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Lipase-Catalyzed Asymmetric Synthesis of (*R*)- and (*S*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethyl-2-cyclohexenone and Their Dihydro Derivatives

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Abstract: Racemic 4-hydroxy-2,6,6-trimethyl-2-cyclohexenone, *trans*- and *cis*-2,6,6-trimethyl-2-cyclohexene-1,4-diols were prepared by reduction of 4-oxoisophorone with sodium borohydride-cerium chloride. Lipase (PS-30)-catalyzed kinetic resolution of (±)-*cis*-2,6,6-trimethyl-2-cyclohexene-1,4-diol with vinyl acetate led to (1*R*, 4*S*)-4-acetoxy-2,6,6-trimethyl-2-cyclohexen-1-ol (81 %ee) and (1*S*,4*R*)-1-acetoxy-2,6,6-trimethyl-2-cyclohexene-4-ol (92 %ee). Hydrolysis of the former monoacetate and recrytallization of the resulting material afforded enantiomerically pure (1*R*, 4*S*)-2,6,6-trimethyl-2-cyclohexene-1,4-diol. On the other hand, recrystallization of (1*S*, 4*R*) monoacetate itself provided an optically pure sample, which was then hydrolyzed to give (1*S*, 4*R*)-2,6,6-trimethylcyclohexene-1,4-diol. Transformation of both diols into (*S*)- and (*R*)-4-*tert*-butyldimethylsilyloxy-2,6,6-trimethyl-2-cyclohexenone was conducted in two steps including silylation and oxidation. Catalytic hydrogenation of these (*S*)- and (*R*)-silyloxy enones over Raney nickel afforded the corresponding dihydro derivatives.

4-Hydroxy-2,6,6-trimethyl-2-cyclohexenone (*S*)- and (*R*)-(**2**) are a versatile class of the chiral building blocks for the synthesis of optically active natural products and their enantiomers, including abscisic acid,[1] carotenoid[2,3,4] and flavour constituents.[2] The dihydro compounds such as (4*R*, 6*R*)-**5** and (4*R*, 6*S*)-**6** are also valuable chirons, which have served as key starting materials for obtaining aroma substances[2] and carotenoids.[2,3,6] Among these chiral enones and their dihydro derivatives, the preparation of tetrahydropyranyl ether (4*R*, 6*S*)-**6** was first reported by Mori,[7] who used the resolution of the tetrahydro compound, derived from 4-oxoisophorone (**1**) with a steroidal carboxylic acid, followed by the chemical transformation into (4*R*, 6*S*)-**6**. Subsequently, a Roche group[8] developed a new approach for the synthesis of (4*R*, 6*R*)- and (4*S*, 6*R*)-**5** in a technical scale, which consisted of a joint procedure of the baker's yeast reduction of **1** and the regioselective reduction of the resulting chiral diketone. The Roche group's chemists[9] also reported the conversion of these chiral ketols to (*S*)- and (*R*)-**2**. This method enabled one to readily access a large number of optically active natural products. In this paper, we describe a novel approach for obtaining *tert*-butyldimethylsilyl ethers (*S*)- and (*R*)-**3** and their dihydro derivatives (4*R*, 6*RS*)- and (4*S*, 6*RS*)-**7**, which involves lipase-catalyzed transesterification of racemic diol (±)-**9**, derived from **1** and subsequent chemical transformation.

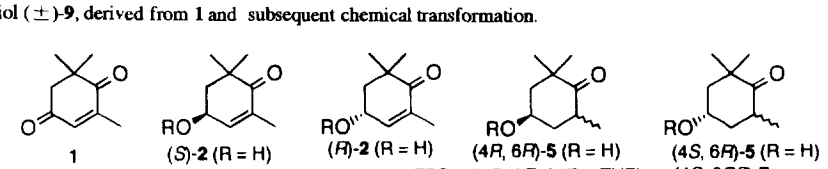
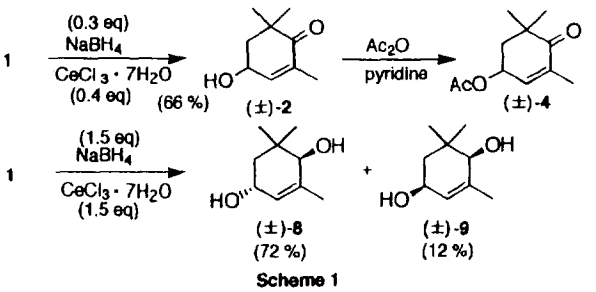


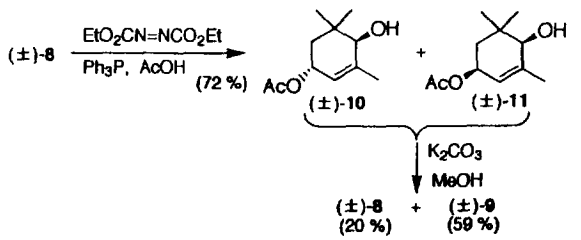
Fig. 1

First of all, we began by preparing the racemic substrates necessary to lipase-catalyzed kinetic resolution. (±)-4-Hydroxy-2,6,6-trimethyl-2-cyclohexenone [(±)-**2**][10] was prepared by regioselective reduction of 4-oxoisophorone (**1**) with a limited amount of sodium borohydride-cerium(III) chloride in methanol (Scheme 1). On the other hand, use of an excess of this reagent system led to (±)-*trans*- and (±)-*cis*-2,6,6-trimethyl-2-cyclohexene-1,4-diol [(±)-**8**] and [(±)-**9**] in 72% and 12% yields, respectively. In

order to access the latter minor diol in quantity, we examined the Mitsunobu reaction on *trans* diol (±)-**8** (Scheme 2). Upon treating with triphenylphosphine, diethyl azodicarboxylate and anhydrous acetic acid in tetrahydrofuran, (±)-**8** afforded a mixture of monoacetates (±)-**10** and (±)-**11**, which without further separation, was converted to (±)-**8** and (±)-**9** in a 1 : 3 ratio by hydrolysis with potassium carbonate in methanol.

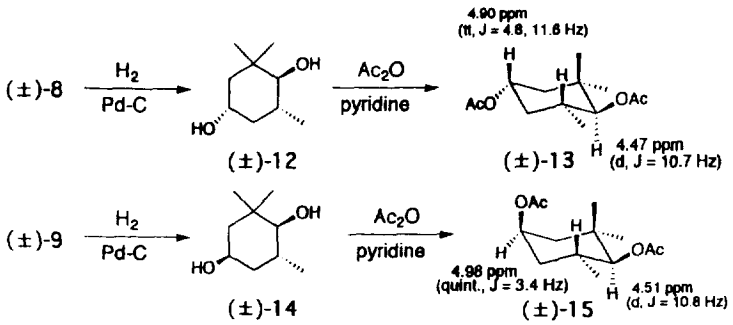


Scheme 1



Scheme 2

The stereochemistry of both diols was next determined as follows (Scheme 3). Catalytic hydrogenation of (±)-**8** and (±)-**9** over palladium on carbon in ethanol led to crystalline saturated diols (±)-**12** and (±)-**14**, which on treatment with acetic anhydride in pyridine in the usual way gave diacetates (±)-**13** and (±)-**15**. The ^{1}H-NMR spectrum of (±)-**13** showed a doublet signal (J = 10.7 Hz) at 4.47 ppm for C-1 methine proton and a triplet of triplet signal (J = 4.8, 11.6 Hz) at 4.90 ppm for C-4 proton, indicating the *trans* relationship of the two hydroxyl groups. On the other hand, (±)-**15** bearing the *cis* stereochemistry showed a doublet (J = 10.8 Hz) at 4.51 ppm for C-1 H and a quintet (J =3.4 Hz) at 4.98 ppm for C-4 H.



Scheme 3

With the requisite racemic substrates (±)-**2**, (±)-**8** and (±)-**9** in hand, we turned to the lipase-catalyzed enantioselective transesterification. Several lipases including those from *Pseudomonas* sp. [P(Amano), PS-30, P(Nagase), 2G] and *Candida* sp. (MY) were examined for the enzymatic resolution (Table 1). This results, coupled with those from the solvent effect experiments (Table 2), revealed that when *cis* diol (±)-**9** was used as substrate, lipase PS-30 in neat vinyl acetate gave the best result in

terms of enantioselectivity and efficiency. Under these conditions, (±)-**9** provided (1*R*, 4*S*)-**11** (81 % ee), (1*S*, 4*R*)-**16** (92 %ee) and (1*S*, 4*R*)-**9** (21 % ee). Hydrolysis of (1*R*, 4*S*) monoacetate with potassium carbonate in methanol and recrystallization of the resulting material afforded enantiomerically pure (1*R*, 4*S*)-**9**. On the other hand, recrystallization of (1*S*, 4*R*)-**16** itself led to an enantiomerically pure sample, which was then hydrolyzed in a similar manner to yield (1*S*, 4*R*)-**9**.

Table 1. Lipase-Catalyzed Kinetic Resolution

substrate	lipase	time, h	acetate			remaining alcohol		
			isomer	yield, %	ee, %	isomer	yield, %	ee, %
(±)-**2**	MY	44	(*R*)-**4**	18	25	(*S*)-**2**	79	5
	P(Amano)	28	(*S*)-**4**	15	34	(*R*)-**2**	59	22
	PS-30	26	(*S*)-**4**	30	28	(*R*)-**2**	59	12
(±)-**8**	MY	120	(1*R*,4*R*)-**10**	11	35	(1*S*,4*S*)-**8**	74	—
	P(Amano)	145	(1*S*, 4*S*)-**10**	9	24	(1*R*,4*R*)-**8**	73	—
	PS-30	114	(1*S*, 4*S*)-**10**	10	8	(1*R*,4*R*)-**8**	64	—
(±)-**9**	MY	28	(1*S*, 4*R*)-**11**	56	32	(1*R*,4*S*)-**9**	44	36
	P(Nagase)	144	(1*R*, 4*S*)-**11**	24	72	(1*S*,4*R*)-**9**	70	15
	2G	144	(1*S*, 4*R*)-**11**	22	25	(1*R*,4*S*)-**9**	73	7
	P(Amano)	50	(1*R*, 4*S*)-**11**	35	53	(1*S*,4*R*)-**9**	34	5
			(1*S*, 4*R*)-**16**	18	78			
	PS-30	48	(1*R*, 4*S*)-**11**	40	81	(1*S*,4*R*)-**9**	32	21
			(1*S*, 4*R*)-**16**	18	92			

Table 2. Solvent Effect

(±)-**9** $\xrightarrow[\text{OAc}\ 30°C]{\text{lipase PS-30}}$ (1*R*, 4*S*)-**11**

solvent	ee, %
Et_2O	41
$i\text{-}Pr_2O$	58
PhH	48
CH_3CN	33
vinyl acetate	81

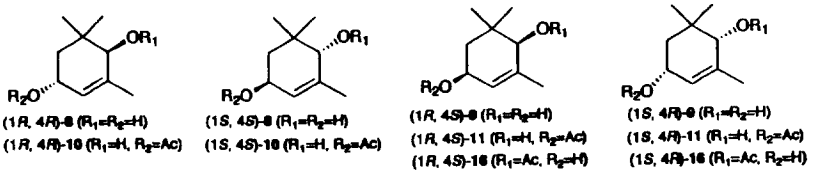
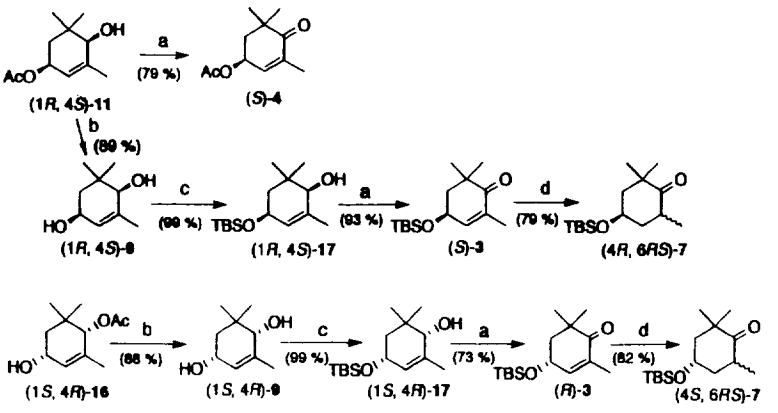


Fig. 2



Scheme 4

Reagents: a) PDC, DMF b) K_2CO_3, MeOH c) TBDMSCl, imidazole, DMF d) H_2, Ra-Ni

Transformation of both enantiomerically pure diols thus obtained into the target compounds was then undertaken (Scheme 4). Upon treating with *tert*-butyldimethylsilyl chloride, (1*R*, 4*S*)- and (1*S*, 4*R*)-**9** furnished monosilylated alcohols (1*R*, 4*S*)- and (1*S*, 4*R*)-**17**. Pyridinium dichromate oxidation of these alcohols in dimethylformamide gave (*S*)- and (*R*)-**3**. Conversion of both silyloxy enones to the corresponding dihydro derivatives (4*R*, 6*RS*)- and (4*S*, 6*RS*)-**7** was attained by the catalytic hydrogenation with Raney nickel in ethanol. The ^{1}H-NMR spectrum of (4*R*, 6*RS*)-**7** revealed that the reduction product was a mixture of (4*R*, 6*S*)- and (4*R*, 6*R*)-**7** (4.5 : 1).

Experimental

General. Lipase MY (*Candida* sp.) was supplied by Meito Sangyo Co., Ltd. Lipase P (Amano) and PS-30 (*Pseudomonas* sp.) were given by Amano Pharm. Co., Ltd. Lipase P (Nagase) and 2G (*Pseudomonas* sp.) were a gift of Nagase Sangyo Co., Ltd. All melting point (mp) values are uncorrected. ^{1}H-NMR spectra were recorded on JEOL GSX-270 and IR spectra were taken with a JASCO IR-810 infrared spectrometer. MS spectra were recorded with a JEOL JMX-DX-300 instrument. Optical rotations were measured with a JASCO DIP-4 polarimeter. For column chromatography, silica gel (from Kanto Chemical Co.,Ltd.) was used and for preparative TLC, silica gel PF_{254} (Merck) was employed. The enantiomeric purities (% ee) were calculated from the ^{1}H-NMR spectra of the esters derived from (-)- α-methoxy- α-trifluoromethylphenylacetyl chloride or from the % ee values reported for the known compounds. Absolute stereochemistry was determined by the chemical correlation with the substrates having the known absolute configurations.

(±)-4-Hydroxy-2,6,6-trimethyl-2-cyclohexenone [(±)-2] and its acetate [(±)-4]. The compound (±)-**2** was prepared by the literature procedure.[10] Purification by column chromatography (hexane : AcOEt=4 : 1) furnished pure (±)-**2** in 66 % yield, which was then converted to the acetate (±)-**4** with Ac_2O in pyridine in the usual manner. Purification by column chromatography (hexane : AcOEt=6 : 1) provided an analytical sample (97 % yield). Data for (±)-**4**: IR ν (film) cm^{-1}:2960, 2930, 1740, 1680, 1450, 1375, 1235, 1020, 960. ^{1}H-NMR($CDCl_3$) δ: 1.17(6H, s), 1.81(3H, dd, J = 1.4, 1.9 Hz), 1.94(1H, dd, J = 9.8, 12.7 Hz), 2.10(3H, s), 2.15(1H, ddd, J = 1.7, 5.6, 12.7 Hz), 5.63(1H, m), 6.51(1H, m). *Anal.* Found : C, 67.23; H, 8.34. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22%.

(±)-trans- and (±)-cis-2,6,6-Trimethyl-2-cyclohexene-1,4-diol [(±)-8] and [(±)-9].

a) *By reduction of 4-oxoisophorone (1)* To a stirred solution of 4-oxoisophorone (**1**) (3.51 g) and $CeCl_3 \cdot 7H_2O$ (12.91 g) in MeOH (40 ml) was added portionwise $NaBH_4$ (1.31 g) at -5 ~ -10°C, the mixture being stirred for 1 hr at that temperature. The reaction mixture was diluted with half-sat. NaCl solution and extracted with EtOAc in the usual manner. Recrystallization of the crude product from EtOAc gave (±)-**8** (1.04 g). Column chromatography (hexane : EtOAc =1 : 2) of the mixture obtained from the mother liquor yielded (±)-**8** (1.56 g) and (±)-**9** (0.45 g). Total yields : (±)-**8** (72 %) and (±)-**9** (12 %). Recrystallization of each diol from AcOEt furnished analytical samples. (±)-**8**: mp 144-145 °C. *Anal.* Found : C, 68.80; H, 10.36. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%. (±)-**9** : mp 98-99 °C. *Anal.* Found : C, 69.09; H, 10.18. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%.

b) *Via Mitsunobu reaction of (±)-8.* To a solution of (±)-**8** (4.20 g), Ph_3P (13.44g) and anhydrous AcOH (2.93 ml) in THF (90 ml) was added dropwise diethyl azodicarboxylate (8.93 g) with ice-cooling, stirring being continued at that temperature for 2 hr and at room temperature for a further 10 hr. Evaporation of the solvent and removal of the resulting triphenylphosphine oxide by filtration provided an oil, which on column chromatography and preparative TLC afforded a mixture of monoacetates (±)-**10** and (±)-**11** (3.83 g, 72 %). Then, this mixture was dissolved in MeOH (20 ml) and treated with K_2CO_3 (4.0 g) under ice-cooling for 1 hr and at room temperature for 3 hr. Half-saturated NaCl solution was added and the mixture was extracted with EtOAc. The usual work-up gave a crystalline product, which upon recrystallization from Et_2O-hexane, afforded pure (±)-**9** (0.36 g). Column chromatography of the mixture obtained from the above mother liquor provided (±)-**8** (0.60 g, 20 %) by elution with hexane-AcOEt (3 : 7) and (±)-**9** (1.41 g) by elution with AcOEt-MeOH (5:1). Total yield of (±)-**9** : 1.77 g (59 %).

(±)-trans-2,2,6-Trimethylcyclohexane-1,4-diol [(±)-12] and its acetate [(±)-13]. A solution of (±)-**8** (150 mg) in EtOH (1 ml) was hydrogenated with 10 % Pd-C (30 mg) in the usual way. Column chromatography (hexane:AcOEt=2:1) of the crude product gave (±)-**12** (44 mg, 29 %). Recrystallization from AcOEt furnished an analytical sample, mp 161-162 °C. *Anal.* Found : C, 68.10; H, 11.26. Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47%. This diol was acetylated with Ac_2O (0.5 ml) and pyridine (0.5 ml) in the usual manner to give (±)-**13** (24 mg) after preparative TLC. ^{1}H-NMR ($CDCl_3$) δ: 0.86(3H, d, J = 6.6Hz), 0.88(3H, s), 0.99(3H, s), 1.17(1H, q, J = 12.2 Hz), 1.38(1H, t, J = 12.2 Hz),

1.80(1H, m), 1.88(1H, m), 2.02(3H, s), 2.07(1H, m), 2.09(3H, s), 4.47(1H, d, J = 10.7 Hz), 4.90(1H, tt, J = 4.8, 12.2 Hz).

(±)-cis-2,2,6-Trimethylcyclohexane-1,4-diol [(±)-14] and *its acetate [(±)-15].* Catalytic hydrogenation of (±)-**9** was carried out as just described. Purification by preparative TLC afforded (±)-**14** in 42 % yield. Recrystallization from AcOEt gave an analytical sample, mp 125-126 ℃. *Anal*. Found : C, 68.45; H, 11.37. Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47 %. This diol was acetylated as mentioned above to yield (±)-**15** in 87 % yield after preparative TLC. ^{1}H-NMR ($CDCl_3$) δ : 0.85(3H, s), 0.86(3H, d, J = 6.2 Hz), 1.06(3H, s), 1.38(1H, ddd, J = 3.4, 12.4, 14.8 Hz), 1.50(1H, dd, J = 3.4, 14.8 Hz), 1.83(1H, dt, J = 3.4, 14.8 Hz), 1.91(1H, dq, J = 3.4, 14.8 Hz), 2.04(3H, s), 2.09(1H, m), 2.10(3H, s), 4.51(1H, d, J = 10.8 Hz), 4.98(1H, quint., J = 3.4 Hz).

Lipase-catalyzed kinetic resolution of (±)-2, (±)-8 and (±)-9. The following procedure is representative. A suspension of (±)-**9** (200 mg) and lipase PS-30 (100 mg) in freshly distilled vinyl acetate (2.4 ml) was stirred at 30℃ for 48 hr. Filtration through a celite pad and evaporation of the solvent left a mixture of products, which on purification by preparative TLC gave (1*R*, 4*S*)-**11** (102 mg, 40 %), (1*S*, 4*R*)-**16** (46 mg, 18 %) and (1*S*, 4*R*)-**9** (64 mg, 32 %). Data for (1*R*, 4*S*)-**11** : $[\alpha]_D^{24}$-20.9 (c 0.56, $CHCl_3$) (81 % ee). IR ν (film) cm^{-1}: 3450, 2950, 2870, 1730, 1450, 1380, 1250, 1050, 1020. ^{1}H-NMR ($CDCl_3$) δ : 0.93(3H, s), 1.03(3H, s), 1.47(1H, d, J = 5.6 Hz, OH), 1.59(1H, dd, J = 8.8, 13.2 Hz), 1.69(1H, dd, J = 6.6, 13.2 Hz), 1.85(3H, t, J = 1.5 Hz), 2.05(3H, s), 3.40(1H, d, J = 5.6 Hz), 5.27(1H, dd, J = 6.6, 8.8 Hz), 5.47 (1H, broad s). *Anal*. Found : C, 66.48; H, 9.12. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. Data for (1*S*, 4*R*)-**16** : mp 71-72 ℃. $[\alpha]_D^{24}$-179(c 2.06, $CHCl_3$) (92 % ee). Recrystallization from hexane provided an enantiomerically pure sample, mp 73-74℃. $[\alpha]_D^{24}$-194 (c 0.11, $CHCl_3$). IR ν (film) cm^{-1}: 3400, 2950, 2860, 1740, 1450, 1370, 1240, 1050, 1020, 970. ^{1}H-NMR ($CDCl_3$) δ : 0.92(3H, s), 0.94(3H,s), 1.51(1H, dd, J=9.5, 12.7 Hz), 1.64(1H, broad, OH), 1.69(3H, t, J = 1.5 Hz), 1.71(1H, dd, J = 7.4, 12.7 Hz), 4.22(1H, dd, J = 7.4, 9.5 Hz), 4.93(1H, s), 5.66(1H, broad s). *Anal*. Found : C, 66.42; H, 9.50. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. Data for (1*S*, 4*R*)-**9** : $[\alpha]_D^{24}$-14.3 (c 0.79, $CHCl_3$)(21 %ee). This diol with a low enantiomeric purity was resubjected to an analogous reaction (lipase PS-30, vinyl acetate, 30℃, 4 days) to produce (1*S*, 4*R*)-**16** of 81 % ee in 34 % yield.

Solvent effects. Solvent effects on enantiomeric purity (% ee) of (1*R*, 4*S*)-**11** obtained in the kinetic resolution of (±)-**9** were examined under the following reaction conditions. A solution of (±)-**9** (80 mg) in each solvent (2 ml) containing vinyl acetate (0.2 ml) was stirred with lipase PS-30 (40 mg) at 30℃ for 48 hr. Filtration and evaporation of the solvent gave a mixture of products, from which (1*R*, 4*S*)-**11** was separated by preparative TLC and optical rotation was measured.

(S)-4-Acetoxy-2,6,6-trimethyl-2-cyclohexenone [(S)-(4)]. A mixture of (1*R*, 4*S*)-**11** ($[\alpha]_D^{24}$-20.9) (56 mg) and PDC (213 mg) in DMF (0.5 ml) was stirred at room temperature for 18 hr. Et_2O was added and the organic layer was washed with water, sat. NaCl and dried. Evaporation gave a crude product, which on preparative TLC afforded (*S*)-**4** (44 mg, 79 %). $[\alpha]_D^{24}$-48.9 (c 0.44, EtOH) [81 % ee, based on the literature value[5a] -60.4 (EtOH)].

Enantiomerically pure (1R, 4S)-2,6,6-trimethyl-2-cyclohexene-1,4-diol [(1R, 4S)-9]. (1*R*, 4*S*)-**11** (81 % ee) (152 mg) was treated with K_2CO_3 (159 mg) in MeOH (2 ml) at room temperature for 17 hr. The reaction mixture was diluted with half-sat. NaCl solution and extracted with AcOEt as usual. Evaporation left a crude diol (107 mg, 89 %), which was recrystallized twice from Et_2O to give enantiomerically pure (1*R*,4*S*)-**9**, mp 129-130℃. $[\alpha]_D^{24}$+67.4 (c 0.27, $CHCl_3$). This sample was converted to the diester by treatment with (-)-α-methoxy-α-trifluoromethylphenylacetyl chloride. The ^{1}H-NMR analysis of this ester revealed that the enatiomeric purity was >95 %ee. The absolute stereochemistry of this (+)-diol was evident from the chemical correlation with (-)-acetate (*S*)-(**4**) described above, of which the absolute configuration had been reported.[5a]

(1R, 4S)-4-tert-Butyldimethylsilyloxy-2,6,6-trimethyl-2-cyclohexen-1-ol [(1R, 4S)-17]. A mixture of enantiomerically pure (1*R*, 4*S*)-**9** (210 mg), TBDMSCl (306 mg) and imidazole (230 mg) in DMF (2 ml) was stirred at room temperature for 4 hr. Water was added and the aq. layer was extracted with Et_2O in the usual way. Purification of the crude product by preparative TLC afforded (1*R*, 4*S*)-**17** (362 mg, 99 %) as crystals. Sublimation *in vacuo* gave an analytically pure sample, mp 81-82℃. $[\alpha]_D^{24}$+16.5 (c 0.46, $CHCl_3$). IR ν (KBr) cm^{-1}: 3300, 2900, 2850, 1470, 1360, 1260, 1070, 860, 840, 780. ^{1}H-NMR ($CDCl_3$) δ : 0.08(6H, s), 0.86(3H, s), 0.90(9H, s), 1.01(3H, s), 1.30(1H, d, J=8.8 Hz, OH), 1.47(1H, dd, J =6.4, 8.7 Hz), 1.52(1H, dd, J =4.1, 8.7 Hz), 1.82(3H, t, J =1.5 Hz), 3.27(1H, d, J = 8.8 Hz), 4.19(1H, m), 5.42(1H, broad s). *Anal*. Found : C, 66.41; H, 11.31. Calcd. for $C_{15}H_{30}O_2Si$: C, 66.60; H, 11.18%.

(S)-4-tert-Butyldimethylsilyloxy-2-cyclohexenone [(S)-3]. This compound was prepared from (1*R*, 4*S*)-**17** as described for (*S*)-**4**. Purification by column chromatography provided a pure sample in 93 % yield. $[\alpha]_D^{24}$-57.0 (c 0.44, $CHCl_3$). IR ν (film) cm^{-1}: 2950, 2925, 1675, 1460,

1360, 1250, 1080, 870, 840, 775. ^{1}H-NMR($CDCl_3$) δ : 0.12(3H, s), 0.13(3H, s), 0.92(9H, s), 1.11(3H, s), 1.78(3H, t, J = 1.5 Hz), 1.87(1H, dd, J = 9.8, 13.2 Hz), 1.99(1H, ddd, J = 1.7, 5.4, 13.2 Hz), 4.55(1H, m), 6.50(1H, broad s). *Anal.* Found : C, 67.33; H, 10.42. Calcd. for $C_{15}H_{28}O_2Si$: C, 67.10; H, 10.51%.

(4R, 6RS)-4-tert-Butyldimethylsilyloxy-2,2,6-trimethylcyclohexanone [(4R, 6RS)-7]. Silyloxy enone (*S*)-**3** (48 mg) was hydrogenated over Ra-Ni (W-2) in EtOH (1 ml) in the usual manner. Preparative TLC of the crude product afforded dihydro derivative (4*R*, 6*RS*)-7 (38 mg, 79 %), which proved to consist of (4*R*, 6*S*)-**7**/(4*R*, 6*R*)-**7** (4.5 :1) from the ^{1}H-NMR spectrum. IR ν (film) cm^{-1}: 2960, 2930, 1710, 1460, 1380, 1250, 1080, 860, 840, 775. ^{1}H-NMR ($CDCl_3$) δ : 0.09(6H, s), 0.90(7.4H, s), 0.92(1.6H, s), 1.01(3H, d, J =6.5Hz), 1.01(0.5H, s), 1.05(2.5H, s), 1.19(2.5H, s), 1.35(0.5H, s), 1.45(1H, m), 1.60(0.8H, dd, J =10.8, 13.0 Hz), 1.71 (0.2H, m), 1.92(0.8H, dt, J =4.0, 13.5 Hz), 2.02(0.2H, m), 2.14(0.8H, m), 2.70(0.8H, heptet, J =5.9 Hz), 3.19(0.2H, heptet, J =5.9 Hz), 4.12(0.2H, quint.,J = 3.0 Hz), 4.27(0.8H, tt, J =4.0, 10.8 Hz). *Anal.* Found : C, 66.36; H, 11.26. Calcd. for $C_{15}H_{30}O_2Si$: C, 66.60; H, 11.18%.

(1S, 4R)-2,6,6-Trimethyl-2-cyclohexene-1,4-diol [(1S, 4R)-9]. This compound was prepared from (1*S*, 4*R*)-**16** as described for (1*R*, 4*S*)-**9**. Purification by preparative TLC provided pure (1*S*, 4*R*)-**9** in 88 % yield. mp 129-130°C. $[\alpha]_D^{24}$-67.0 (*c* 0.20, $CHCl_3$).

(1S, 4R)-4-tert-Butyldimethylsilyloxy-2,6,6-trimethyl-2-cyclohexen-1-ol [(1S, 4R)-17]. This compound was prepared from (1*S*, 4*R*)-**9** as described for (1*R*, 4*S*)-**17**. Purification by preparative TLC gave (1*S*, 4*R*)-**17** in 99 % yield, which on recrystallization from hexane afforded a pure sample, mp 92-93°C. $[\alpha]_D^{24}$ -17.3 (*c* 0.3, $CHCl_3$).

(R)-4-tert-Butyldimethylsilyloxy-2,6,6-trimethyl-2-cyclohexenone [(R)-3]. This compound was prepared from (1*S*, 4*R*)-**17** as described for (*S*)-**3**. Purification by preparative TLC afforded (*R*)-**3** in 73 % yield. $[\alpha]_D^{24}$+55.0 (*c* 0.34, $CHCl_3$).

(4S, 6RS)-4-tert-Butyldimethylsilyloxy-2,2,6-trimethylcyclohexanone [(4S, 6RS)-7]. This compound was prepared from (*R*)-**3** as described for (4*R*, 6*RS*)-**7**. Purification by preparative TLC provided (4*S*, 6*RS*)-**7** in 82 % yield, which was composed of a 4.5 : 1 ratio of (4*S*, 6*R*)- and (4*S*, 6*S*)-**7**, based on ^{1}H-NMR analysis.

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