New ways to determine the absolute configurations of alkyl 6-R-cyclohexa-1,3-dienecarboxylates*

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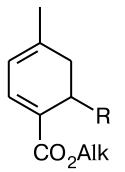
Two new methods for the determinatuion of the absolute configuration of methyl 4-methyl-6-(2-methylprop-1-enyl)cyclohexa-1,3-dienecarboxylate are proposed, and the configurations attributed previously to its (+)- and (−)-enantiometers are confirmed. Chiral methyl carboxylate is converted into the corresponding alcohol whose configuration is deduced from either the rate of hydrolysis of the respective racemic acetate in the presence of pancreatic lipase (method 1) or from the difference between the $Eu(fod)_3$-induced shifts of the MeO signals in the ^1H NMR spectra of the diastereomeric esters of *S*- or *R*-Mosher´s acid (method 2).

Key words: [4-methyl-6-(2-methylprop-1-enyl)cyclohexa-1,3-diene]methanol, synthesis and acylation; pancreatic lipase, hydrolysis of acetates; europium(III); complexation with esters of Mosher´s acid.

Originally, the absolute configuration of cyclohexadienecarboxylates of the type **1** was deduced from the signs of displacement of diagnostic chemical shifts δ_H in their ^1H NMR spectra induced by chiral solvating agents, (*S*)-BINOL and (*R*)-BINOL.[1] Previously, this method has been used to determine the absolute configurations of chiral sulfoxides.[2] The assignments made in the study cited[1] relied only on the known similarity between the carbonyl and sulfoxide groups.[3] The purpose of the present work is to verify the validity of the absolute configurations attributed to the (+)- and (−)-enantiomers of esters **1** by employing some other independent methods. Two ways of determining the configuration have been tried in relation to scalemic ester (+)-**1a** (R = Me_2C=CH, Alk = Me); specimens of this ester with different *ee* have been obtained previously.[1,4] Both procedures start with the hydride reduction of ester **1a** to give the corresponding primary alcohol **2**.



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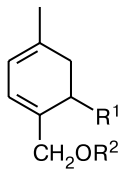
R = Ph, α-furyl, PhCH=CH, Me_2CH, Me_2CHCH_2, Me_2C=CH, Me; Alk = Me, Et, Bu^t



2, 3

R^1 = Me_2C=CH; R^2 = H (**2**), Ac (**3**)

* Dedicated to Academician I. P. Beletskaya on the occasion of her anniversary.

Procedure 1. Determination of the configuration using pancreatic lipase

An original approach to the determination of the configurations of the (+)- and (−)-enantiomers of alcohol **2** is based on enzymatic hydrolysis of the acetates of racemic alcohols mediated by porcine pancreatic lipase (PPL). The enantioselectivity of this reaction has been studied rather comprehensively. Several models have been proposed to explain the enantioselectivity of ester hydrolysis inherent in PPL.[5] A general interpretation explains this selectivity in terms of a conformational substrate model (CSM).[6] According to the CSM, hydrolysis is faster for that component of a racemic acetate whose fixation *in a conventional mode* on a *conventional* diastereofaceous plane in a specific W-shaped conformation (no less than five coplanar C and O atoms in succession at the end of the chain including the reaction center) results in a situation where the bulkiest substituent at the asymmetric carbon atom nearest to the reaction center in the alcohol fragment falls into the sterically less hindered sector located *conventionally* on the α-side of this plane. A similar fixation of the W-shaped conformation of the second enantiomer forces this substituent into the sterically congested ("viscous") sector, located *conventionally* on the β-side of the diastereodiscriminating plane, and thus retards the hydrolysis. The configurations of esters (+)-**1a** and (−)-**1a** were deduced by comparing the specimens of alcohol **2** obtained by hydride reduction of ester (+)-**1a** and by partial hydrolysis of racemic acetate (±)-**3** in the presence of PPL.

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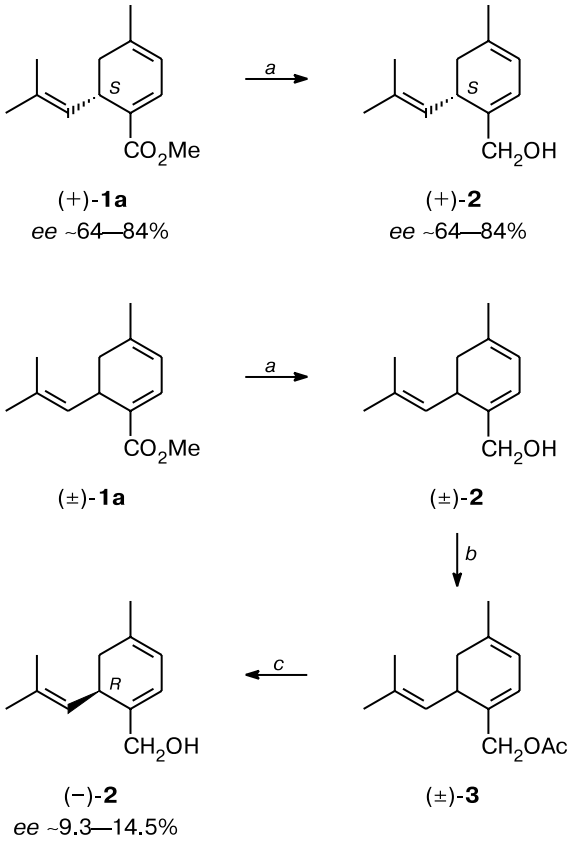
Specimens of ester (+)-**1a** with $[\alpha]_D^{20}$ +248 or +190 (*c* 1.0, PhH) were reduced with $LiAlH_4$ in an Et_2O—THF mixture, and specimens of alcohol (+)-**2** with $[\alpha]_D^{20}$ +148 and +134, respectively (*c* 1.0, PhH), were isolated in 66—74% yields. According to the assignment made previously for ester (+)-**1a**,[1] they had to be identified as having the *S*-configuration and *ee* ~84 and ~64%, respectively. The known racemic ester (±)-**1a** [7] was converted in the same way into alcohol (±)-**2**, which was transformed into acetate (±)-**3** by the standard method. Hydrolysis of acetate (±)-**3** in an 0.1 *M* phosphate buffer (pH 6.8, 20 °C; **3** : PPL = 2 : 1 w/w), to ~10% and 32% degrees of conversion afforded specimens of alcohol (−)-**2** with $[\alpha]_D^{20}$ −41 and −27.5 (*c* 1.0, PhH), respectively. In conformity with previous data,[1] the *R*-configuration and *ee* ~14.5 and 9.3% were ascribed to the levorotatory enantiomer of acetate **3** whose hydrolysis was faster (Scheme 1). To verify these assignments, we calculated the G°_{298} values for the most stable configuration and the W-shaped conformation of acetate **3** in order to estimate the population of the W-shaped conformer under the conditions of hydrolysis.

Scheme 1



Reagents: *a*. $LiAlH_4$/THF—Et_2O (66—74%); *b*. Ac_2O/Py—DMAP (71%); *c*. H_2O (pH 6.8)/PPL (conversion *C* ~10 or 32%).

Using the CSM, these data would help to determine which of the enantiomers of acetate **3** has the $Me_2C{=}CH$ ligand at C(6) in the α-sector.

MNDO calculations showed that acetate **3** is most stable in conformation **A** where the $Me_2C{=}CH$ group and the AcO group are located on opposite sides of the ring at a maximum distance from each other (Fig. 1, *a*). The calculated ΔG°_{298} value for the transition of conformation **A** into the W-shaped conformation **B**, in which the CH_2OAc fragment is almost coplanar with the ring diene system (Fig. 1, *b*), was 1.17 kcal mol^{-1}. Thus, it follows that the equilibrium constant K = [**B**]/[**A**] amounts to ~0.14 and the [**B**]/[**A**] ratio is ~12 : 88. Therefore, the binding of conformation **B** to the active site of PPL, as on the postulated plane, is energetically admissible. According to the CSM, of the two enantiomers of acetate **3**, the *R*-enantiomer is fixed on the diastereofaceous plane in a position favorable for hydrolysis, because its $Me_2C{=}CH$ group is directed toward the sterically less hindered α-side. When molecule (*S*)-**3** in conformation **B** is fixed on the diastereofaceous plane, the $Me_2C{=}CH$ group falls into the sterically hindered β-sector and hydrolysis is decelerated.

Since the sign of $[\alpha]_D$ did not change upon the reduction of ester (+)-**1a** into alcohol **2**, alcohol (−)-**2** resulting from enzymatic hydrolysis should correspond to ester (−)-**1a**, which has previously been identified[1] as *R*-enantiomer. Thus, within the framework of the CSM the configurations of (+)-**2** and (−)-**2** are consistent with configurations assigned previously for esters (*S*)-(+)-**1a** and (*R*)-(−)-**1a**.

Procedure 2. Determination of the configuration from the Eu^{III}-induced shift (δ_H) in the ^1H NMR spectra of Mosher´s esters (MTPA esters)

Yet another way of validating the configurations assigned to esters (+)-**1a** and (−)-**1a** involves the determination of absolute configuration of the β-C atom in alcohols of the type $RCH(R^1)CH_2OH$ from the europium β-diketonate-induced shift of the signals for the protons of the CH_3O group in the ^1H NMR spectra of their (*R*)- and (*S*)-MTPA esters.[8] It was important to find out whether this method can be extended to the MTPA esters of alcohols like **2** (esters **4**) in which the asymmetric center is remote from the reaction center. We proceeded from the premises given in the original publication,[8a] namely, (*1*) coordination of Eu ion to two *O*-atoms of the MTPA moiety occurs in the most stable conformation of the MTPA ester and from the side favorable for complexation; in this particular case, this is either the front or the rear of the plane through the C(4) and C(1) atoms and the O—C(=O)—C* group; (*2*) the stronger the coordination of Eu to the MTPA ester the larger the downfield shift of δ_{OCH_3} (Scheme 2).

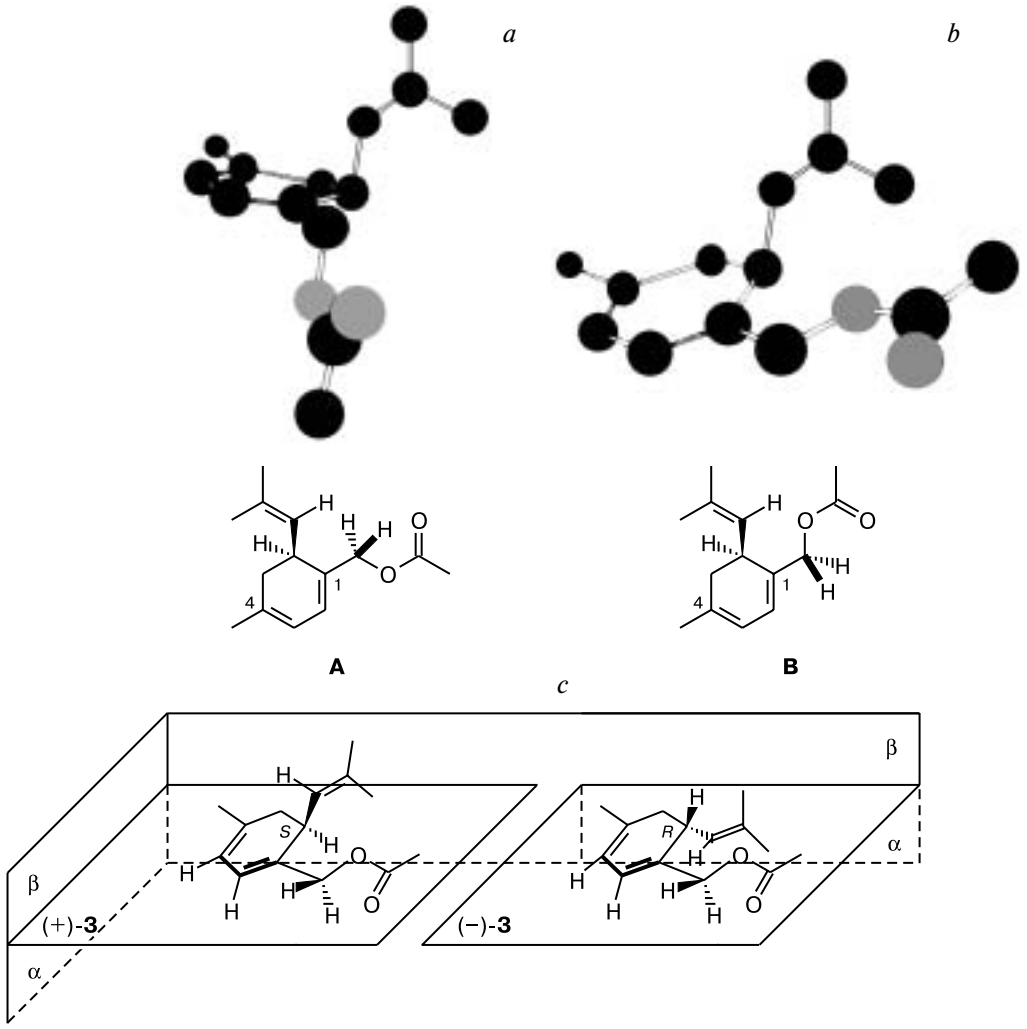


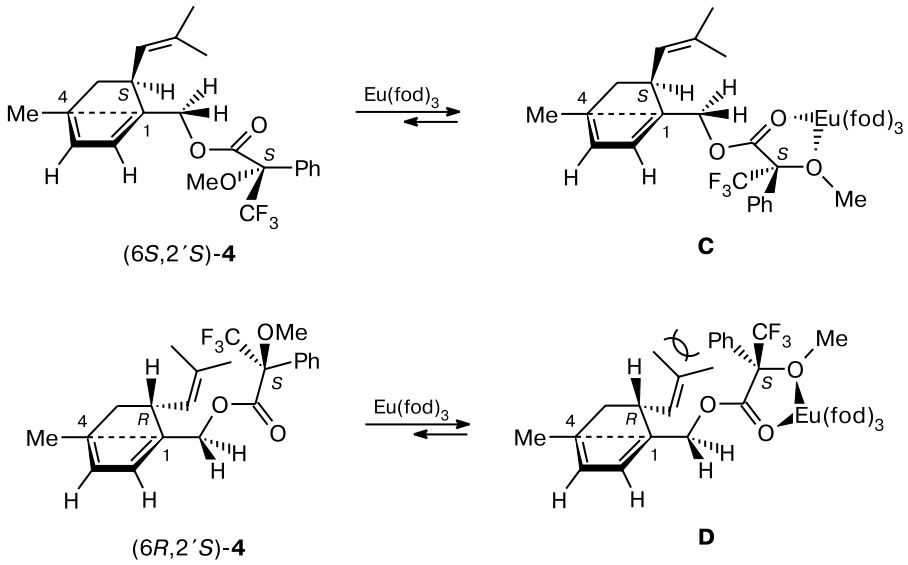
Fig. 1. *a*. Stable conformation **A** of acetate (*S*)-**3**. The C(1) and C(4) atoms of the ring and the 4-CH_3 and CH_2OAc groups lie in the plane orthogonal to the diastereofaceous plane that accommodates the substrate molecule; the $Me_2C{=}CH$ and CH_2OAc groups are removed as far as possible from each other. *b*. W-conformation **B**. The C and O atoms of the CH_2OCOCH_3 group lie in the diastereozero plane of molecule **3**. *c*. Determination of the absolute configuration of alcohols (+)-**2** and (−)-**2** from the rates of hydrolysis of their acetates in terms of the conformational substrate model with PPL. The fixation of the W-conformation of molecule (−)-**3** on the diastereonought plane is consistent with a higher rate of hydrolysis for (*R*)-**3** compared to (*S*)-**3**; α is the α-side (sterically nonhindered), fast hydrolysis in the presence of PPL; β is the β-side (sterically hindered), slow hydrolysis in the presence of PPL.

In the case where the lanthanide approaches the less hindered side of the *S*,*S*-diastereomer (Scheme 2), the resulting chelate **C** is sterically less hindered than its diastereomer **D**. The downfield shift of the OMe signal in the ^{1}H NMR spectrum of **C** is relatively large. When the lanthanide comes from the less hindered side of the (6*R*,2′*S*)-diastereomer (Scheme 2), the resulting chelate **D** is sterically more congested than diastereomer **C**. The downfield shift of the OMe signal in its ^{1}H NMR spectrum is relatively small.

Scalemic alcohol **2** with $[\alpha]_D^{20}$ +134 (*ee* ~64%) was acylated with (*R*)- or (*S*)-MTPA chloride to give a binary mixture of diastereomeric MTPA esters (Scheme 3); their ^{1}H NMR spectra in $CDCl_3$ were recorded. Then $Eu(fod)_3$ was added to solutions of the diastereomeric MTPA esters (in the pair of (*S*)-MTPA esters, [(6*S*,2′*S*)-**4**] > > [(6*R*,2′*S*)-**4**], while in the pair of (*R*)-MTPA esters, [(6*S*,2′*R*)-**4**] > [(6*R*,2′*R*′)-**4**]), and the shifts of the signals for the OMe groups were measured in the spectra of binary mixtures of the chelates thus formed.

The values of the lanthanide-induced downfield shifts (LIDS) of the OMe-group signals for the major and minor diastereomers were used to determine the strength of the $Eu(fod)_3$ complexes with each of the four MTPA esters. This provided grounds for deducing the configurations of the major and minor enantiomer in the starting scalemic alcohol (+)-**2**. The results are presented in Table 1. Tentative MNDO calculations showed that the

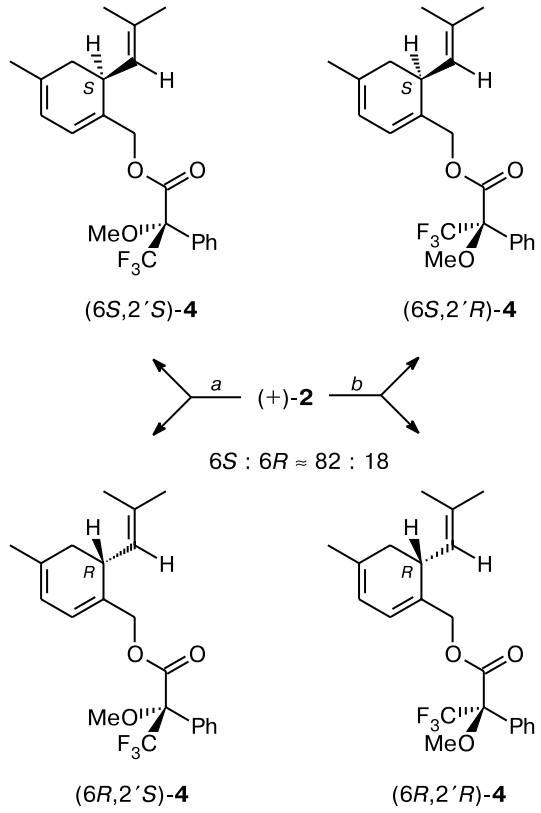
Scheme 2



stable conformation of the four MTPA esters of alcohol **2** is similar to conformation **A** of acetate **3** (see Fig. 1, *a*).

It can be seen (see Table 1 and Scheme 2) that in the pair of diastereomeric (*S*)-MTPA esters formed by the major alcohol (+)-**2** and by its minor (levorotatory) enantiomer, a larger LIDS for OCH_3 belongs to the chelate of the major diastereomer. This diastereomer is formed upon such an approach of $Eu(fod)_3$ to the stable conformer of the MTPA ester where the bulky substituents in the alcoholic (Me_2C=CH) and acyl (Ph) fragments of the molecule occupy opposite sides of the plane passing through the C(4) and C(1) atoms and the O—C(=O)—C* triad. In the case of *S*-configuration of the acyl fragment, this approach is expected to be from the "rear" side of this plane, which is possible only when the distance between $Eu(fod)_3$ and Me_2C=CH is substantial, and this implies *S*-configuration of the C(6) center in the alcoholic fragment. The smaller LIDS (see Scheme 2) should refer to the minor diastereomer (6*R*,2′*S*)-**4** and its complex with $Eu(fod)_3$ in which both the Me_2C=CH and Ph groups are located on one side of the plane accommodating the C(4) and C(1) atoms and the O—C(=O)—C* fragment (in this case, the approach of $Eu(fod)_3$ to the stable conformer of ester (6*R*,2′*S*)-**4** occurs from the "frontal" side of the plane). In the pair of diastereomeric (*R*)-MTPA esters, the stereochemical situation for the major and minor components is reversed: the complex formed by the minor (*R*,*R*)-ester is more stable, while the complex of the (6*S*,2′*R*)-ester with $Eu(fod)_3$ is more labile. The LIDS in the ^{1}H NMR spectrum change accordingly.

Scheme 3



a. (*R*)-(−)-MTPA-Cl; *b*. (*S*)-(+)-MTPA-Cl

Thus, determination of the configurations of the major and minor enantiomers in scalemic alcohol (+)-**2** led to the same conclusion as the use of CSM, namely, alcohol (+)-**2** has the *S*-configuration. Since (+)-**2** was prepared by hydride reduction of ester (+)-**1a**, this confirms the *S*-configuration of this ester determined previously. In previous studies[1,4] where ^{1}H NMR spectroscopy was used in combination with BINOL, *S*-configurations were

Table 1. Determination of the absolute configuration of alcohols (+)-**2** and (−)-**2** from the induced shift ($\Delta\delta_H$) of the OMe-group signals in the ^{1}H NMR spectra of binary mixtures of MTPA esters **4**

MTPA fragment in the Eu chelate	$Eu(fod)_3$ in the sample (mol.%)	δ_{OCH_3} ($\Delta\delta_H$)		Configuration of alcohol **2** with greater $\Delta\delta_H$
		major peak	minor peak	
(*S*)-MTPA	0	3.47	3.43	
	25	3.59	3.49	*S*
		(0.12)	(0.06)	
(*R*)-MTPA	0	3.42	3.46	
	25	3.49	3.57	*R*
		(0.07)	(0.11)	

assigned to all dextrorotatory cyclohexadienes (when R = Me, this is formally the *R*-enantiomer) and *R*-configurations were found for the levorotatory compounds (except for the case where R = Me). Moreover, the agreement of the results of the determining of the absolute configuration of ester (+)-**1a** by three independent methods validates other previous assignments of the absolute configurations of these esters.[1,4]

This allows one to interpret more reliably the effects of various factors on the stereoselectivity of the catalytic asymmetric synthesis of cyclohexadienes.[1,4]

Experimental

NMR spectra were recorded in $CDCl_3$ at 20 °C on Bruker AM-300 (operating at 300.13 MHz, for ^{1}H) and Bruker AC-200 (operating at 50.3 MHz, for ^{13}C) spectrometers. IR spectra were measured for solutions in $CHCl_3$ on a Specord IR-80 instrument. The $[\alpha]_D$ values were determined on a JASCO DIP-360 polarimeter for solutions in C_6H_6 at 16—22 °C. Mass spectra were run on a Finnigan MAT INCOS-50 mass spectrometer (EI, 70 eV, direct inlet). The completeness of the reactions and the product purity were checked by TLC on Silufol UV-254 plates. Column chromatography was carried out on neutral Silica gel 40 (Fluka, particle size 0.04—0.06 mm). All solvents were purified[9] prior to use. Porcine pancreatic lipase with a specific activity of 14.7 units mg^{-1} (Serva) or 47 units mg^{-1} (OlainFarm, Latvia), $LiAlH_4$, $Eu(fod)_3$, and (*S*)- and (*R*)-MTPA (Fluka) were used as purchased. Specimens of ester (+)-**1a** were prepared by a known procedure,[1] and the specimen of ester (±)-**1a** was prepared similarly.[7]

(+)-[4-Methyl-6-(2-methylprop-1-enyl)cyclohexa-1,3-diene]methanol, (*S*)-2. A 1.4 *M* solution (0.5 mL) of $LiAlH_4$ (~27 mg, 0.7 mmol) in anhydrous THF was added at 20 °C under argon to a solution of ester (+)-**1a** (70 mg, 0.34 mmol) in 5 mL of anhydrous Et_2O (5 mL). The mixture was stirred for 15 min, 1 mL of water was added dropwise, and the precipitate was filtered off and washed with Et_2O (2×5 mL). The combined organic filtrate was dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was chromatographed on a column with SiO_2 (3 g). Elution with benzene gave alcohol (+)-**1a** as a colorless oil with R_f 0.69 (PhH—AcOEt 2 : 1, v/v). ^{1}H NMR, δ: 1.60 (br.s, 1 H); 1.72 (s, 3 H); 1.75 (s, 3 H); 1.83 (s, 3 H); 1.95 (dd, 1 H, C(5)H_A, J_{AB} = 9 Hz, J_{AM} = 12 Hz); 2.40 (dd,, 1 H, C(5)H_B, J_{AB} = 9 Hz, J_{BM} = 18 Hz); 3.15 (ddd, 1 H, C(6)H_2, J_{AM} = 12 Hz, J_{BM} = 18 Hz, J_{vic} = 10 Hz); 4.03 (s, 2 H, CH_2OH); 5.22 (d, 1 H, J_{vic} = 10 Hz); 5.65 (d, C(3)H, 1 H, $J_{2,3}$ = 6 Hz); 5.85 (d, C(2)H, 1 H, $J_{2,3}$ = 6 Hz). ^{13}C NMR, δ: 18.03; 23.36; 25.84; 33.59; 35.54; 65.18; 118.25, 119.79; 125.59; 131.90; 134.32; 137.88. IR, ν/cm^{-1}: 3600, 1600, 1032. MS, *m/z* (I_{rel} (%)): 178 $[M]^+$ (52), 160 $[M - H_2O]^+$ (20), 147 (62), 119 (31), 105 (100), 91 (54). A specimen of (+)-**1a** with $[\alpha]_D^{20}$ +248 (*c* 1.0, PhH), *ee* ~82—84%, was converted into alcohol (+)-**2** with $[\alpha]_D^{20}$ + 148 (*c* 1.0, PhH), yield 40 mg (66%). Another specimen of (+)-**1a** with $[\alpha]_D^{20}$ +190 (*c* 1.0, PhH), *ee* ~63—64%, gave a specimen of (+)-**2** with $[\alpha]_D^{19}$ + 134 (*c* 1.0, PhH) with a similar ^{1}H NMR spectrum, yield 45 mg (74%).

Alcohol (±)-**2a** was prepared in a similar way in 71% yield from 70 mg (0.34 mmol) of specimen (±)-**1a**; the R_f value and the spectroscopic characteristics of the product fully coincided with those given above. An increase in the amount of a 1.4 *M* solution of $LiAlH_4$ to 1 mL (~54 mg, ~1.4 mmol) or in the reaction time (to 1 h) gave rise to a product of "overhydrogenation" of **2** containing only two double bonds, which was difficult to separate. This impurity (colorless oil, 8.5 mg) was isolated in a nearly pure state by repeated chromatography on SiO_2. ^{1}H NMR, δ: 1.52 (br.s, 1 H, O<u>H</u>); 1.66 (s, 3 H); 1.70 (s, 3 H); 1.73 (s, 3 H); 1.86—2.21 (m, 5 H); 3.64 (d, 2 H, *J* = 6.8 Hz); 5.22 (d, 1 H, J_{vic} = 10 Hz); 5.38 (nar.m, 1 H). IR, ν/cm^{-1}: 3640 (s), 1650 (w), 1040 (s). On the basis of these data, the product was identified as (±)-[4-methyl-2-(2-methylprop-1-enyl)cyclohex-3-ene]methanol.

(±)-[4-Methyl-6-(2-methylprop-1-enyl)cyclohexa-1,3-diene]methanol acetate, (±)-3. Pyridine (31 μL, 0.38 mmol), Ac_2O (36 μL, 0.38 mmol), and DMAP (3 mg) were added to a solution of alcohol (±)-**2** (57 mg, 0.32 mmol) in 2 mL of hexane. After 18 h, the solution was concentrated *in vacuo*, and the residue was chromatographped on a column with SiO_2; elution with a hexane—PhH mixture (1 : 1, v/v) gave acetate (±)-**3** as a colorless oil. Yield 50 mg (71%). ^{1}H NMR, δ: 1.65 (s, 3 H); 1.69 (s, 3 H); 1.78 (s, 3 H); 1.97 (dd, 1 H, C(5)H_A, J_{AB} = 8 Hz, J_{AM} = 2 Hz); 2.04 (s, 3 H); 2.39 (dd, C(5)H_B, 1 H, J_{AB} = 8 Hz, J_{BM} = 9 Hz); 3.12 (ddd, C(6)H, 1 H, J_{AM} = 2 Hz, J_{BM} = 9 Hz, J_{vic} = 10 Hz); 4.48 (dd, 2 H, CH_2OAc, *J* = 13 Hz, *J*′ = 6 Hz); 5.16

(d, 1 H, J_{vic} = 10 Hz); 5.64 (m, 1 H, C(3)H); 5.88 (d, 1 H, C(2)H, $J_{2,3}$ = 6 Hz). IR, ν/cm^{-1}: 1738, 1600.

(−)-[4-Methyl-6-(2-methylprop-1-enyl)cyclohexa-1,3-diene]methanol, (*R*)-2. ***A.*** *Enzymatic hydrolysis, low degree of conversion*. PPL (Serva) powder (30 mg) was added in one portion with vigorous stirring at 20 °C to an emulsion of acetate (±)-**3** (76 mg, 0.34 mmol) in an 0.1 *M* phosphate buffer, pH 6.8 (0.5 mL). The resulting slurry was stirred for 7 h and extracted with benzene (3×2 mL); the organic layer was washed with saturated brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was chromatographed on a column with SiO_2 (1 g). Elution with a hexane—AcOEt mixture (10 : 1, v/v) yielded first a fraction of the unchanged acetate (32 mg) and then levorotatory alcohol (*R*)-**2** as a colorless oil whose R_f and IR spectrum were the same as for specimens of (+)-**2** but with $[\alpha]_D^{21}$ −41 (*c* 0.5, PhH). Yield 6.2 mg (10%).

B. *Enzymatic hydrolysis, ~32% conversion*. A heterogeneous mixture containing acetate (±)-**3** (220 mg, 1 mmol), PPL powder (100 mg, OlainFarm), and an 0.1 *M* phosphate buffer, pH 6.8 (2 mL) was vigorously stirred for 3.5 h at 20 °C and worked up as described above. Elution of the column with 11 column volumes of a hexane—AcOEt mixture (10 : 1, v/v) gave alcohol (−)-**2** with $[\alpha]_D^{20}$ −27.5 (*c* 1.0, PhH) and with R_f value and ^{1}H NMR spectrum identical to those found for alcohols (+)-**2** and (±)-**2**. Yield 57 mg (32%).

Esters of alcohol (+)-2 with (*S*)-Mosher´s acid, (6*S*,2´*S*)-4 and (6*R*,2´*S*)-4. A solution of (*R*)-(methoxy)(phenyl)(trifluoromethyl)acetyl chloride ((*R*)-MTPA-Cl), prepared from acid (*S*)-MTPA (39 mg, 0.38 mmol) by a known procedure,[10] in 0.5 mL of Py was added to a solution of alcohol (+)-**2** (20 mg, 0.11 mmol) in CCl_4 (30 μL). The reaction mixture was stirred at 20 °C for 24 h, treated with a solution of *N*,*N*-dimethylethylenediamine (14 mg, ~0.15 mmol) in a minimum volume of CCl_4 by a known procedure,[11] and acidified with 1 *M* HCl (2.5 mL). The organic layer was separated and the aqueous phase was extracted with Et_2O (2×1 mL). The combined organic phase was washed repeatedly with 1 *M* HCl, a saturated solution of $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated *in vacuo*. The thick liquid residue was chromatographed on a column with SiO_2 (2 g); elution with benzene gave a binary mixture of MTPA esters. Yield 31.4 mg (71%). ^{1}H NMR ($CDCl_3$), δ: 1.48 and 1.49 (both s, 3 H); 1.58 and 1.60 (both s, 3 H); 1.86 (m, 3 H); 2.26—2.31 (m, 2 H); 3.00—3.10 (m, 1 H); 3.43 < 3.47 (both s, 3 H); 4.62 (br.s, 2 H); 5.04 (br.d, 1 H); 5.54 (d, 1 H, *J* = 6 Hz); 5.84 (br.d, 1 H, *J* = 6 Hz); 7.25—7.60 (m, 5 H).

Esters of alcohol (+)-2 and (*R*)-Mosher´s acid, (6*S*,2´*R*)-4 and (6*R*,2´*R*)-4. The reaction of 20 mg of the same specimen of the alcohol with (*S*)-(methoxy)(phenyl)(trifluoromethyl)acetyl chloride ((*S*)-MTPA-Cl), prepared from acid (*R*)-MTPA (40 mg) carried out by the same procedure gave 40 mg of a binary mixture of (*R*)-MTPA esters. ^{1}H NMR ($CDCl_3$), δ: 1.56 and 1.59 (both s, 3 H); 1.60 and 1.62 (both s, 3 H); 1.85 (m, 3 H); 2.24—2.29 (m, 2 H); 3.00—3.10 (m, 1 H); 3.42 > 3.46 (both s, 3 H); 4.69 (m, 2 H); 5.11 (br.d, 1 H); 5.54 (d, 1 H, *J* = 6 Hz); 5.85 (br.d, 1 H, *J* = 6 Hz); 7.25—7.66 (m, 5 H).

Complexation of MTPA esters 4 with Eu(fod) was carried out by a procedure used previously.[12] The results are presented in Table 1.

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