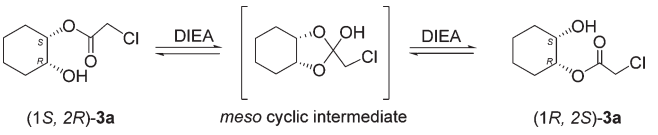


Therefore, efficient and practical desymmetrization of *meso*-1,2-diols is still highly desirable.

Results and Discussion

1-Methylhistidine-containing oligopeptides or 1-methylhistidinol derivatives as effective nucleophilic catalysts have been successfully applied to the kinetic resolution (KR) and the desymmetrization of alcohols.[5−7] We recently reported that a thioamide-modified 1-methylhistidine methyl ester **1**, which has a low molecular weight and can be readily synthesized, could catalyze the kinetic resolution of the secondary alcohols containing a hydrogen bond accepting auxiliary with high selective factors (Scheme 1).[8] During the course of this work, we found that when using *cis*-cyclohexane-1,2-diol monochloroacetate (**3a**) as the substrate, the ee value of the product was 51% but the ee value of the starting material was only 3% at 53% conversion of the starting material (Scheme 1). The racemization of the unreacted (1*S*,2*R*)-**3a** can be explained by an intramolecular chloroacetoxy migration process as shown in Scheme 2. The intramolecular acetoxy migration was observed before in enzymatic and nonenzymatic asymmetric acylations of 1,2-diols or desymmetrizations of *meso*-1,2-diols via asymmetric acylation and was considered as an harmful side reaction that could cause partial racemization of the optically active product (this problem can be avoided by protecting the hydroxy group in the product immediately after the reaction).[1c,2,9] We think the fast racemizing chloroacetoxy migration in *cis*-1,2-diol monochloroacetate can be utilized to enable a dynamic kinetic resolution (DKR), which is highly valued for both economical and environmental reasons.[10] The DKR of *meso*-1,2-diol

SCHEME 2. The Racemizing Intramolecular Transesterification in 3a



monochloroacetates give optically active *cis*-1,2-diol heterosubstituted diesters which actually accomplish the desymmetrization of *meso*-1,2-diols. The racemization without a reaction at the asymmetric center is an uncommon racemization method and many of them are through multiple steps and not an in situ racemization.[11] It is also of interest to determine if a racemizing intramolecular transesterification can work together with an enantioselective acylation.

In a successful DKR, the reaction rate of the racemization reaction should be fast enough to keep a 1:1 ratio of two substrate enantiomers during the whole reaction otherwise the er value of the product would decrease gradually as the reaction proceeds as happens in a KR. The enantiomeric purity of the acylated product **3b** was monitored during the DKR of **3a**. The er value of **3b** declined from 82:18 at the beginning of the reaction to 61:39 at the end of the reaction, which implied that the racemizing chloroacetoxy migration in **3a** was not fast enough. If the chloroacetoxy carbonyl is made more electron deficient by attaching more electron-withdrawing atoms to it, it is more susceptible to the nucleophilic attack and thus the racemizing intramolecular transesterification will be accelerated. On the other hand, an electron-rich acetoxy group in the 1,2-diol substrate is desired for the formation of a strong intermolecular hydrogen bond with the thioamide NH in catalyst **1**. The electron-withdrawing atoms substituted acetoxy group becomes a worse hydrogen bond acceptor and this will deteriorate the enantioselectivity of the resolution reaction. To find a suitable balance that can benefit both processes, five *cis*-cyclohexane-1,2-diol monoacetates with one, two, or three halogen atoms on the acetoxy group were synthesized and subjected to the DKR condition.

The results obtained from the DKR of **3a**−**8a** were shown in Table 1. The pK_a values of the halogen-substituted acetic acids representing the leaving abilities of the halogen-substituted acetoxy groups were also listed for the understanding of the experimental results. As anticipated, a low er value of 70:30 was observed for the trifluoroacetoxy protected diol **4a** with a poor hydrogen bond acceptor. The er value increased with the increase of the pK_a value and the highest er value was obtained with the dichloroacetoxy protected diol **6a**. Then the er value decreased as the pK_a value further increased because the corresponding racemization reaction slowed down. The er value of the acylated product **6b** in the DKR of **6a** did not change as a function of percent conversion of **6a**, which suggested a satisfactory racemization rate was reached.

To obtain the information about the rate of the intramolecular dichloroacetoxy migration, we studied the dichloroacetoxy migration in methyl-substituted *cis*-1,2-cyclohexanediol monodichloroacetate **9** where the dichloroacetoxy migration

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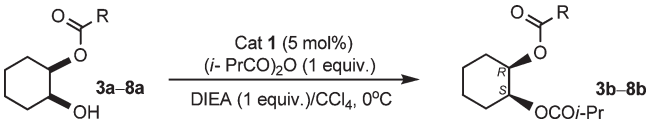
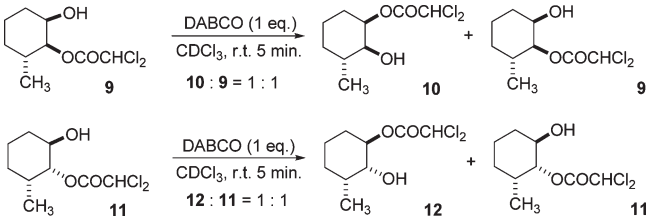
TABLE 1. Screening of the Monoester Group on *cis*-1,2-Cyclohexanediol[a]



R	time (h)	pK_a of RCOOH	er of isobutyrate diester
CF_3 (**4a**)	5	0.50	70:30[b]
CCl_3 (**5a**)	4	0.52	77:23[c]
$CHCl_2$ (**6a**)	3	1.26	83:17[b]
$CHBr_2$ (**7a**)	3	1.39	73:27[c]
CH_2Cl (**3a**)	3	2.87	61:39[b]
CH_2Br (**8a**)	2.5	2.90	60:40[b]

[a]Conditions: alcohol (0.2 mmol), catalyst (5 mol %), DIEA (0.2 mmol), and $(i\text{-PrCO})_2O$ (0.2 mmol) in CCl_4 (4 mL) were stirred at 0 °C. [b]Determined by GC analysis. [c]Determined by HPLC analysis.

SCHEME 3. Base-Catalyzed Dichloroacetoxy Migrations in Compounds 9 and 11



between two hydroxy groups in the molecule can be monitored by ^{1}H NMR analysis (Scheme 3). A ^{1}H NMR spectrum was taken immediately after the addition of 1 equiv of DABCO in an NMR tube containing compound **9** in $CDCl_3$. The reaction reached equilibrium within 5 min and the ratio of compound **9** and compound **10** was 1:1 judging from the integration of their ^{1}H NMR signals.[12] This indicated that the dichloroacetoxy migration proceeded very fast at room temperature. It took 9 days for the dichloroacetoxy migration to proceed 10% without a base catalyst. The dichloroacetoxy migration in methyl-substituted *trans*-1,2-cyclohexanediol monodichloroacetate **11** proceeded with a similar reaction rate. Nevertheless, the dichloroacetoxy migration in *trans*-1,2-cyclohexanediol monodichloroacetate is useless because the migration gave back the original molecule.

The enantioselectivity for monodichloroacetate **6a** is lower than that for **2a** in which a carbamate carbonyl serves as the hydrogen bond acceptor. One technique for improving the enantioselectivity for **6a** is to reinforce the hydrogen bond between the substrate and the catalyst. Catalyst **13** with a hydroxy group forming an intramolecular hydrogen bond with the thioamide and making the thioamide NH a better hydrogen bond donor was synthesized. The more acidic thioamide NH was supported by the evidence that the chemical shift of the NH moved downfield to 9.5 ppm (the chemical shift of the thioamide NH in **1** is at 8.1 ppm).[8] Unfortunately, the observed er value in the DKR of **6a** with catalyst **13** was lower than that from the DKR with catalyst **1** (Scheme 4). We cannot explain why increasing the hydrogen bond-forming ability of the amide NH does not improve the enantioselectivity of the catalyst. The same phenomenon

(12) See the Supporting Information for details.

SCHEME 4. DKR of Monodichloroacetate 6a by Catalyst 13

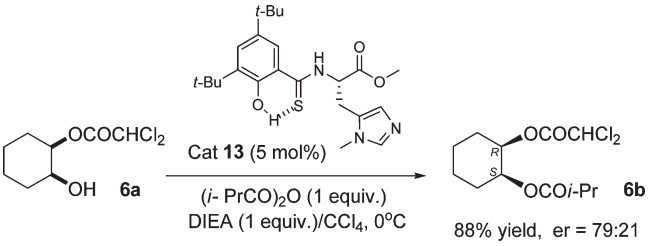
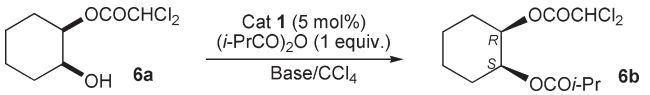


TABLE 2. Screening of the Racemizing Bases[a]



base	amount (equiv)	time (h)	er of isobutyrate diester[b]
none	0	5	65:35
DIEA	1	3	83:17
DIEA	2	3	83:17
pyridine	1	4	79:21
collidine	1	4	78:22
Et_3N	1	2.5	80:20
HMTA	1	3	80:20
TMEDA	1	2.5	82:18
PMP	1	3	83:17
DABCO	1	3	85:15
DBU	1	2	59:41
Cs_2CO_3	1	4	84:16

[a]Conditions: alcohol (0.2 mmol), catalyst (5 mol %), $(i\text{-PrCO})_2O$ (0.2 mmol), and base in CCl_4 (4 mL) were stirred at 0 °C. [b]Determined by GC analysis.

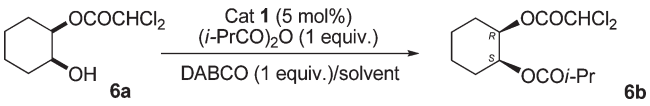
has also been observed before by Prof. Ishihara's research group.[6b]

The base catalyzing the racemization reaction in the DKR was screened by using **6a** as the substrate (Table 2). A lower er value of 65:35 was obtained when no base was added, while using 2 equiv of DIEA gave a similar result compared with using 1 equiv of DIEA. But the use of a weaker base such as pyridine or collidine gave a lower er value. Trialkylamines and solid base Cs_2CO_3 gave comparable results. Using DABCO as the base provided a slightly higher er value than using other bases. A strong base such as DBU deteriorated the enantioselectivity significantly.

Other organic solvents such as toluene and methylene dichloride were also tested in the DKR of **6a**. Running the reaction in toluene at 0 °C afforded a slightly lower enantioselectivity and further decreasing the reaction temperature to −78 °C greatly retarded the reaction. The corresponding reaction in methylene dichloride constantly gave very slow reaction rates and lower enantioselectivities. It was found that carbon tetrachloride, the solvent used in our initial study, was the best choice. Lowing the reaction temperature to −20 °C could further increase the er value to 87:13, but a longer reaction period was needed (Table 3).

The optimized reaction condition was then applied to the DKR of various monodichloroacetates derived from *meso*-1,2-diols (Table 4). All reactions were carried out at −20 °C and went to completion within 24 h with the isolated yields between 83% and 95%. Analogous enantioselectivities were observed for all tested cyclic 1,2-diol monodichloroacetates

TABLE 3. Solvent and Temperature Effects on the DKR[a]



solvent	temp (°C)	time (h)	conversion (%)	er of isobutyrate diester[b]
$PhCH_3$	0	5	100	77:23
$PhCH_3$	−40	24	75	79:21
$PhCH_3$	−78	24	18	71:29
CH_2Cl_2	0	24	20	75:25
CH_2Cl_2	−40	24	11	78:22
CCl_4	0	3	100	85:15
CCl_4	−20	24	100	87:13

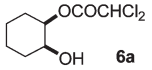
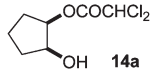
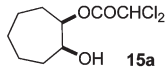
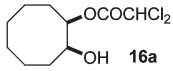
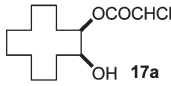
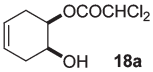
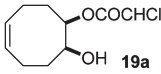
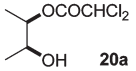
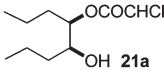
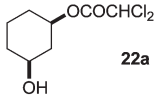
[a]Conditions: alcohol (0 2 mmol), catalyst (5 mol %), DABCO (0.2 mmol), and $(i\text{-PrCO})_2O$ (0.2 mmol)) in solvent (4 mL) were stirred at the temperature indicated. [b]Determined by GC analysis.

except in the case of *cis*-cyclododecane-1,2-diol monodichloroacetate **17a**. The flexible conformation of this substrate led to the substantial lower er value. For **18a** and **19a** having a double bond in their ring structure, the er values of the products were slightly lower than those from **6a** and **16a**. This further supported the conclusion we made in our previous studies that catalyst **1** recognized the hydrogen bond accepting auxiliary in the substrates rather than the skeleton of the substrates.[8] The enantioselectivities for acyclic substrates such as **20a** and **21a** did not drop significantly compared with those of the cyclic substrates. *cis*-1,3-Cyclohexanediol monoacetates can also be racemized through acetoxy migration[13] and thus compound **22a** was also tested in the standard condition, but it turned out that **22a** was not a suitable substrate for the current system.

The dichloroacetoxy group in the heterosubstituted diester product is more liable toward a basic deprotection and is supposed to be selectively removed in the standard condition (triethylamine in methanol). However, partial racemization due to the facile acyl migration occurred during the deprotection. Using a milder base could largely avoid the racemization problem. Treating **6b** (er of 87:13) in methanol/water (4/1) mixture solvent containing 1.1 equiv of collidine at room temperature for 1.5 h gave (1*S*,2*R*)-diol monoisobutyrate **6c** (er of 86:14) in 93% isolated yield.[14] The enantiomerically enriched **6c** is stable in aprotic solvents such as CH_2Cl_2 solution for at least 3 days at room temperature and this period is long enough for carrying further organic transformations. When enantiomerically enriched *cis*-2-(2,2-dichloroacetoxy)cyclopentyl isobutyrate **14b** (er of 83:17) was treated with this deprotection system, the er ratio of the isolated 1,2-diol monoisobutyrate **14c** decreased to 60:40. Careful examination of the reaction mixture found that the er ratio of **14c** did not decline considerably after the reaction completed. The severe racemization happened in the workup and column chromatography processes owing to the facile acyl migration in this product. Two other substrates including **18b** and the acyclic heterosubstituted diester **20b** were not racemized significantly during the above-mentioned deprotection procedure (Table 5).

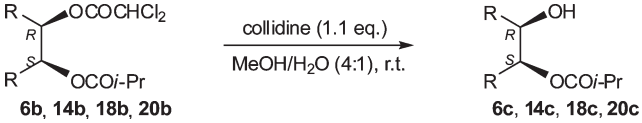
(13) Edin, M.; Bäckvall, J.-E. *J. Org. Chem.* **2003**, *68*, 2216.
(14) Johnson, F.; Starkkovsky, N. A.; Paton, A. C.; Carlson, A. A. *J. Am. Chem. Soc.* **1964**, *86*, 118.

TABLE 4. Dynamic Kinetic Resolution of *cis*-Diol Monodichloroacetates by Catalyst 1 and DABCO[a]

entry	substrate	time (h)	yield (%)	er of isobutyrate diester
1	 6a	20	90	87 :13[b]
2	 14a	18	85	83 : 17[b]
3	 15a	20	91	87 : 13[c]
4	 16a	24	93	85 : 15[c]
5	 17a	24	95	77 : 23[c]
6	 18a	20	87	83 : 17[b]
7	 19a	24	89	80 : 20[c]
8	 20a	18	83	84: 16[c]
9	 21a	24	90	81 : 19[c]
10	 22a	28	91	60 : 40[c]

[a]Conditions: alcohol (0.2 mmol), catalyst (5 mol %), DABCO (0.2 mmol), and $(i\text{-PrCO})_2O$ (0.2 mmol) in CCl_4 (4 mL) were stirred at −20 °C. [b]Determined by GC analysis. [c]Determined by HPLC analysis.

TABLE 5. Selective Deprotection of the Dichloroacetoxy Group in Heterosubstituted Diesters[a]



6b, **14b**, **18b**, **20b** → **6c**, **14c**, **18c**, **20c**

isobutyrate diester (er)	time (h)	yield (%)[a]	er of monoisobutyrate[b]
6b (87:13)	1.5	93	86:14
14b (83:17)	1.5	91	60:40
18b (83:17)	1.5	91	81:19
20b (84:16)	1.0	90	81:19

[a]Isolated yield. [b]Determined by GC analysis.

In summary, the desymmetrization of cyclic and acyclic *meso*-1,2-diols was achieved via the DKR of their monodichloroacetates. The resulting enantiomerically enriched (1*S*,2*R*)-heterosubstituted diol diesters are stable in enantiomerically pure form and can be readily used for further

organic transformations. The in situ racemization of the substrate through the fast dichloroacetoxy migration enables the dynamic kinetic resolution in which 90% of the starting materials are converted into the products, which is much higher than the 50% theoretical yield in a kinetic resolution.

Experimental Section

Typical Procedure for the Dynamic Kinetic Resolution of Monoprotected *meso*-1,2-Diols Catalyzed by Catalyst 1 and DABCO. To the CCl_4 (4 mL) solution containing (±)-**6a** (45 mg, 0.2 mmol) and catalyst **1** (4 mg, 0.01 mmol) was added DABCO (22 mg, 0.2 mmol) and isobutyric anhydride (33 uL, 0.2 mmol) at −20 °C under nitrogen atmosphere. After completion, the reaction mixture was quenched with water and extracted with EtOAc. The organic phase was washed with aqueous NH_4Cl, water, and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (eluent: 5% Et_2O/petroleum ether) to afford product **6b** as a colorless oil (53 mg, 90%);

^{1}H NMR Analysis of Dichloroacetoxy Migration in Compounds 9 and 11.[16] Compound **9** (6.0 mg, 0.025 mmol) in $CDCl_3$ (0.5 mL) was added to a dry NMR tube. A ^{1}H NMR spectrum was taken at room temperature. Then DABCO (2.8 mg, 0.025 mmol) was added to the mixture and the mixture was monitored by ^{1}H NMR within 5 min.

Procedure for the Deprotection of the Dichloroacetoxy Group.[14] *cis*-2-(2,2-dichloroacetoxy)cyclohexyl isobutyrate **6b** (0.1 mmol, 30 mg, er 87:13) was dissolved in a mixture of 10 mL of MeOH and 3 mL of H_2O. Collidine (0.11 mmol, 13 mg, 15 μL) in 2 mL of MeOH was added to the mixture. The mixture was stirred at room temperature for 1.5 h and diluted with EtOAc, washed by aqueous solution of citric acid and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (eluent:15% EtOAc/petroleum ether) to give the desired product **6c** (18 mg, 93%, er 86:14) as a colorless oil.

***cis*-2-Hydroxycyclohexyl 2-chloroacetate (3a):**[17] white solid; mp 59−62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (dt, J = 2.8, 8.0 Hz, 1H), 4.11 (s, 2H), 3.89−3.92 (m, 1H), 1.87−1.96 (m, 1H), 1.74−1.76 (m, 2H), 1.57−1.71(m, 4H), 1.34−1.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 76.2, 69.0, 41.1, 30.2, 26.8, 21.7, 21.1.

***cis*-2-(2-Chloroacetoxy)cyclohexyl isobutyrate (3b):** yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07−5.11 (m, 2H), 4.04 (s, 2H), 2.55 (septet, J = 7.0 Hz, 1H), 1.81−1.91 (m, 2H), 1.63−1.70 (m, 4H), 1.40−1.50 (m, 2H), 1.17 (dd, J = 3.6, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 166.6, 73.3, 70.0, 40.9, 34.1, 27.7, 27.3, 21.8, 21.3, 19.0, 18.9; HRMS (ESI) for $C_{12}H_{19}ClO_4$ calcd for $[M + Na]^+$ m/z 285.0864, found 285.0868; $[\alpha]^{20}_D$ −0.8 (c 1.0, CH_2Cl_2) for 61:39 er; GC analysis: Beta DEX 120 column (30 m × 0.25 mm × 0.25 μm film thickness), 165 °C for 50 min, 1 deg/min to 190 °C, 13.6 psi, t_R = 24.7 min (1*R*,2*S*, minor), 25.3 min (1*S*,2*R* major). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxycyclohexyl 2,2,2-trifluoroacetate (4a):**[18] Compound **4a** was synthesized from *cis*-cyclohexane-1,2-diol and trifluoroacetic anhydride catalyzed by DMAP in CH_2Cl_2: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14−5.18 (m, 1H), 3.92−3.95 (m, 1H), 1.94−2.05 (m, 1H), 1.57−1.83 (m, 6H), 1.37−1.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0 (q, J = 42 Hz), 114.5 (q, J = 284 Hz), 78.7, 68.7, 29.9, 26.8, 21.3, 21.0.

***cis*-2-(2,2,2-Trifluoroacetoxy)cyclohexyl isobutyrate (4b):** yield 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25−5.28 (m, 1H), 5.04−5.08 (m, 1H), 2.53 (septet, J = 7.0 Hz, 1H), 1.94−2.01 (m, 1H), 1.80−1.88 (m, 1H), 1.63−1.79 (m, 4H), 1.43−1.54 (m, 2H), 1.15 (dd, J = 2.0, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 156.8 (q, J = 42 Hz), 114.5 (q, J = 284 Hz), 75.5, 69.8, 34.0, 27.5, 27.1, 21.7, 20.9, 18.7, 18.6; HRMS (ESI) for $C_{12}H_{17}F_3O_4$ calcd for $[M + Na]^+$ m/z 305.0971, found 305.0972; $[\alpha]^{20}_D$ −1.5 (c 1.0, CH_2Cl_2) 70:30 er; GC analysis: Beta DEX 120 column (30 m × 0.25 mm × 0.25 μm film thickness), 100 °C for 50 min, 1 deg/min to 190 °C, 11 psi, t_R = 42.9 min (1*S*,2*R*, major), 44.2 min (1*R*,2*S*, minor). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxycyclohexyl 2,2,2-trichloroacetate (5a):** white solid; mp 49 °C−51 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11−5.14 (m, 1H), 3.91−3.93 (m, 1H), 2.01−2.10 (m, 1H), 1.71−1.74 (m, 4H), 1.58−1.69 (m, 2H), 1.34−1.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 90.2, 79.8, 69.3, 30.1, 27.0, 21.7, 21.0; HRMS (ESI) for $C_8H_{11}Cl_3O_3$ calcd for $[M + Na]^+$ m/z 282.9666, found 282.9666.

***cis*-2-(2,2,2-Trichloroacetoxy)cyclohexyl isobutyrate (5b):** yield 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24−5.26 (m, 1H), 5.02 (dt, J = 3.0, 9.4 Hz, 1H), 2.53 (septet, J = 7.0 Hz, 1H), 2.00−2.06 (m, 1H), 1.84−1.94 (m, 1H), 1.64−1.77 (m, 4H), 1.38−1.43 (m, 2H), 1.16 (dd, J = 2.4, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 161.2, 90.1, 76.4, 70.7, 34.1, 27.9, 26.9, 22.3, 20.6, 18.9, 18.8; HRMS (ESI) for $C_{12}H_{17}Cl_3O_4$ calcd for $[M + Na]^+$ m/z 353.0085, found 353.0081; $[\alpha]^{20}_D$ −4.0 (c 1.0, CH_2Cl_2) 77:23 er; HPLC (Chiralcel OJ-H, hexane:2-propanol = 99:1, flow rate = 0.3 mL/min) 210 nm; t_R = 15.1 min (1*S*,2*R*, major), 16.0 min (1*R*,2*S*, minor). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxycyclohexyl 2,2-dichloroacetate (6a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (s, 1H), 5.05−5.07 (m, 1H), 3.91−3.93 (m, 1H), 1.94−2.02 (m, 1H), 1.63−1.83 (m, 6H), 1.35−1.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 77.6, 69.0, 64.5, 30.1, 26.8, 21.3, 21.2; HRMS (ESI) for $C_8H_{12}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 249.0056, found 249.0059.

***cis*- 2-(2,2-Dichloroacetoxy)cyclohexyl isobutyrate (6b):**[15] yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.17−5.19 (m, 1H), 5.03 (dt, J = 2.8, 8.8 Hz, 1H), 2.54 (septet, J = 7.2 Hz, 1H), 1.82−1.99 (m, 2H), 1.65−1.75 (m, 4H), 1.43−1.51 (m, 2H), 1.16 (dd, J = 2.8, 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 163.8, 74.5, 70.4, 64.5, 34.1, 27.6, 27.2, 21.9, 21.0, 18.9, 18.8; HRMS (ESI) for $C_{12}H_{18}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 319.0474, found 319.0479; $[\alpha]^{20}_D$ −4.8 (c 1.0, CH_2Cl_2) for 87:13 er; GC analysis: Beta DEX 120 (30 m × 0.25 mm × 0.25 μm film thickness), 152 °C for 100 min, 3 deg/min to 190 °C, 8.6 psi, t_R = 90.1 min (1*R*,2*S*, minor), 91.6 min (1*S*,2*R*, major). The absolute configuration of **6b** was determined by comparing the optical rotation value with reported (1*R*,2*S*)-2-hydroxycyclohexyl isobutyrate after removal of the dichloroacetoxy group.

***cis*-2-Hydroxycyclohexyl isobutyrate (6c):**[15] yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.93−4.95 (m, 1H), 3.84−3.87 (m, 1H), 2.60 (septet, J = 7.0 Hz, 1H), 1.82−1.87 (m, 2H), 1.73−1.79 (m, 1H), 1.64−1.70 (m, 2H), 1.54−1.58 (m, 2H), 1.32−1.42 (m, 2H), 1.19 (d, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 73.6, 69.4, 34.2, 30.1, 27.1, 21.7, 21.3, 19.1, 18.9; GC analysis: Gamma DEX 225 column (30 m × 0.25 mm × 0.25 μm film thickness), 115 °C for 45 min, 10 deg/min to 200 °C, 11 psi, t_R = 41.8 min (1*R*,2*S*, minor), 42.1 min (1*S*,2*R* major).

***cis*-2-Hydroxycyclohexyl 2,2-dibromoacetate (7a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 (s, 1H), 5.04 (dt, J = 2.6, 7.2 Hz, 1H), 3.91 (dt, J = 2.8, 8.0 Hz, 1H), 1.94−2.02 (m, 1H), 1.70−1.84 (m, 4H), 1.60−1.65 (m, 2H), 1.34−1.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 77.6, 69.1, 32.9, 30.2, 26.7, 21.4, 21.3; HRMS (ESI) for $C_8H_{12}Br_2O_3$ calcd for $[M + Na]^+$ m/z 336.9045, found 336.9045.

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***cis*-2-(2,2-Dibromoacetoxy)cyclohexyl isobutyrate (7b):** yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (s, 1H), 5.16−5.17 (m, 1H), 5.02 (dt, J = 3.0, 9.2 Hz, 1H), 2.54 (septet, J = 7.0 Hz, 1H), 1.84−1.99 (m, 2H), 1.66−1.74 (m, 4H), 1.42−1.54 (m, 2H), 1.17 (dd, J = 2.8, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 163.9, 74.4, 70.6, 34.1, 32.7, 27.7, 27.1, 22.1, 20.9, 19.0, 18.9; HRMS (ESI) for $C_{12}H_{18}Br_2O_4$ calcd for $[M + Na]^+$ m/z 406.9464, found 406.9458; $[\alpha]^{20}_D$ −6.8 (c 1.0, CH_2Cl_2) 73:27 er; HPLC (Chiralcel OD-H, hexane:2-propanol = 93:7, flow rate = 0.4 mL/min) 210 nm, t_R = 12.6 min (1*S*,2*R*, major), 13.5 min (1*R*,2*S*, minor). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxycyclohexyl 2-bromoacetate (8a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.00 (dt, J = 3.0, 8.0 Hz, 1H), 3.88−3.91 (m, 3H), 1.89−1.95 (m, 1H), 1.75−1.82 (m, 2H), 1.60−1.71 (m, 4H), 1.13−1.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 76.2, 69.0, 30.2, 26.8, 26.1, 21.7, 21.1; HRMS (ESI) for $C_8H_{13}BrO_3$ calcd for $[M + Na]^+$ m/z 258.9940, found 258.9941.

***cis*-2-(2-Bromoacetoxy)cyclohexyl isobutyrate (8b):** yield 94%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05−5.09 (m, 2H), 3.82 (s, 2H), 2.55 (septet, J = 7.0 Hz, 1H), 1.82−1.91 (m, 2H), 1.64−1.70 (m, 4H), 1.44−1.49 (m, 2H), 1,17 (dd, J = 3.6, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 166.5, 73.2, 70.1, 34.1, 27.6, 27.4, 25.9, 21.6, 21.5, 19.0, 18.9; HRMS (ESI) for $C_{12}H_{19}BrO_4$ calcd for $[M + Na]^+$ m/z 329.0359, found 329.0357; $[\alpha]^{20}_D$ −1.3 (c 1.0, CH_2Cl_2) 60:40 er; GC analysis: Beta DEX 120 column (30 m × 0.25 mm × 0.25 μm film thickness), 177 °C for 40 min, 3 deg/min to 190 °C, 11 psi, t_R = 20.9 min (1*R*,2*S*, minor), 21.3 min (1*S*,2*R*, major). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxy-*trans*-6-methylcyclohexyl 2,2-dichloroacetate (9):**[16] white solid; mp 70−72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 (s, 1H), 4.65 (dd, J = 2.6, 10.0 Hz, 1H), 4.09−4.11 (m, 1H), 2.10−2.21 (m, 1H), 1.90−1.96 (m, 1H), 1.75−1.81 (m, 2H), 1.64−1.72 (m, 1H), 1.44−1.54 (m, 2H), 1.04−1.16 (m, 1H), 0.95 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 83.8, 67.3, 64.5, 32.5, 31.0, 30.7, 18.7, 17.7; HRMS (ESI) for $C_9H_{14}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 263.0212, found 263.0219.

***cis*-2-Hydroxy-*trans*-3-methylcyclohexyl 2,2-dichloroacetate (10):**[16] Compound **9** was crystallized from the mixture of compounds **9** and **10**. But pure compound **10** was inseparable from the mixture of compounds **9** and **10**. The NMR data of compound **10** were deduced from the mixture's NMR spectrum. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (s, 1H), 5.22 (br s, 1H), 3.16−3.43 (m, 1H), 2.05−2.10 (m, 1H), 1.76−1.78 (m, 1H), 1.49−1.68 (m, 5H), 1.26 (br s, 1H), 1.05 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 77.3, 75.9, 64.6, 34.4, 32.3, 28.7, 19.5, 18.3.

***trans*-2-Hydroxy-*cis*-6-methylcyclohexyl 2,2-dichloroacetate (11):**[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 (s, 1H), 4.81 (dd, J = 4.0, 6.4 Hz, 1H), 3.94−3.97 (m, 1H), 2.26−2.31 (m, 1H), 2.05−2.19 (m, 1H), 1.90 (br s, 1H), 1.46−1.64 (m, 5H), 0.96 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 81.2, 67.0, 64.5, 30.5, 30. 4, 29.2, 18.8, 14.9; HRMS (ESI) for $C_9H_{14}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 263.0212, found 263.0221.

***trans*-2-Hydroxy-*trans*-3-methylcyclohexyl 2,2-dichloroacetate (12):**[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (s, 1H), 4.96−4.98 (m, 1H), 3.75 (br s, 1H), 2.03−2.08 (m, 1H), 1.92−1.97 (m, 1H), 1.76 (br s, 1H), 1.54−1.58 (m, 3H), 1.47−1.49 (m, 2H), 1.0 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 76.6, 71.9, 64.5, 32.6, 28.4, 26.5, 19.3, 14.9; HRMS (ESI) for $C_9H_{14}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 263.0212, found 263.0220.

(*S*)-Methyl 2-(3,5-di-*tert*-butyl-2-hydroxyphenylthioamido)-3-(1-methyl-1*H*-imidazol-5-yl)propanoate (13):[8]**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.38 (s, 1H), 7.01 (s, 1H), 6.80 (s, 1H), 5.44−5.48 (m, 1H), 3.85 (s, 3H), 3.56−3.61 (m, 4H), 3.38 (d, J = 15.6 Hz, 1H), 1.42 (s, 9H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7, 170.7, 154.8, 141.2, 138.7, 138.6, 128.5, 128.1, 125.9, 123.1, 118.7, 56.6, 53.1, 35.4, 34.3, 31.6, 31.3, 29.5, 24.6; HRMS (ESI) for $C_{23}H_{33}N_3O_3S$ calcd for $[M + H]^+$ m/z 432.2315, found 432.2321.

***cis*-2-Hydroxycyclopentyl 2,2-dichloroacetate (14a):** white solid; mp 46−49 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (s, 1H), 5.09−5.13 (m, 1H), 4.25−4.29 (m, 1H), 1.84−2.06 (m, 5H), 1.69−1.78 (m, 1H), 1.58−1.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 80.0, 73.3, 64.4, 30.6, 27.8, 19.3; HRMS (ESI) for $C_7H_{10}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 234.9899, found 234.9902.

***cis*-2-(2,2-Dichloroacetoxy)cyclopentyl isobutyrate (14b):** yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (s, 1H), 5.27−5.31 (m, 1H), 5.14−5.19 (m, 1H), 2.53 (septet, J = 7.0 Hz, 1H), 2.01−2.08 (m, 2H), 1.77−1.98 (m, 3H), 1.63−1.72 (m, 1H), 1.16 (d, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 163.8, 77.5, 73.8, 64.3, 33.9, 29.7, 28.1, 27.8, 19.1, 18.8; HRMS (ESI) for $C_{11}H_{16}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 305.0318, found 305.0323; $[\alpha]^{20}_D$ −4.2 (c 1.0, CH_2Cl_2) for 83:17 er; GC analysis: Beta DEX 120 column (30 m × 0.25 mm × 0.25 μm film thickness), 152 °C for 100 min, 1 deg/min to 190 °C, 11 psi, t_R = 63.5 min (1*R*,2*S*, minor), 64.8 min (1*S*,2*R*, major). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxycyclopentyl isobutyrate (14c):** yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97 (q, J = 5.4, 10.8 Hz, 1H), 4.19 (q, J = 4.8, 9.6 Hz, 1H), 2.60 (septet, J = 7.2 Hz, 1H), 1.96−2.04 (m, 1H), 1.83−1.94 (m, 2H), 1.67−1.78 (m, 2H), 1.52−1.61 (m, 2H), 1.19 (dd, J = 2.4, 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 76.4, 73.2, 34.0, 30.6, 28.1, 19.4, 19.0, 18.9; HRMS (ESI) for $C_9H_{16}O_3$ calcd for $[M + Na]^+$ m/z 195.0992, found 195.0994; GC analysis: Gamma DEX 225 column (30 m × 0.25 mm × 0.25 μm film thickness), 120 °C for 28 min, 11 psi, t_R = 20.1 min (1*R*,2*S*, minor), 20.8 min (1*S*,2*R*, major).

***cis*-2-Hydroxycycloheptyl 2,2-dichloroacetate (15a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (s, 1H), 5.09 (dt, J = 2.6, 9.0 Hz, 1H), 4.03−4.06 (m, 1H), 2.03−2.12 (m, 1H), 1.68−1.90 (m, 6H), 1.56−1.64 (m, 2H), 1.42−1.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 81.2, 72.0, 64.5, 31.4, 27.0, 26.6, 22.1, 21.7; HRMS (ESI) for $C_9H_{14}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 263.0212, found 263.0210.

***cis*-2-(2,2-Dichloroacetoxy)cycloheptyl isobutyrate (15b):** yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.22 (dt, J = 2.6, 7.6 Hz, 1H), 5.10 (dt, J = 2.6, 9.0 Hz, 1H), 2.54 (septet, J = 7.0 Hz, 1H), 1.93−2.04 (m, 2H), 1.52−1.85 (m, 8H), 1.16 (dd, J = 1.8, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 163.7, 78.1, 73.7, 64.5, 34.1, 28.5, 28.3, 26.4, 22.4, 22.1, 18.9, 18.8; HRMS (ESI) for $C_{13}H_{20}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 333.0631, found 333.0634; $[\alpha]^{20}_D$ −5.4 (c 1.0, CH_2Cl_2) 87:13 er; HPLC (Chiralcel OD-H, hexane:2-propanol = 96:4, flow rate = 0.15 mL/min) 210 nm, t_R = 29.7 min (1*S*,2*R*, major), 31.4 min (1*R*,2*S*, minor). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxycyclooctyl 2,2-dichloroacetate (16a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 1H), 5.16 (dt, J = 2.4, 9.6 Hz, 1H), 4.05 (br s, 1H), 2.12−2.21 (m, 1H), 2.02 (br s, 1H), 1.82−1.93 (m, 2H), 1.48−1.79 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 80.8, 71.2, 64.5, 30.2, 26.9, 26.8, 25.3, 24.2, 21.7; HRMS (ESI) for $C_{10}H_{16}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 277.0369, found 277.0371.

***cis*-2-(2,2-Dichloroacetoxy)cyclooctyl isobutyrate (16b):** yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (s, 1H), 5.23−5.26 (m, 1H), 5.17−5.19 (m, 1H), 2.53 (septet, J = 6.8 Hz, 1H), 2.01−2.09 (m, 2H), 1.61−1.83 (m, 10H), 1.16 (dd, J = 2.4, 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 163.8, 77.5, 72.7, 64.5, 34.1, 28.1, 27.9, 26.3, 25.9, 23.2, 22.4, 18.9, 18.8; HRMS (ESI) for $C_{14}H_{22}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 347.0787, found 347.0788; $[\alpha]^{20}_D$ −2.0 (c 1.0, CH_2Cl_2) for 85:15 er; HPLC (Chiralcel OJ-H, hexane:2-propanol = 96:4, flow rate = 0.2 mL/min) 210 nm, t_R = 23.5 min (1*S*,2*R*, major), 26.1 min (1*R*,2*S*, minor). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-2-Hydroxycyclododecyl 2,2-dichloroacetate (17a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 1H), 5.19 (t, J = 6 Hz, 1H), 3.91−3.94 (m, 1H), 1.62−1.84 (m, 5H), 1.35−1.63 (m, 16H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.6, 79.5, 71.1, 64.5, 29.6, 28.8, 24.5, 24.4, 24.2, 23.6, 23.5, 21.7, 21.6, 21.1; HRMS (ESI) for $C_{14}H_{24}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 333.0995, found 333.0990.

***cis*-2-(2,2-Dichloroacetoxy)cyclododecyl isobutyrate (17b):** yield 95%; white solid; mp 30−33 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (s, 1H), 5.16−5.21 (m, 2H), 2.53 (septet, J = 7.0 Hz, 1H), 1.80−1.86 (m, 2H), 1.61−1.67 (m, 2H), 1.25−1.52 (m, 16H), 1.16 (dd, J = 2.5, 7.0 Hz, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 176.8, 164.1, 77.3, 71.5, 71.4, 64.5, 34.1, 29.7, 24.42, 24.38, 24.3, 23.6, 23.5, 21.7, 21.6, 21.0, 18.9, 18.8; HRMS (ESI) for $C_{18}H_{30}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 403.1413, found 403.1407; $[\alpha]^{20}_D$ −4.5 (c 1.0, CH_2Cl_2) for 77:23 er; HPLC (Chiralcel OD-H, hexane:2-propanol = 99:1, flow rate = 0.4 mL/min) 210 nm, t_R = 10.5 min (1*S*,2*R*, major), 11.1 min (1*R*,2*S*, minor). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-6-Hydroxycyclohex-3-enyl 2,2-dichloroacetate (18a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 (s, 1H), 5.59−5.66 (m, 2H), 5.19−5.21 (m, 1H), 4.12−4.15 (m, 1H), 2.45−2.48 (m, 3H), 2.29−2.34 (m, 1H), 2.02 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 123.8, 122.7, 75.7, 66.8, 64.4, 31.3, 27.5; HRMS (ESI) for $C_8H_{10}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 246.9899, found 246.9902.

***cis*-6-(2,2-Dichloroacetoxy)cyclohex-3-enyl isobutyrate (18b):** yield 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.60−5.68 (m, 2H), 5.34 (t, J = 5 Hz, 1H), 5.20 (t, J = 6.4 Hz, 1H), 2.51−2.58 (m, 2H), 2.39−2.41 (m, 3H), 1.16 (t, J = 6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 164.0, 123.9, 122.6, 72.5, 68.3, 64.4, 34.1, 28.6, 27.8, 18.9, 18.8; HRMS (ESI) for $C_{12}H_{16}Cl_2O_4$ calcd for $[M+Na]^+$ m/z 317.0318, found 317.0315; $[\alpha]^{20}_D$ −5.5 (c 1.0, CH_2Cl_2) for 83:17 er; GC analysis: Beta DEX 120 column (30 m × 0.25 mm × 0.25 μm film thickness), 148 °C for 100 min, 1 deg/min to 200 °C, 12 psi, t_R = 80.1 min (1*R*,2*S*, minor), 81.9 min (1*S*,2*R*, major). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-6-Hydroxycyclohex-3-enyl isobutyrate (18c):** yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57−5.63 (m, 2H), 5.06−5.09 (m, 1H), 4.05 (t, J = 6.4 Hz, 1H), 2.60 (septet, J = 6.8 Hz, 1H), 2.32−2.44 (m, 3H), 2.28−2.30 (m, 1H), 2.19 (br s, 1H), 1.18 (dd, J = 3.6, 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 123.7, 123.3, 71.7, 67.4, 34.1, 31.3, 28.0, 19.0, 18.9; HRMS (ESI) for $C_{10}H_{16}O_3$ calcd for $[M + Na]^+$ m/z 207.0992, found 207.0991; GC analysis: Beta DEX 120 column (30 m × 0.25 mm × 0.25 μm film thickness), 155 °C for 18 min, 10.6 psi, t_R = 14.4 min (1*S*,2*R*, major), 14.7 min (1*R*,2*S*, minor).

***cis*-8-Hydroxycyclooct-4-enyl 2,2-dichloroacetate (19a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 1H), 5.70−5.81 (m, 2H), 5.16 (dd, J = 3.8, 8.6 Hz, 1H), 4.11 (t, J = 6.2 Hz, 1H), 2.49−2.64 (m, 2H), 2.26 (br s, 1H), 1.98−2.26 (m, 3H), 1.78−1.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 130.9, 129.6, 83.1, 73.3, 64.5, 33.1, 29.2, 21.6, 21.3; HRMS (ESI) for $C_{10}H_{14}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 275.0212, found 275.0213.

***cis*-8-(2,2-Dichloroacetoxy)cyclooct-4-enyl isobutyrate (19b):** yield 89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (s, 1H), 5.76 (t, J = 5 Hz, 2H), 5.23 (dd, J = 4, 7.6 Hz, 1H), 5.19 (dd, J = 4.8, 8.4 Hz, 1H), 2.52−2.63 (m, 3H), 1.99−2.09 (m, 4H), 1.75−1.91 (m, 2H), 1.18 (dd, J = 3.2, 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 163.8, 130.1, 129.8, 79.8, 74.6, 64.5, 34.1, 29.9, 29.8, 21.4, 21.2, 18.9, 18.8; HRMS (ESI) for $C_{14}H_{20}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 345.0631, found 345.0631; $[\alpha]^{20}_D$ −4.4 (c 1.0, CH_2Cl_2) for 80:20 er; HPLC (Chiralcel OJ-H, hexane:2-propanol = 98:2, flow rate = 0.5 mL/min) 210 nm, t_R = 10.9 min (1*S*,2*R*, major), 12.5 min (1*R*,2*S*, minor). The absolute stereochemistry was determined by analogy with that of **6b**.

***cis*-3-Hydroxybutan-2-yl 2,2-dichloroacetate (20a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (s, 1H), 4.97 (dq, J = 3.6, 6.4 Hz, 1H), 3.96 (dq, J = 3.6, 6.4 Hz, 1H), 1.93 (br s, 1H), 1.31 (d, J = 6.4 Hz, 3H), 1.23 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 78.0, 69.0, 64.4, 17.9, 13.8; HRMS (ESI) for $C_6H_{10}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 222.9899, found 222.9903.

***cis*−3-(2,2-Dichloroacetoxy)butan-2-yl isobutyrate (20b):** yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (s, 1H), 5.13 (dq, J = 3.5, 6.6 Hz, 1H), 5.04 (dq, J = 3.5, 6.6 Hz, 1H), 2.54 (septet, J = 7.0 Hz, 1H), 1.32 (d, J = 6.6 Hz, 3H), 1.26 (d, J = 6.6 Hz, 3H), 1.16 (dd, J = 3.4, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 163.8, 74.9, 70.4, 64.4, 34.1, 18.9, 18.8, 14.9, 14.5; HRMS (ESI) for $C_{10}H_{16}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 293.0318, found 293.0321; $[\alpha]^{20}_D$ −1.3 (c 1.0, CH_2Cl_2) for 84:16 er; HPLC (Chiralcel OD-H, hexane:2-propanol = 96:4, flow rate = 0.3 mL/min) 210 nm, t_R = 14.8 min (major), 15.9 min (minor).

***cis*-3-Hydroxybutan-2-yl isobutyrate (20c):** yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87 (dq, J = 3.2, 6.4 Hz, 1H), 3.86−3.91 (m, 1H), 2.56 (septet, J = 6.8 Hz, 1H), 1.97 (br s, 1H), 1.16−1.22 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 74.0, 69.7, 34.1, 19.0, 18.9, 17.8, 14.2; GC analysis: Gamma DEX 225 column (30 m × 0.25 mm × 0.25 μm film thickness), 120 °C for 10 min, 11 psi, t_R = 8.5 min (minor), 8.8 min (major).

***cis*-5-Hydroxyoctan-4-yl 2,2-dichloroacetate (21a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 1H), 4.98 (dt, J = 3.4, 9.6 Hz, 1H), 3.77−3.80 (m, 1H), 1.75−1.79 (m, 1H), 1.71−1.72 (m, 1H), 1.53−1.64 (m, 2H), 1.28−1.48 (m, 5H), 0.92−0.97 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 80.9, 72.4, 64.5, 34.1, 30.5, 18.9, 18.6, 13.9, 13.8; HRMS (ESI) for $C_{10}H_{18}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 279.0523, found 279.0520.

***cis*-5-(2,2-Dichloroacetoxy)octan-4-yl isobutyrate (21b):** yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (s, 1H), 5.12 (dt, J = 3.4, 9.6 Hz, 1H), 5.03 (dt, J = 3.4, 10.0 Hz, 1H), 2.54 (septet, J = 7.0 Hz, 1H), 1.51−1.74 (m, 4H), 1.27−1.47 (m, 4H), 1.16 (dd, J = 1.6, 7.0 Hz, 6H), 0.91−0.96 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 164.1, 77.9, 73.1, 64.5, 34.1, 31.4, 30.8, 18.9, 18.8, 18.7, 18.6, 13.8, 13.7; HRMS (ESI) for $C_{14}H_{24}Cl_2O_4$ calcd for $[M+Na]^+$ m/z 349.0944, found 349.0943; $[\alpha]^{20}_D$ −1.0 (c 1.0, CH_2Cl_2) for 81:19 er; HPLC (Chiralcel OD-H, hexane:2-propanol = 99:1, flow rate = 0.4 mL/min) 210 nm, t_R = 9.8 min (major), 10.3 min (minor).

***cis*-3-Hydroxycyclohexyl 2,2-dichloroacetate (22a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (s, 1H), 4.82−4.90 (m, 1H), 3.71−3.77 (m, 1H), 2.29−2.32 (m, 1H), 2.12−2.14 (m, 1H), 1.86−1.99 (m, 3H), 1.25−1.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 74.7, 68.1, 64.4, 39.8, 34.0, 30.0, 19.6; HRMS (ESI) for $C_8H_{12}Cl_2O_3$ calcd for $[M + Na]^+$ m/z 249.0056, found 249.0057.

***cis*-3-(2,2-Dichloroacetoxy)cyclohexyl isobutyrate (22b):**[19] yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (s, 1H), 4.85−4.92 (m, 1H), 4.74−4.81 (m, 1H), 2.52 (septet, J = 7.0 Hz, 1H), 2.29−2.33 (m, 1H), 2.01−2.03 (m, 1H), 1.87−1.96 (m, 2H), 1.56−1.64 (m, 1H), 1.30−1.48 (m, 3H), 1.16 (dd, J = 1.0, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 163.7, 74.1, 69.5, 64.4, 36.3, 34.0, 30.4, 30.1, 19.6, 18.9, 18.8; HRMS (ESI) for $C_{12}H_{18}Cl_2O_4$ calcd for $[M + Na]^+$ m/z 319.0479, found 319.0471; $[\alpha]^{20}_D$ −0.6 (c 1.0, CH_2Cl_2) for 20% ee (60:40 er); HPLC (Chiralpeak AD-H, hexane:2-propanol = 97:3, flow rate = 0.4 mL/min) 210 nm, t_R = 21.6 min (1*R*,3*S*, minor), 23.2 min (1*S*,3*R*, major). The absolute configuration was determinded by comparing the optical rotation value with that reported for (1*S*,3*R*)-3-hydroxycyclopentyl acetate after removal of the dichloroacetoxy group.

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Supporting Information Available: General procedure for the synthesis of substrates and products in Schemes 3 and 4 and Tables 1, 4, and 5, ^{1}H NMR, ^{13}C NMR, and HRMS spectra, and ^{1}H NMR analysis of the dichloroacetoxy migration. This material is available free of charge via the Internet at http://pubs.acs.org.