June 1994 Chem. Pharm. Bull. 42(6) 1191—1197 (1994)

Lipase-Catalyzed Hydrolysis of Some Racemic 1-Acetoxy-2-arylpropanes

Takashi MATSUMOTO,*,[a] Yoshio TAKEDA,[a] Eiko IWATA,[a] Mitsuo SAKAMOTO,[a] and
Takashi ISHIDA[b]

Faculty of Integrated Arts and Sciences, University of Tokushima,[a] Minamijosanjima, Tokushima 770, Japan and Hiroshima Institute of Technology,[b] Miyake, Saeki-ku, Hiroshima 731-51, Japan.

Received November 19, 1993; accepted January 24, 1994

Racemic 1-acetoxy-2-phenylpropane (12) and 1-acetoxy-2-(2-naphthyl)propane (33) were hydrolyzed with lipase at 35—36 °C for 2 and 24 h to give predominantly (*S*)-2-phenyl-1-propanol (11) and (*S*)-2-(2-naphthyl)-1-propanol (32), respectively. However, racemic 1-acetoxy-2-(1-naphthyl)propane (25) was recovered intact even when the reaction was carried out for 240 h. On the other hand, the enantioselectivities towards racemic 2-phenyl (16), 2-(*p*-tolyl) (20), 2-(1-naphthyl) (28), and 2-(2-naphthyl) (36) derivatives of 1-acetoxy-2-propanol were very low.

Keywords lipase; resolution; 1-acetoxy-2-arylpropane; hydrolysis; stereoselectivity

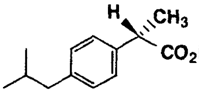
There are a number of nonsteroidal anti-inflammatory and analgesic drugs, such as ibuprofen (**1**), fenoprofen (**2**), naproxen (**3**), cicloprofen (**4**), pranoprofen (**5**), benoxaprofen (**6**), and so on. These drugs possess an asymmetric carbon atom in the molecule and can exist as the (*R*)- and (*S*)-enantiomers. Although most of these drugs are used in racemic form, it is known that only the (*S*)-(+)-enantiomers have high prostaglandin synthetase-inhibiting and anti-inflammatory activities.[1,2]

In a previous paper,[3] we have reported the biotransformation of racemic 2-(*p*-tolyl)-1-propanol (**7**) in rabbits leading to the optically active acids, 2-(*p*-tolyl)propanoic acid (**8**, *R*/*S*=6:94) and *p*-(1-carboxyethyl)benzoic acid (**9**, *R*/*S*=23:77), possessing a 2-arylpropanoic acid moiety similar to that of the drugs (**1**—**6**). This biotransformation suggests that 2-aryl-1-propanol can serve as a precursor of 2-arylpropanoic acid *in vivo*. In order to obtain the optically active 2-aryl-1-propanols, therefore, we examined the resolution of some racemic 1-acetoxy-2-arylpropanes by the use of lipase.[4-12]

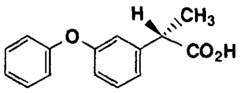
Synthesis of Racemic 1-Acetoxy-2-arylpropanes Some racemic 1-acetoxy-2-arylpropanes (**12**, **16**, **20**, **25**, **28**, **33**, and **36**) were synthesized in the following manner. Methyl (±)-2-phenylpropanoate (**10**), prepared from propiophenone according to the method of Fujii *et al.*,[13] was reduced with lithium aluminum hydride in ether and the resulting alcohol (**11**) was acetylated with acetic anhydride in pyridine to give (±)-1-acetoxy-2-phenylpropane (**12**).

α-Methylstyrene (**13**) was oxidized with *m*-chloroperbenzoic acid and anhydrous disodium hydrogen phosphate in dichloromethane to give a (±)-epoxide (**14**), which was converted into (±)-2-phenyl-1,2-propanediol (**15**) by hydrolysis with dilute sulfuric acid in ether. Acetylation of **15** with acetic anhydride in pyridine afforded (±)-1-acetoxy-2-phenyl-2-propanol (**16**). Similarly, 4-isopropenyltoluene[3] (**17**) was converted into (±)-1-acetoxy-2-(*p*-tolyl)-2-propanol (**20**) *via* the (±)-epoxide (**18**) and (±)-2-(*p*-tolyl)-1,2-propanediol (**19**).

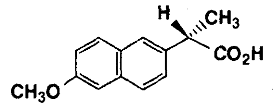
Subsequently, some naphthyl derivatives were also synthesized as follows. The Grignard reaction of 1′-



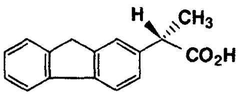
(S)-1



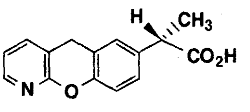
(S)-2



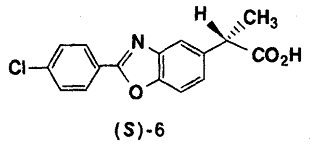
(S)-3



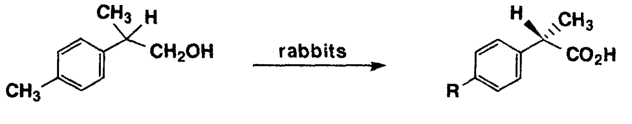
(S)-4



(S)-5

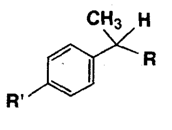


(S)-6

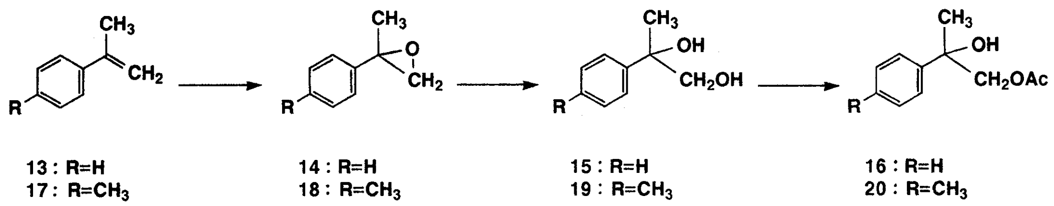


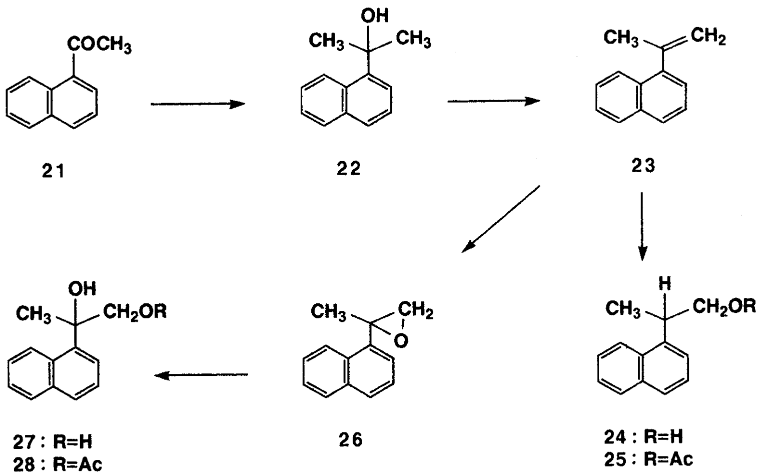
(±)-7

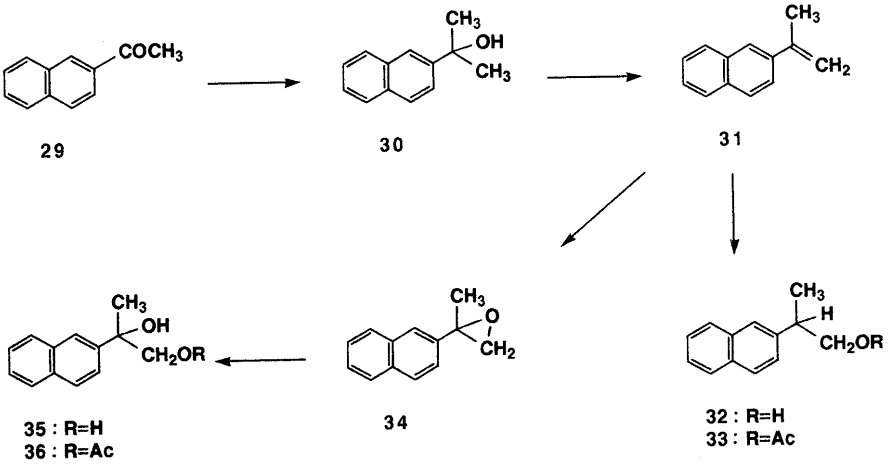
(S)-8 : R=CH$_3$
(S)-9 : R=CO$_2$H



10 : R=CO$_2$CH$_3$, R'=H
11 : R=CH$_2$OH, R'=H
12 : R=CH$_2$OAc, R'=H
37 : R=CH$_2$OAc, R'=CH$_3$



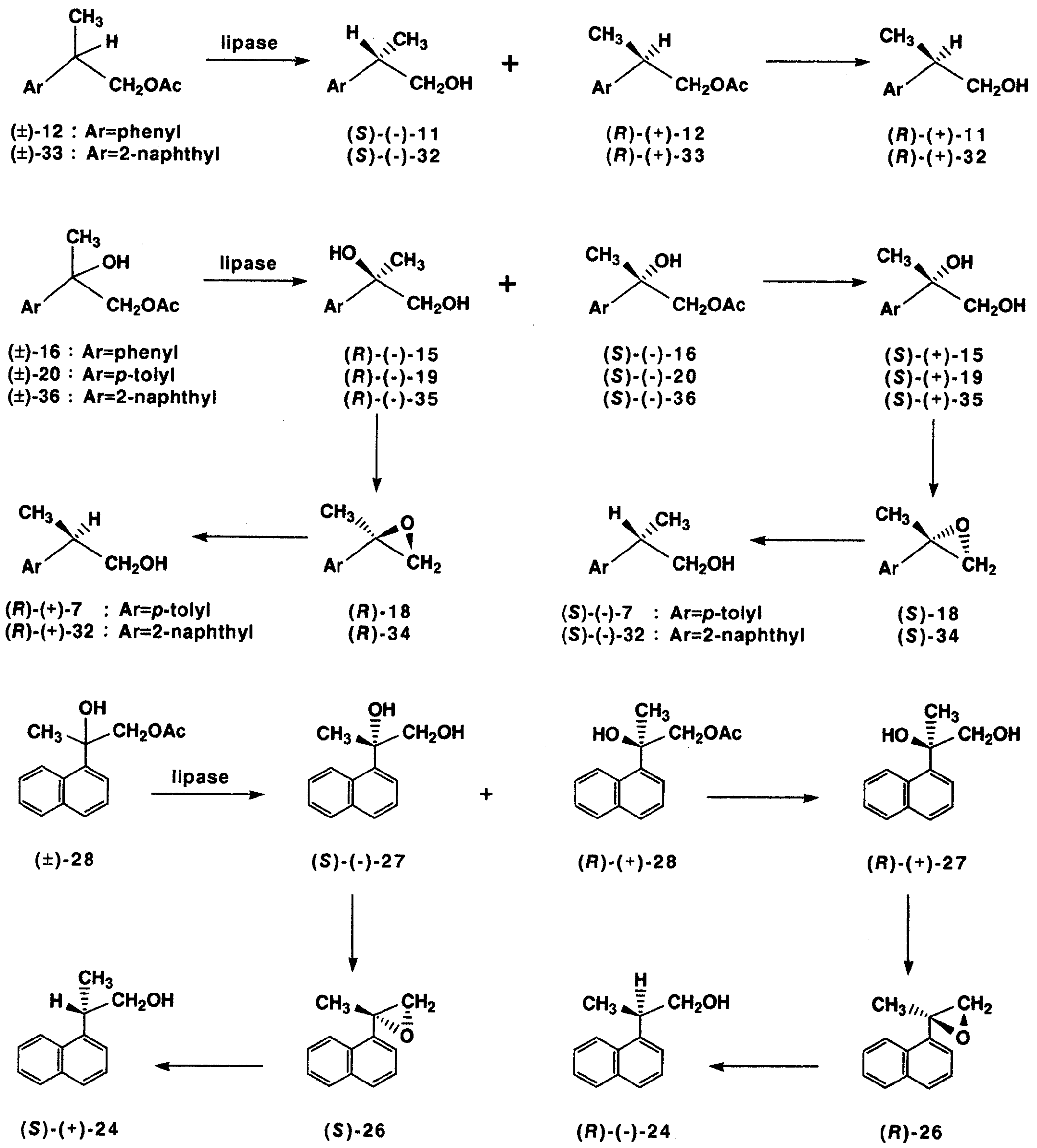




acetonaphthone (**21**) with methylmagnesium iodide afforded 2-(1-naphthyl)-2-propanol (**22**), which was dehydrated with dilute sulfuric acid to give an isopropenyl derivative (**23**). Hydroboration of **23** with borane–tetrahydrofuran complex, followed by oxidation with alkaline hydrogen peroxide afforded (±)-2-(1-naphthyl)-1-propanol (**24**), which was converted into the (±)-acetate (**25**) with acetic anhydride in pyridine. Oxidation of **23** with *m*-chloroperbenzoic acid and subsequent hydrolysis of the resulting (±)-epoxide (**26**) with dilute sulfuric acid produced a (±)-1,2-propanediol derivative (**27**), which was acetylated with acetic anhydride in pyridine to give (±)-1-acetoxy-2-(1-naphthyl)-2-propanol (**28**).

Similarly, 2′-acetonaphthone (**29**) was also converted into (±)-1-acetoxy-2-(2-naphthyl)propane (**33**) *via* a *tert*-alcohol (**30**), an isopropenyl derivative (**31**), and (±)-2-(2-naphthyl)-1-propanol (**32**). Compound **31** was further transformed into (±)-1-acetoxy-2-(2-naphthyl)-2-propanol (**36**) *via* a (±)-epoxide (**34**) and a (±)-1,2-propanediol derivative (**35**).

Lipase-Catalyzed Hydrolysis of Racemic 1-Acetoxy-2-arylpropanes Each of the racemic acetates (**12**, **16**, **20**, **25**, **28**, **33**, and **36**) in methanol was shaken with lipase (PPL-Sigma L-3126) in the presence of 0.1 M phosphate buffer (pH 7.0) at 35—36 °C for 2—240 h. The reaction was monitored by proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy and was stopped when about half of the substrate was hydrolyzed. The reaction mixture was then separated into the unchanged acetate and the hydrolyzed alcohol by silica gel column chromatography. Lipase-catalyzed hydrolysis of the racemic acetates (**12**, **16**, **20**, **28**, **33**, and **36**) produced the hydrolyzed alcohols [(−)-**11**, (−)-**15**, (−)-**19**, (−)-**27**, (−)-**32**, and (−)-**35**] and the unchanged acetates [(+)-**12**, (−)-**16**, (−)-**20**, (+)-**28**, (+)-**33**, and (−)-**36**], which were respectively treated with lithium aluminum hydride in ether to give the alcohols [(+)-**11**, (+)-**15**, (+)-**19**, (+)-**27**, (+)-**32**, and (+)-**35**]. However, the racemic 1-acetoxy-2-(1-naphthyl)-



propane (**25**) was recovered intact even when the hydrolysis was carried out for 240 h. The enantiomeric ratios of the optically active alcohols (**11**, **15**, and **32**) were determined by comparisons of the sign and value of specific rotations with those given in the literature.[3,14,15] In order to determine the enantiomeric ratios of the other optically-active 2-aryl-1,2-propanediol derivatives [(−)-**19**, (+)-**19**, (−)-**27**, (+)-**27**, (−)-**35**, and (+)-**35**], the following conversions were carried out.

Each of the diols was tosylated with *p*-toluenesulfonyl chloride in pyridine at room temperature and the resulting monotosylate in ether was treated with sodium methoxide in methanol at 0—3 °C to give the epoxide, which was then submitted to catalytic hydrogenolysis using 10% Pd–C and alcoholic sodium hydroxide to give the known optically-active 2-aryl-1-propanol derivative. Mitsui and Imaizumi[14] found that the hydrogenolysis of α-alkylstyrene oxides proceeded with predominant inversion of the configuration using a Pd–C catalyst in the presence of base. Application of Mitsui's rule to the epoxide suggested that the configuration (*R* or *S*) of the hydrogenolyzed 2-aryl-1-propanol derivative was the same as that of 2-aryl-1,2-propanediol derivative. The enantiomeric ratios of the optically active 2-aryl-1-propanol derivatives (**7**, **24**, and **32**) were also determined by comparisons of their specific rotations with those given in the literature.[3,15] From the above correlation, the enantiomeric ratios of the hydrolyzed alcohols [(−)-**19**, (−)-**27**, and (−)-**35**] and the unchanged acetates [(−)-**20**, (+)-**28**, and (−)-**36**] were finally determined. The results are summarized in Table I, including a previous result[16] with racemic 1-acetoxy-2-(*p*-tolyl)propane (**37**) for comparison.

The racemic acetates (**12** and **33**) were hydrolyzed by lipase to give predominantly the (*S*)-2-arylpropanol derivatives, (−)-**11** ($R/S = 12.1:87.9$) and (−)-**32** ($R/S = 3.3:96.7$), showing high enantioselectivities, and the results were in good agreement with that ($R/S = 5:95$)[16] for 1-acetoxy-2-(*p*-tolyl)propane (**37**). However, the racemic acetate **25**, possessing an 1-(acetoxymethyl)ethyl moiety at the α-position on the naphthalene nucleus, was recovered intact, contrary to our expectation that it would readily afford an optically active 1-propanol derivative

TABLE I. Lipase-Catalyzed Hydrolysis of Racemic 1-Acetoxy-2-arylpropane Derivatives

Racemic substrate	Reaction time (h)	Hydrolyzed alcohol				Unchanged acetate			
		Product	Yield (%)[a]	$[\alpha]_D$ (°) (solvent)[b]	R/S	Product	Yield (%)[a]	$[\alpha]_D$ (°) (solvent)[b]	R/S
12	2	(−)-**11**	30	−10.31 (C)	12.1 : 87.9	(+)-**12**	52	+1.58 (C)	78.0 : 22.0
16	220	(−)-**15**	24	−0.53 (E)	54.4 : 45.6	(−)-**16**	39	−0.73 (C)	45.4 : 54.6
20	200	(−)-**19**	28	−0.88 (C)	52.5 : 47.5	(−)-**20**	51	−0.50 (C)	47.9 : 52.1
25	240		0			(±)-**25**	94		
28	240	(−)-**27**	46	−0.73 (C)	43.9 : 56.1	(+)-**28**	54	+5.42 (C)	56.0 : 44.0
33	24	(−)-**32**	40	−24.61 (B)	3.3 : 96.7	(+)-**33**	46	+13.64 (B)	88.4 : 11.6
36	192	(−)-**35**	45	−0.22 (C)	50.5 : 49.5	(−)-**36**	48	−0.17 (C)	49.4 : 50.6
37[16]	2.5	(−)- **7**	43	−14.7 (C)	5 : 95	(+)-**37**	54	+5.50 (C)	86 : 14

a) Isolated yield. *b)* The abbreviations used are as follows: B, benzene; C, chloroform; E, ethanol.

(**24**). The enantioselectivities towards the racemic 1-acetoxy-2-aryl-2-propanol derivatives (**16**, **20**, **28**, and **36**) were very low. Thus, it is clear that the lipase (PPL-Sigma L-3126)-catalyzed hydrolyses of these compounds are unsuitable for optical resolution.

Experimental

All melting points are uncorrected. The infrared (IR) spectra and optical rotations were measured in chloroform. The ^{1}H-NMR spectra were recorded with a Hitachi R-1500 spectrometer (60 MHz) in deuteriochloroform using tetramethylsilane as an internal standard, and the following abbreviations are used: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. Column chromatography was performed using Merck silica gel (0.063—0.200 mm).

(±)-1-Acetoxy-2-phenylpropane (12) Methyl (±)-2-phenylpropanoate (**10**) (2.289 g), prepared from propiophenone according to the method of Fujii *et al.*,[13] was reduced with lithium aluminum hydride (584 mg) in dry ether (45 ml) at room temperature for 70 min. The mixture was poured into ice-dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo* to give (±)-2-phenyl-1-propanol (**11**) (1.801 g: 94.8% yield). IR: 3575, 3400 cm^{-1}.

A mixture of the above alcohol **11** (1.801 g) and acetic anhydride (7.0 ml) in pyridine (7.0 ml) was allowed to stand at room temperature for 22.5 h. After the usual work-up, the crude product was chromatographed on silica gel (20 g), using chloroform as an eluent, to give an acetate **12** (2.291 g: 97.2% yield). The IR and ^{1}H-NMR spectra of **12** were identical with those of an authentic sample.[3]

(±)-1-Acetoxy-2-phenyl-2-propanol (16) *m*-Chloroperbenzoic acid (80%, 4.746 g) was added to a stirred mixture of α-methylstyrene (**13**) (2.364 g) and anhydrous disodium hydrogen phosphate (3.691 g) in dichloromethane (50 ml) with cooling in an ice-water bath at 2—6 °C for 16 min. The mixture was further stirred at this temperature for 29 min, diluted with cold ether, and washed successively with water, aqueous sodium hydrogensulfite, water, aqueous sodium hydrogencarbonate, and water. The dried solution was evaporated *in vacuo*. The residue was chromatographed on silica gel (30 g), using chloroform as an eluent, to give an epoxide (**14**) (2.286 g: 85.2% yield). ^{1}H-NMR δ: 1.72 (3H, s, $-CH_3$), 2.78 and 2.98 (each 1H, d, J = 5.6 Hz, $-CH_2O-$), 7.34 (5H, s, aromatic protons).

A solution of the above epoxide (**14**) (2.286 g) in ether (38 ml) was stirred with dilute sulfuric acid (2%, 23 ml) at 2—5 °C for 20 min. The ether solution was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (30 g), using ether–chloroform (1 : 1) as an eluent, to give (±)-2-phenyl-1,2-propanediol (**15**) (701 mg: 27.0% yield). IR: 3550, 3380 cm^{-1}. ^{1}H-NMR δ: 1.51 (3H, s, $-CH_3$), 2.16 (1H, br s, $-OH$), 2.77 (1H, br s, $-OH$), 3.57 and 3.80 (each 1H, d, J = 11.1 Hz, $-C\underline{H}_2OH$), 7.23—7.50 (5H, m, aromatic protons). *Anal.* Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.24; H, 7.79.

A solution of (±)-**15** (820 mg) and acetic anhydride (3.0 ml) in pyridine (3.0 ml) was allowed to stand at room temperature for 23.5 h. After the usual work-up, the crude product was chromatographed on silica gel (20 g), using chloroform as an eluent, to give a racemic acetate (**16**) (1.031 g: 98.6% yield). IR: 3575, 3435, 1725 cm^{-1}. ^{1}H-NMR δ: 1.56 (3H, s, $-CH_3$), 2.04 (3H, s, $-OCOCH_3$), 2.54 (1H, s, $-OH$), 4.25 (2H, s, $-C\underline{H}_2OAc$), 7.26—7.52 (5H, m, aromatic protons). *Anal.* Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.18; H, 7.39.

(±)-1-Acetoxy-2-(*p*-tolyl)-2-propanol (20) *m*-Chloroperbenzoic acid (80%, 6.299 g) was added to a stirred mixture of 4-isopropenyltoluene[3] (**17**) (3.500 g) and anhydrous disodium hydrogen phosphate (4.898 g) in dichloromethane (65 ml) with cooling in an ice-water bath at 0—8 °C for 20 min. The mixture was further stirred at this temperature for 40 min and then treated as described for the preparation of **14** to give an ether solution (*ca.* 50 ml) containing a crude epoxide (**18**).

The above ether solution (*ca.* 50 ml) was stirred with dilute sulfuric acid (2%, 50 ml) at 2—4 °C for 20 min. The ether solution was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (60 g), using ether–chloroform (1 : 1) as an eluent, to give (±)-2-(*p*-tolyl)-1,2-propanediol (**19**) (1.294 g: 29.4% yield from **17**). IR: 3550 sh, 3400 cm^{-1}. ^{1}H-NMR δ: 1.44 (3H, s, $-CH_3$), 2.29 (3H, s, $-CH_3$), 3.47 and 3.70 (each 1H, d, J = 11.4 Hz, $-C\underline{H}_2OH$), 3.90 (2H, s, 2-OH), 7.09 and 7.30 (each 2H, d, J = 8.8 Hz, aromatic protons). *Anal.* Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.11; H, 8.37.

A solution of (±)-**19** (1.274 g) and acetic anhydride (4.0 ml) in pyridine (4.0 ml) was allowed to stand at room temperature for 24 h. After the usual work-up, the crude product was chromatographed on silica gel (20 g), using chloroform as an eluent, to give a racemic acetate (**20**) (1.506 g: 94.1% yield). IR: 3575, 3400, 1725 cm^{-1}. ^{1}H-NMR δ: 1.53 (3H, s, $-CH_3$), 2.02 (3H, s, $-OCOCH_3$), 2.33 (3H, s, $-CH_3$), 2.72 (1H, s, $-OH$), 4.22 (2H, t, J = 11.7 Hz, $-C\underline{H}_2OAc$), 7.13 and 7.36 (each 2H, d, J = 8.5 Hz, aromatic protons). *Anal.* Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.39; H, 7.61.

1-Isopropenylnaphthalene (23) A solution of 1′-acetonaphthone (**21**) (5.00 g) in dry ether (25 ml) was added dropwise to a stirred solution of methylmagnesium iodide (prepared from magnesium turnings (858 mg) and methyl iodide (2.4 ml) in dry ether (6.0 ml)) at room temperature for 40 min. The mixture was further stirred at room temperature for 2 h, poured into a mixture of ice and aqueous ammonium chloride (15%, 80 ml), and extracted with ethyl acetate. The ethyl acetate extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was recrystallized from acetone–hexane to give a *tert*-alcohol (**22**) (5.347 g: 97.7% yield), mp 83—85 °C. IR: 3600, 3420 cm^{-1}. ^{1}H-NMR δ: 1.86 (7H, s, 2-CH_3 and $-OH$), 7.36—7.95 (6H, m) and 8.74—8.91 (1H, m) (aromatic protons). *Anal.* Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.70; H, 7.71.

A stirred suspension of **22** (1.280 g) in dilute sulfuric acid (2%, 25 ml) was refluxed for 80 min. The mixture was cooled and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (40 g), using hexane as an eluent, to give **23** (1.059 g: 91.6% yield). ^{1}H-NMR δ: 2.21 (3H, s, $-CH_3$), 5.07 and 5.41 (each 1H, br s, $=CH_2$), 7.25—8.20 (7H, m, aromatic protons). *Anal.* Calcd for $C_{13}H_{12}$: C, 92.81; H, 7.19. Found: C, 92.65; H, 7.41.

(±)-1-Acetoxy-2-(1-naphthyl)propane (25) A solution of tetrahydrofuran–borane (1 : 1) addition compound (1 mol dm^{-3}: 4.3 ml) was added dropwise to a stirred solution of **23** (1.020 g) in dry tetrahydrofuran (5.1 ml) at −29 to −27 °C for 5 min under a stream of nitrogen. After the mixture had been stirred at 0—5 °C for 80 min and at room temperature for 2.5 h, the following solutions were added successively at

−24 to −3 °C: aqueous tetrahydrofuran (50%, 1.9 ml), aqueous sodium hydroxide (12%, 1.9 ml), and hydrogen peroxide (30%, 1.9 ml). The mixture was stirred at 0—5 °C for 30 min and at room temperature for 1 h, then diluted with brine, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (25 g), using benzene as an eluent, to give the recovered **23** (277 mg: 27.2% yield). Further elution with benzene and ether–benzene (5 : 95) afforded (±)-2-(1-naphthyl)-1-propanol (**24**) (693 mg: 61.4% yield). IR: 3580, 3400 cm^{-1}. ^{1}H-NMR δ: 1.43 (3H, d, J=6.7 Hz, –CH(C$\underline{H}_3$)–), 1.49 (1H, s, –OH), 3.80 (1H, d, J=7.6 Hz) and 3.96 (1H, d, J=7.9 Hz) (–C$\underline{H}_2$OH), *ca.* 3.88 (1H, m, overlap, –C$\underline{H}$(CH$_3$)–), 7.34—8.24 (7H, m, aromatic protons). *Anal.* Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 84.02; H, 7.79.

A solution of (±)-**24** (91 mg) and acetic anhydride (0.5 ml) in pyridine (0.5 ml) was heated at 80—85 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (5 g), using chloroform as an eluent, to give a racemic acetate (**25**) (106 mg: 94.6% yield). IR: 1720 cm^{-1}. ^{1}H-NMR δ: 1.45 (3H, d, J=6.4 Hz, –CH(C$\underline{H}_3$)–), 2.00 (3H, s, –OCOCH$_3$), 3.81—4.60 (3H, m, –C$\underline{H}$(CH$_3$)C$\underline{H}_2$–), 7.38-8.25 (7H, m, aromatic protons). *Anal.* Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.69; H, 7.21.

(±)-1-Acetoxy-2-(1-naphthyl)-2-propanol (28) *m*-Chloroperbenzoic acid (80%, 2.563 g) was added to a stirred mixture of 1-isopropenylnaphthalene (**23**) (1.815 g) and anhydrous disodium hydrogen phosphate (1.987 g) in dichloromethane (36 ml) at room temperature for 5 min. The mixture was further stirred at room temperature for 3 h and then treated as described for the preparation of **14** to give a crude epoxide (**26**) (2.059 g). ^{1}H-NMR δ: 1.74 (3H, s, –CH$_3$), 2.95 and 3.15 (each 1H, d, J=5.3 Hz, –CH$_2$O–), 7.36—8.24 (7H, m, aromatic protons).

A solution of the above crude epoxide (**26**) (2.059 g) in tetrahydrofuran (20 ml) was stirred with dilute sulfuric acid (2%, 20 ml) in an ice-water bath for 1.5 h. The mixture was extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (30 g), using ether–chloroform (1 : 1) as an eluent, to give (±)-2-(1-naphthyl)-1,2-propanediol (**27**) (1.565 g: 71.7% yield from **23**). IR: 3565, 3415 cm^{-1}. ^{1}H-NMR δ: 1.79 (3H, s, –CH$_3$), 2.15 (2H, br s, 2-OH), 3.84 and 4.29 (each 1H, d, J=11.4 Hz, –C$\underline{H}_2$OH), 7.27—7.96 (6H, m) and 8.56—8.73 (1H, m) (aromatic protons). *Anal.* Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.36; H, 7.13.

A solution of (±)-**27** (1.272 g) and acetic anhydride (5.0 ml) in pyridine (5.0 ml) was allowed to stand at room temperature for 44.5 h. After the usual work-up, the crude product was chromatographed on silica gel (30 g), using ether–chloroform (1 : 9) as an eluent, to give a racemic acetate (**28**) (1.440 g: 93.8% yield). IR: 3600, 3470, 1730 cm^{-1}. ^{1}H-NMR δ: 1.83 (3H, s, –CH$_3$), 2.06 (3H, s, –OCOCH$_3$), 2.72 (1H, br s, –OH), 4.45 and 4.78 (each 1H, d, J=11.4 Hz, –C$\underline{H}_2$OAc), 7.32—8.83 (7H, m, aromatic protons). *Anal.* Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.91; H, 6.47.

2-Isopropenylnaphthalene (31) A solution of 2′-acetonaphthone (**29**) (25.00 g) in dry ether (170 ml) was added dropwise to a stirred solution of methylmagnesium iodide (prepared from magnesium turnings (4.287 g) and methyl iodide (11.9 ml) in dry ether (70 ml)) at room temperature for 1 h. The mixture was further stirred at room temperature for 2 h, poured into a mixture of ice and aqueous ammonium chloride (15%, 150 ml), and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The residue was recrystallized from hexane to give 2-(2-naphthyl)-2-propanol (**30**) (25.715 g: 94.0% yield), mp 64—65 °C. IR: 3580, 3400 cm^{-1}. ^{1}H-NMR δ: 1.67 (6H, s, 2-CH$_3$), 1.87 (1H, br s, –OH), 7.25—7.92 (7H, m, aromatic protons). *Anal.* Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.69; H, 7.46.

A stirred suspension of **30** (4.006 g) in dilute sulfuric acid (2%, 80 ml) was refluxed for 2 h. The mixture was cooled and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was recrystallized from hexane to give an isopropenyl compound (**31**) (3.004 g: 83.0% yield), mp 53—53.5 °C. ^{1}H-NMR δ: 2.26 (3H, s, –CH$_3$), 5.19 and 5.52 (each 1H, br s, =CH$_2$), 7.23—7.84 (7H, m, aromatic protons). *Anal.* Calcd for $C_{13}H_{12}$: C, 92.81; H, 7.19. Found: C, 92.60; H, 7.42. The mother liquor of recrystallization was evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using hexane as an eluent, to give additional **31** (480 mg: 13.3% yield).

(±)-1-Acetoxy-2-(2-naphthyl)propane (33) A solution of tetrahydrofuran–borane (1 : 1) addition compound (1 mol dm^{-3}: 61.6 ml) was added dropwise to a stirred solution of **31** (14.807 g) in dry tetrahydrofuran (74 ml) at −42 to −23 °C for 10 min under a stream of nitrogen. After the mixture had been stirred at 0—5 °C for 1 h and at room temperature for 2.5 h, the following solutions were added successively at −35 to −3 °C: aqueous tetrahydrofuran (50%, 27.6 ml), aqueous sodium hydroxide (12%, 27.6 ml), and hydrogen peroxide (30%, 27.6 ml). The mixture was stirred at 0—5 °C for 30 min and at room temperature for 1 h, then diluted with brine, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was recrystallized from a mixture of chloroform and hexane to give (±)-2-(2-naphthyl)-1-propanol (**32**) (14.822 g: 90.4% yield), mp 60.5—61 °C. IR: 3610, 3440 cm^{-1}. ^{1}H-NMR δ: 1.36 (3H, d, J=6.7 Hz, –CH(C$\underline{H}_3$)–), 3.11 (1H, m, –C$\underline{H}$(CH$_3$)–), 3.79 (2H, d, J=6.5 Hz, –C$\underline{H}_2$OH), 7.25—7.90 (7H, m, aromatic protons). *Anal.* Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.61; H, 7.39.

A solution of (±)-**32** (1.001 g) and acetic anhydride (4.0 ml) in pyridine (4.0 ml) was heated at 75—80 °C for 1.5 h. After the usual work-up, the crude product was chromatographed on silica gel (50 g), using hexane–chloroform (1 : 1 and then 1 : 4) as eluents, to give a racemic acetate (**33**) (1.207 g: 98.3% yield). IR: 1720 cm^{-1}. ^{1}H-NMR δ: 1.38 (3H, d, J=7.0 Hz, –CH(C$\underline{H}_3$)–), 2.00 (3H, s, –OCOCH$_3$), 3.26 (1H, m, –C$\underline{H}$(CH$_3$)–), 4.26 (2H, d, J=7.2 Hz, –C$\underline{H}_2$OAc), 7.18—7.89 (7H, m, aromatic protons). *Anal.* Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.17; H, 7.28.

(±)-1-Acetoxy-2-(2-naphthyl)-2-propanol (36) *m*-Chloroperbenzoic acid (80%, 1.275 g) was added to a stirred mixture of **31** (912 mg) and anhydrous disodium hydrogen phosphate (995 mg) in dichloromethane (25 ml) at 0—5 °C for 15 min. The mixture was further stirred at 0—5 °C for 45 min, diluted with cold ether (40 ml), and washed successively with cold water, aqueous sodium hydrogensulfite, water, aqueous sodium hydrogencarbonate, and water. The dried solution was evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g), using ether–benzene (1 : 3) as an eluent, to give (±)-2-(2-naphthyl)-1,2-propanediol (**35**) (489 mg: 44.6% yield from **31**), which was recrystallized from a mixture of acetone and hexane, mp 96—96.5 °C. IR: 3535, 3375 cm^{-1}. ^{1}H-NMR δ: 1.62 (3H, s, –CH$_3$), 3.69 and 3.94 (each 1H, d, J=11 Hz, –C$\underline{H}_2$OH), 7.26—7.96 (7H, m, aromatic protons). *Anal.* Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.08; H, 6.77.

A solution of (±)-**35** (238 mg) and acetic anhydride (1.0 ml) in pyridine (1.0 ml) was allowed to stand at room temperature for 28 h. After the usual work-up, the crude product was chromatographed on silica gel (15 g), using ether–benzene (1 : 9) as an eluent, to give a racemic acetate (**36**) (250 mg: 91.6% yield). IR: 3575, 3450, 1730 cm^{-1}. ^{1}H-NMR δ: 1.65 (3H, s, –CH$_3$), 2.03 (3H, s, –OCOCH$_3$), 2.67 (1H, br s, –OH), 4.27 and 4.48 (each 1H, d, J=11.5 Hz, –C$\underline{H}_2$OAc), 7.38—7.94 (7H, m, aromatic protons). *Anal.* Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.58; H, 6.51.

Lipase-Catalyzed Hydrolyses of the Racemic Acetates (12, 16, 20, 25, 28, 33, and 36) Each of the racemic acetates was hydrolyzed with lipase (PPL-Sigma L-3126) using phosphate buffer (pH 7.0) in methanol at 35—36 °C for 2—240 h. The reaction mixture was extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel to give the recovered acetate and the hydrolyzed alcohol.

a) (±)-**12** (537 mg) was hydrolyzed with lipase (537 mg) and 0.1 M phosphate buffer (45.0 ml) in methanol (15.0 ml) for 2.0 h to give a crude product (457 mg) (**11**/**12**=43 : 57 by ^{1}H-NMR). The crude product was chromatographed on silica gel (30 g), using chloroform as an eluent, to give the recovered acetate (+)-**12** (279 mg: 52.0% yield), $[\alpha]_D$ +1.58° (c=3.80), R/S=78.0 : 22.0, and an alcohol (−)-**11** (125 mg: 30.4% yield), $[\alpha]_D$ −10.31° (c=2.69), R/S=12.1 : 87.9. The recovered acetate (+)-**12** (234 mg) in dry ether (3.0 ml) was treated with lithium aluminum hydride (82 mg) at room temperature for 1 h. After the usual work-up, the crude product was purified by column chromatography on silica gel (20 g), using chloroform as an eluent, to give an alcohol (+)-**11** (145 mg: 80.9% yield), $[\alpha]_D$ +7.62° (c=2.60), R/S=78.0 : 22.0.

b) (±)-**16** (477 mg) was hydrolyzed with lipase (477 mg) and 0.1 M phosphate buffer (45.0 ml) in methanol (15.0 ml) for 220 h to give a crude product (364 mg) (**15**/**16**=47 : 53 by ^{1}H-NMR). The crude product was chromatographed on silica gel (15 g), using chloroform as an eluent, to give the recovered acetate (−)-**16** (184 mg: 38.6% yield), $[\alpha]_D$ −0.73°

($c=5.64$). Further elution with ether–chloroform (3 : 7) afforded a diol (−)-**15** (88 mg: 23.5% yield), $[\alpha]_D$ −0.53° (ethanol, $c=1.33$), $R/S=54.4:45.6$.

The recovered acetate (−)-**16** (177 mg) in dry ether (3.0 ml) was treated with lithium aluminum hydride (58 mg) at room temperature for 1 h. The crude product was chromatographed on silica gel (20 g), using ether–chloroform (3 : 7) as an eluent, to give a diol (+)-**15** (68 mg: 50.4% yield), $[\alpha]_D$ +0.56° (ethanol, $c=1.45$), $R/S=45.4:54.6$.

c) (±)-1-Acetoxy-2-(p-tolyl)-2-propanol (**20**) (419 mg) was hydrolyzed with lipase (419 mg) and 0.1 M phosphate buffer (42.0 ml) in methanol (14.0 ml) for 200 h to give a crude product (357 mg) (**19**/**20**=40 : 60 by ^{1}H-NMR). The crude product was chromatographed on silica gel (10 g), using chloroform as an eluent, to give the recovered acetate (−)-**20** (214 mg: 51.1% yield) $[\alpha]_D$ −0.50° ($c=2.63$). Further elution with ether–chloroform (3 : 7) afforded a diol (−)-**19** (94 mg: 28.1% yield), $[\alpha]_D$ −0.88° ($c=3.42$).

Conversion of the hydrolyzed diol (−)-**19** into (+)-2-(*p*-tolyl)-1-propanol (**7**): A solution of the hydrolyzed diol (−)-**19** (92 mg) and p-toluenesulfonyl chloride (126 mg) in pyridine (1.0 ml) was allowed to stand at room temperature for 26 h. The mixture was poured into a mixture of ice and dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo* to give a crude monotosylate (168 mg). ^{1}H-NMR δ: 1.53, 2.32, and 2.42 (each 3H, s, 3-CH_3), 2.80 (1H, br s, –OH), 4.03 (2H, s, –CH_2O–), 7.00—7.80 (8H, m, aromatic protons).

A solution of sodium methoxide (30 mg) in methanol (0.8 ml) was added to a stirred solution of the crude tosylate (168 mg) in dry ether (1.6 ml) with cooling in an ice-water bath. The mixture was further stirred for 1 h and then diluted with ether. The precipitates were removed by filtration and the filtrate was evaporated *in vacuo*. The residue was extracted with ether and the ether extract was evaporated *in vacuo* to give a crude epoxide (**18**) (88 mg). ^{1}H-NMR δ: 1.70 and 2.32 (each 3H, s, 2-CH_3), 2.78 and 2.97 (each 1H, d, $J=5.6$ Hz, –CH_2O–).

A mixture of 10% Pd–C (23 mg) and alcoholic sodium hydroxide (2%, 0.2 ml) in ethanol (5.0 ml) was stirred at room temperature for 1 h. After the addition of a solution of the crude epoxide (**18**) (88 mg) in ethanol (5.0 ml), the mixture was stirred at room temperature under an atmosphere of hydrogen for 2 h. The mixture was filtered and the filtrate was acidified with acetic acid (0.03 ml). The acidic solution was evaporated *in vacuo* and the residue was extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using chloroform as an eluent, to give an alcohol (+)-**7** (36 mg: 43.3% yield from (−)-**19**), $[\alpha]_D$ +0.84° ($c=1.78$), $R/S=52.5:47.5$.

Conversion of the recovered acetate (−)-**20** into (−)-**7**: The recovered acetate (−)-**20** (104 mg) in dry ether (2.0 ml) was treated with lithium aluminum hydride (57 mg) at room temperature for 2 h. The crude product was chromatographed on silica gel (10 g), using ether–chloroform (3 : 7) as an eluent, to give a diol (+)-**19** (57 mg: 68.7% yield), $[\alpha]_D$ +0.74° ($c=2.83$).

A mixture of the diol (+)-**19** (57 mg) and *p*-toluenesulfonyl chloride (78 mg) in pyridine (1.0 ml) was allowed to stand at room temperature for 70 h to give a crude tosylate (91 mg).

A solution of the crude tosylate (91 mg) in dry ether (1.0 ml) was treated with a solution of sodium methoxide (18 mg) in methanol (0.5 ml) at 0—3 °C for 1 h to give a crude epoxide (**18**) (48 mg).

A mixture of 10% Pd–C (13 mg) and alcoholic sodium hydroxide (2%, 0.1 ml) in ethanol (5.0 ml) was stirred at room temperature for 1 h. After the addition of a solution of the crude epoxide (**18**) (48 mg) in ethanol (5.0 ml), the mixture was stirred at room temperature under an atmosphere of hydrogen for 2 h. The crude product was chromatographed on silica gel (5 g), using chloroform as an eluent, to give an alcohol (−)-**7** (14 mg: 26.9% yield from (+)-**19**), $[\alpha]_D$ −0.71° ($c=0.42$), $R/S=47.9:52.1$.

d) (±)-**25** (32 mg) was submitted to lipase-catalyzed hydrolysis for 240 h to give the unchanged acetate (30 mg).

e) (±)-**28** (1.440 g) was hydrolyzed with lipase (1.440 g) and 0.1 M phosphate buffer (144 ml) in methanol (48.0 ml) for 240 h to give a crude product (1.398 g) (**27**/**28**=46 : 54 by ^{1}H-NMR). The crude product was chromatographed on silica gel (30 g), using ether–chloroform (1 : 9) as an eluent, to give the recovered acetate (+)-**28** (777 mg: 54.0% yield), $[\alpha]_D$ +5.42° ($c=5.24$). Further elution with the same solvent afforded a diol (−)-**27** (543 mg: 45.6% yield), $[\alpha]_D$ −0.73° ($c=5.89$).

Conversion of the hydrolyzed diol (−)-**27** into (+)-**24**: A solution of the hydrolyzed diol (−)-**27** (292 mg) and p-toluenesulfonyl chloride (330 mg) in pyridine (1.5 ml) was allowed to stand at room temperature for 67 h to give a crude tosylate (506 mg). ^{1}H-NMR δ: 1.83 and 2.40 (each 3H, s, 2-CH_3), 2.13 (1H, s, –OH), 4.32 and 4.61 (each 1H, d, $J=10.0$ Hz, –CH_2O-), 7.13—8.56 (11H, m, aromatic protons). IR: 3590 cm^{-1}.

A solution of sodium methoxide (78 mg) in methanol (2.5 ml) was added to a stirred solution of the crude tosylate (506 mg) in dry ether (5.0 ml) with cooling in an ice-water bath. The mixture was further stirred for 1 h, diluted with ether, and then filtered. The filtrate was evaporated *in vacuo*. The residue was chromatographed on silica gel (15 g), using chloroform as an eluent, to give an epoxide (+)-**26** (252 mg: 94.7% yield from (−)-**27**), $[\alpha]_D$ +15.3° ($c=3.87$).

A mixture of 10% Pd–C (60 mg) and alcoholic sodium hydroxide (2%, 0.6 ml) in ethanol (7.5 ml) was stirred at room temperature for 1 h. After the addition of a solution of the epoxide (+)-**26** (238 mg) in ethanol (7.5 ml), the mixture was stirred at room temperature under an atmosphere of hydrogen for 3 h. The crude product was chromatographed on silica gel (10 g), using chloroform as an eluent, to give an alcohol (+)-**24** (212 mg: 88.0% yield), $[\alpha]_D$ +0.98° (benzene, $c=2.24$), $R/S=43.9:56.1$.

Conversion of the recovered acetate (+)-**28** into (−)-**24**: A mixture of the recovered acetate (+)-**28** (341 mg) and lithium aluminum hydride (85 mg) in dry ether (3.0 ml) was stirred at room temperature for 2.5 h. After the usual work-up, the crude product was chromatographed on silica gel (10 g), using ether–chloroform (3 : 7) as an eluent, to give a diol (+)-**27** (235 mg: 83.3% yield), $[\alpha]_D$ +0.73° ($c=2.87$).

A solution of the diol (+)-**27** (198 mg) and *p*-toluenesulfonyl chloride (225 mg) in pyridine (1.0 ml) was stirred at room temperature for 67 h to give a crude tosylate (341 mg). IR: 3590 cm^{-1}.

A solution of sodium methoxide (53 mg) in methanol (1.5 ml) was added to a stirred solution of the crude tosylate (319 mg) in dry ether (3.0 ml) with cooling in an ice-water bath. The mixture was stirred for 1 h and then treated as described above. The crude product was chromatographed on silica gel (15 g), using chloroform as an eluent, to give an epoxide (−)-**26** (149 mg: 82.8% yield from (+)-**27**), $[\alpha]_D$ −17.4° ($c=3.12$).

A mixture of 10% Pd–C (40 mg) and alcoholic sodium hydroxide (2%, 0.4 ml) in ethanol (5.0 ml) was stirred at room temperature for 1 h. After the addition of a solution of the epoxide (−)-**26** (146 mg) in ethanol (5.0 ml), the mixture was stirred at room temperature under an atmosphere of hydrogen for 4 h. The crude product was chromatographed on silica gel (10 g), using chloroform as an eluent, to give an alcohol (−)-**24** (120 mg: 81.1% yield), $[\alpha]_D$ −0.97° (benzene, $c=2.78$), $R/S=56.0:44.0$.

f) (±)-1-Acetoxy-2-(2-naphthyl)propane (**33**) (1.077 g) was hydrolyzed with lipase (1.077 g) and 0.1 M phosphate buffer (108 ml) in methanol (36.0 ml) for 24 h to give a crude product (928 mg) (**32**/**33**=45 : 55 by ^{1}H-NMR). The crude product was chromatographed on silica gel (20 g), using hexane–chloroform (1 : 4) as an eluent, to give the recovered acetate (+)-**33** (494 mg: 45.9% yield), $[\alpha]_D$ +13.64° (benzene, $c=3.35$). Further elution with the same solvent gave an alcohol (−)-**32** (353 mg: 40.2% yield), $[\alpha]_D$ −24.61° (benzene, $c=1.30$), $R/S=3.3:96.7$.

A solution of the recovered acetate (+)-**33** (60 mg) in dry ether (2.0 ml) was treated with lithium aluminum hydride (15 mg) at room temperature for 1 h. After the usual work-up, the crude product was chromatographed on silica gel (10 g), using chloroform as an eluent, to give an alcohol (+)-**32** (48 mg: 98.0% yield), $[\alpha]_D$ +20.23° (benzene, $c=2.66$), $R/S=88.4:11.6$.

g) (±)-**36** (1.587 g) was hydrolyzed with lipase (1.587 g) using 0.1 M phosphate buffer (159 ml) in methanol (53 ml) for 192 h to give a crude product (1.429 g) (**35**/**36**=50 : 50 by ^{1}H-NMR). The crude product was chromatographed on silica gel (25 g), using ether–chloroform (5 : 95) as an eluent, to give the recovered acetate (−)-**36** (765 mg: 48.2% yield), $[\alpha]_D$ −0.17° ($c=23.1$). Further elution with the same solvent gave a diol (−)-**35** (590 mg: 44.9% yield), $[\alpha]_D$ −0.22° ($c=7.91$).

Conversion of the hydrolyzed diol (−)-**35** into (+)-**32**: A solution of the diol (−)-**35** (311 mg) and p-toluenesulfonyl chloride (353 mg) in pyridine (1.5 ml) was allowed to stand at room temperature for 48 h to give a crude tosylate (576 mg). ^{1}H-NMR δ: 1.61 and 2.32 (each 3H, s, 2-CH_3), 2.71 (1H, s, –OH), 4.17 (2H, s, –CH_2O–), 7.04—7.81 (11H, m, aromatic protons). IR: 3590 cm^{-1}.

A solution of sodium methoxide (83 mg) in methanol (2.9 ml) was added to a stirred solution of the crude tosylate (576 mg) in dry ether (5.8 ml) with cooling in an ice-water bath. The mixture was further stirred for 1 h to give a crude epoxide (**34**) (321 mg). ^{1}H-NMR δ: 1.78 (3H, s, $-CH_3$), 2.83 and 3.00 (each 1H, d, J = 5.6 Hz, $-CH_2O-$), 7.15—7.83 (7H, m, aromatic protons).

A mixture of 10% Pd–C (80 mg) and alcoholic sodium hydroxide (2%, 0.8 ml) in ethanol (10 ml) was stirred at room temperature for 1 h. After the addition of a solution of the crude epoxide (321 mg) in ethanol (10 ml), the mixture was stirred at room temperature under an atmosphere of hydrogen for 2 h. The crude product was chromatographed on silica gel (20 g), using hexane–chloroform (1 : 4) as an eluent, to give an alcohol (+)-**32** (241 mg: 76.8% yield from (−)-**35**), $[\alpha]_D$ +0.27° (benzene, c = 4.44), R/S = 50.5 : 49.5.

Conversion of the recovered acetate (−)-**36** into (−)-**32**: A mixture of the recovered acetate (−)-**36** (303 mg) and lithium aluminum hydride (75 mg) in dry ether (3.0 ml) was stirred at room temperature for 1 h. The crude product was chromatographed on silica gel (10 g), using ether–chloroform (3 : 7) as an eluent, to give a diol (+)-**35** (212 mg: 84.6% yield), $[\alpha]_D$ +0.27° (c = 5.19).

A solution of the diol (+)-**35** (166 mg) and p-toluenesulfonyl chloride (187 mg) in pyridine (1.0 ml) was stirred at room temperature for 48 h to give a crude tosylate (341 mg). IR: 3590 cm^{-1}.

A solution of sodium methoxide (44 mg) in methanol (1.5 ml) was added to a stirred solution of the crude tosylate (341 mg) in dry ether (3.0 ml) with cooling in an ice-water bath. The mixture was stirred at room temperature for 1 h and then treated as described above to give a crude epoxide (**34**) (180 mg).

A mixture of 10% Pd–C (50 mg) and alcoholic sodium hydroxide (2%, 0.5 ml) in ethanol (6.0 ml) was stirred at room temperature for 1 h. After the addition of a solution of the epoxide (**34**) (180 mg) in ethanol (6.0 ml), the mixture was stirred at room temperature under an atmosphere of hydrogen for 2 h. The crude product was chromatographed on silica gel (15 g), using hexane–chloroform (1 : 4) as an eluent, to give an alcohol (−)-**32** (142 mg: 92.8% yield from (+)-**35**), $[\alpha]_D$ −0.33° (benzene, c = 3.64), R/S = 49.4 : 50.6.

References

1) Y. Nakamura, T. Yamaguchi, *Drug. Metab. Dispos.*, **15**, 529 (1987), and references cited therein.
2) T. Nomura, T. Imai, M. Otagiri, *Biol. Pharm. Bull.*, **16**, 298 (1993), and references cited therein.
3) T. Matsumoto, T. Ishida, T. Yoshida, H. Terao, Y. Takeda, Y. Asakawa, *Chem. Pharm. Bull.*, **40**, 1721 (1992).
4) T. Itoh, E. Ohira, Y. Takagi, S. Nishiyama, K. Nakamura, *Bull. Chem. Soc. Jpn.*, **64**, 624 (1991), and references cited therein.
5) T. Sasaki, Y. Iida, S. Kikuyama, S. Tsuboi, M. Utaka, *Chem. Lett.*, **1991**, 1651.
6) T. Itoh, T. Ohta, *Chem. Lett.*, **1991**, 217.
7) H. Akita, T. Kawaguchi, Y. Enoki, T. Oishi, *Chem. Pharm. Bull.*, **38**, 323 (1990).
8) R. Chenevert, M. Desjardins, R. Gagnon, *Chem. Lett.*, **1990**, 33.
9) H. Suemune, M. Hizuka, T. Kamashita, K. Sakai, *Chem. Pharm. Bull.*, **37**, 1379 (1989).
10) T. Miyazawa, H. Iwanaga, S. Ueji, T. Yamada, S. Kuwata, *Chem. Lett.*, **1989**, 2219, and references cited therein.
11) Y. Hirose, M. Anzai, M. Saitoh, K. Naemura, H. Chikamatsu, *Chem. Lett.*, **1989**, 1939.
12) K. Mori, T. Takeuchi, *Tetrahedron*, **44**, 333 (1988).
13) K. Fujii, K. Nakao, T. Yamaguchi, *Synthesis*, **1982**, 456.
14) S. Mitsui, S. Imaizumi, *Nippon Kagaku Zasshi*, **86**, 219 (1965).
15) R. Menicagli, O. Piccolo, L. Lardicci, M. L. Wis, *Tetrahedron*, **35**, 1301 (1979).
16) T. Matsumoto, Y. Takeda, H. Terao, T. Takahashi, M. Wada, *Chem. Pharm. Bull.*, **41**, 1459 (1993).