(BTAF) (482 mg, 1.5 equiv) in THF (4 mL) containing 4-Å molecular sieves (0.5 g). The reaction was allowed to stir for 3 h. Filtration and removal of the solvent in vacuo followed by chromatography (silica gel, 5% ethyl acetate–hexane) afforded 275 mg (61.9%) of product whose NMR analysis indicated it to be a 1:1 mixture of epimers. This mixture was dissolved in methanol (25 mL) containing potassium bicarbonate (0.7g) and allowed to stir for 3 h. The solvent was evaporated, followed by dissolving the resultant product in methylene chloride. After a quick filtration through Florisil, the solvent was again removed in vacuo to afford 261 mg (58.7%) of 11: $[\alpha]^{24}_D$–20° (c 1.4, $CHCl_3$); IR ($CHCl_3$) 2940, 1699, 16408 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (3 H, s), 0.92 (3 H, s), 1.13 (3 H, s), 1.20–2.68 (14 H, complex), 4.95–5.03 (2 H, m), 5.71–5.86 (1 H, m); mass spectrum, *m/e* 234.1982 (M^+ calcd for $C_{16}H_{26}O$, 234.1984).

Anal. Calcd for $C_{16}H_{26}O$: C, 82.05; H, 11.10. Found: C, 82.10; H, 11.10.

Keto Aldehyde 12. Ozone was passed through a solution of **11** (62 mg, 0.27 mmol) in methylene chloride (25 mL) for 15 min at −78 °C. Triphenylphosphine (0.4 mmol) was then added to the solution as it was allowed to warm to room temperature. After 2 h the solvent was evaporated and the resultant material chromatographed (silica gel, 10% ethyl acetate–hexane) to yield 54 mg (85%) of **12**: $[\alpha]^{25}_D$ −19° (c 1.2, $CHCl_3$); IR ($CHCl_3$) 2735, 1725, 1705, 1463, 1390, 1380, 1362, 995 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (3 H, s), 0.92 (3 H, s), 1.19 (3 H, s), 1.06–2.22 (12 H, complex), 2.88 (1 H, dd, J = 17, 7 Hz), 3.27 (1 H, m), 9.79 (1 H, br s); mass spectrum, *m/e* 237.1841 (M^+ calcd for $C_{15}H_{25}O_2$, 237.1858).

(+)-Pallescensin A (8). Keto aldehyde **12** (17 mg, 0.07 mmol) was added to a solution of dry benzene (30 mL) containing 2 drops of boron trifluoride–etherate. The solution was heated to reflux for 1 h with water removal (Dean–Stark apparatus). The solution was allowed to cool and then diluted with ether (50 mL) and water (40 mL). The organic layer was washed with brine, dried over anhydrous magnesium sulfate, concentrated in vacuo, and chromatographed (silica gel, hexanes) to afford 5.6 mg (35%) of **8**, the spectroscopic data (NMR and IR) of which were identical with those of authentic spectra of natural pallescensin A (**8**):[17b] $[\alpha]^{25}_D$ +81.3° (c 1.3, $CHCl_3$); IR ($CHCl_3$) 2930, 2858, 1500, 1460, 1375 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.92 (6 H, s), 1.18 (3 H, s), 1.20–2.70 (11 H, complex), 6.08 (1 H, d, J = 2 Hz), 7.15 (1 H, d, J = 2 Hz); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.91 (3 H, s), 0.93 (3 H, s) 1.19 (3 H, s), 1.21–1.90 (8 H, complex), 2.08–2.16 (1 H, m), 2.30–2.57 (2 H, m), 6.11 (1 H, d, J = 1.8 Hz), 7.18 (1 H, d, J = 1.8 Hz).

Acknowledgment. It is a pleasure to acknowledge the support of this investigation by the National Institutes of Health (Institute of Neurology, Communication Disorders and Stroke) through Grant No. 18254. In addition, we thank Drs. G. Furst and T. Terwilliger of the University of Pennsylvania Spectroscopic Facilities for aid in obtaining the high-field NMR and MS spectral data, respectively.

Registry No. **1a**, 91547-50-1; **1b**, 91547-51-2; **1c**, 91444-81-4; **1d**, 91444-82-5; **1e**, 91444-83-6; **1f**, 91547-52-3; **1g**, 91444-84-7; **4**, 91444-85-8; **5**, 33878-99-8; **6**, 61950-54-7; **7**, 91547-53-4; **8**, 56881-68-6; **9**, 91547-54-5; **10**, 60134-39-6; **11**, 91444-86-9; **12**, 91444-87-0; methyl iodide, 74-88-4; allyl bromide, 106-95-6; benzyl bromide, 100-39-0; *trans*-cinnamyl bromide, 26146-77-0; butyl iodide, 542-69-8; *trans*-3-pentenyl iodide, 56399-98-5.

Enantioselectivity of Microbial Hydrolysis of (±)-Decahydro-2-naphthyl Acetates. Preparations and Absolute Configurations of Chiral Decahydro-2-naphthols

Takayuki Oritani* and Kyohei Yamashita

Department of Agricultural Chemistry, Faculty of Agriculture, Tohoku University, Sendai 980, Japan

Chizuko Kabuto

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

Received August 16, 1983

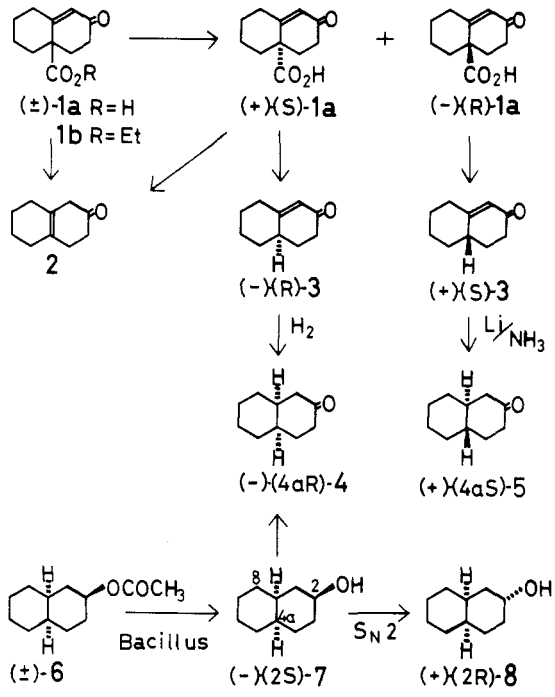
Absolute configurations of chiral decahydro-2-naphthols, which were obtained by microbial hydrolysis of corresponding (±)-acetates and chloroacetates, were elucidated by chemical correlation to (4a*S*,8a*S*)-*trans*-octahydro-2(1*H*)-naphthalenone (**5**). Decarboxylation of the (−)-α-methylbenzylamine salt of (−)-2-oxo-2,3,4,4a,5,6,7,8-octahydro-4a-naphthalenecarboxylic acid (**1a**) gave (+)-(*S*)-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (**3**), which was reduced with lithium in liquid ammonia to (+)-(4a*S*,8a*S*)-*trans*-octahydro-2-(1*H*)-naphthalenone (**5**). Catalytic hydrogenation of (−)-**3** gave (−)-(4a*R*,8a*S*)-*cis*-octahydro-2(1*H*)-naphthalenone (**4**), which was already obtained by oxidation of (−)-*cis*,*cis*-decahydro-2-naphthol (**7**) with chromic acid. These results mean that (−)-**7** has the 2*S*,4a*R*,8a*S* configuration. Furthermore, the absolute configuration of (−)-**7** was confirmed by X-ray analysis of its *p*-bromobenzoate.

(±)-Monocyclic monoterpene alcohols can be effectively resolved by microbial hydrolysis of corresponding acetates[1] and chlforoacetates.[2] In order to extend this enzymic resolution to (±)-bicyclic sesquiterpene alcohols, it is necessary to elucidate the stereochemistry on the microbial hydrolysis of (±)-decahydro-1- and 2-naphthyl acetates[2,3] having their fundamental ring structure. Already, chiral decahydronaphthols having an (*S*)-hydroxyl group had been prepared by microbial reduction of (±)-octahydronaphthalenones by Prelog et al.[4] But the reduction of (±)-*cis*-octahydro-2(1*H*)-naphthalenone (**4**) gave only racemic decahydro-2-naphthols, cis,cis form[5] **7**, and cis,trans

(1) Oritani, T.; Yamashita, K. *Agric. Biol. Chem.* **1973**, *37*, 1695.
(2) Oritani, T., Ichimura, M.; Yamashita, K. *Agric. Biol. Chem.* **1983**, *47*, 2613.
(3) Oritani, T.; Yamashita, K. *Agric. Biol. Chem.* **1974**, *38*, 1965.
(4) Prelog, V.; Smith, H. E. *Helv. Chim. Acta* **1959**, *42*, 2624.
(5) First cis for C-4a and C-8a hydrogens, second cis for C-2 and C-8a hydrogens on decahydro-2-naphthols, see: "Dictionary of Organic Compounds", 5th ed.; Chapman and Hall: London, 1982.

0022-3263/84/1949-3689$01.50/0

Scheme I



form 8. In the previous paper[3] the authors obtained chiral *cis,cis*-decahydro-2-naphthol (−)-7 by microbial hydrolysis of the corresponding acetate (±)-6, but the absolute stereochemistry of (−)-7 has not been clarified. Here, we elucidated the absolute configuration of (−)-7 and its related analogues by chemical correlation to (+)-(4a*S*,8a*S*)-*trans*-octahydro-2(1*H*)-naphthalenone (5), and the structure of (−)-7 was confirmed by X-ray analysis of its *p*-bromobenzoate. Furthermore, we clarified the enantioselectivity of microbial hydrolysis of (±)-decahydro-2-naphthyl acetate and chloroacetates.

Results and Discussion

Absolute Configuration of (−)-*cis*-Octahydro-2-(1*H*)-naphthalenone (4) and Its Related Analogue by Chemical Correlation. The condensation of ethyl 2-oxo-1-cyclohexanecarboxylate with 3-buten-2-one gave (±)-ethyl 2-oxo-2,3,4,4a,5,6,7,8-octahydronaphthalene-4a-carboxylate (**1b**),[6] hydrolysis of which with aqueous potassium hydroxide under reflux,[7] followed by decarboxylation, afforded (±)-α,β-unsaturated ketone, 4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (**3**), with a minor product of β,γ-unsaturated ketone, 3,4,5,6,7,8-hexahydro-2(1*H*)-naphthalenone (**2**).[8] Hydrolysis of (±)-**1b** with methanolic potassium hydroxide at 5 °C gave (±)-carboxylic acid **1a** (70% yield). Optical resolution of (±)-**1a** with (−)-(*S*)-α-methylbenzylamine gave an unstable levorotatory salt, which was treated with dilute hydrochloric acid to give (−)-2-oxo-2,3,4,4a,5,6,7,8-octahydronaphthalene-4a-carboxylic acid (**1a**). The salt of the dextrorotatory acid in the mother liquor was decarboxylated spontaneously on standing to afford (−)-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (**3**) with a minor product **2**. Also, the levorotatory salt was decarboxylated by warming to (+)-α,β-unsaturated ketone **3**, which was reduced with lithium in liquid ammonia to give

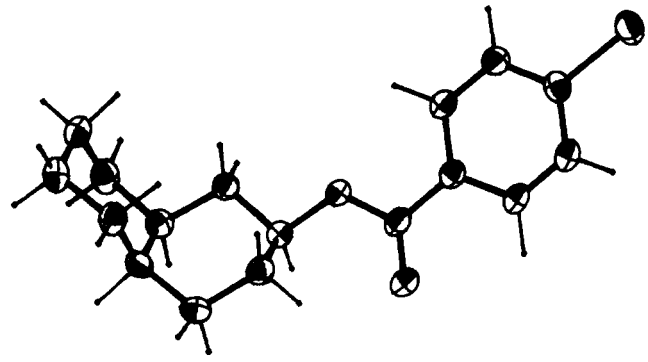
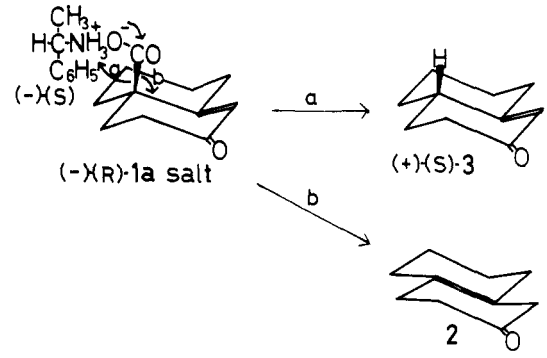


Figure 1. A perspective drawing of the *p*-bromobenzoate of (−)-*cis,cis*-decahydro-2-naphthol (−)-7. Ellipsoids of nonhydrogen atoms are scaled to include 30% probability.

Scheme II. The Proposed Mechanism for Decarboxylation of the (−)-(*S*)-α-Methylbenzylamine Salt of 2-Oxo-2,3,4,4a,5,6,7,8-octahydro-4a-naphthalenecarboxylic Acid (−)-1a



(+)-*trans*-octahydro-2(1*H*)-naphthalenone (**5**). As (+)-**5** with a positive Cotton effect has the 4a*S*,8a*S* configuration,[4] it is obvious that (+)-α,β-unsaturated ketone **3** has the *S* configuration. Decarboxylation of a primary amine salt of (−)-**1a** gave mainly (+)-α,β-unsaturated ketone **3** as described above in the case of α-methylbenzylamine salt. But the salt of a tertiary amine, quinine, or the free acid (−)-**1a** by heating over the melting point gave β,γ-unsaturated ketone **2**. From the steric course of this decarboxylation (S_Ei), it was deduced that (−)-**1a** has the *R* configuration as shown in Scheme II. Catalytic hydrogenation of (−)-**3** with palladium catalyst in ethanol[9] gave (−)-(4a*R*,8a*S*)-*cis*-octahydro-2(1*H*)-naphthalenone (**4**) which was contaminated with 4% of trans-ketone **5**. Optical resolution of (±)-**4** via the hydrazone derivative of (−)-menthyl *N*-aminocarbamate[10] gave partially resolved (−)-**4** without the contamination of the trans-isomer **5**.

Chiral Decahydro-2-naphthols Obtained by Microbial Hydrolysis of Corresponding (+)-Acetates and Chloroacetates. We already reported that microbial hydrolysis of (±)-*cis,cis*-decahydro-2-naphthyl acetate (**6**) by *Bacillus subtilis* var. *niger* IFO 3108 gave (−)-*cis,cis*-decahydro-2-naphthol (**7**),[11] which was oxidized with chromic acid to give (−)-cis-ketone **4**. From the above result, it was deduced that (−)-*cis,cis*-decahydro-2-naphthol (**7**) has the 2*S*,4a*R*,8a*S* configuration. Furthermore, recrystallization of (−)-**7** (54% enantiomeric excess, ee) gave optically pure (−)-**7**, which reacted with *p*-bromobenzoyl chloride in pyridine to give the crystalline *p*-bromo-

(6) Dreiding, A. S.; Tomasewski, A. J. *J. Am. Chem. Soc.* **1955**, *77*, 411.
(7) du Feu, E. C.; McQuillin, F. T.; Robinson, A. *J. Chem. Soc.* **1937**, 53.
(8) Augustine, R. E.; Caputo, J. A. "Organic Synthesis"; Wiley: New York, 1973; Collect. Vol. 5, pp 869–871. Birch, A. J. *J. Chem. Soc.* **1946**, 593; *J. Chem. Soc.* **1944**, 430.
(9) van Tamelen, E. E.; Proost, Jr., W. C. *J. Am. Chem. Soc.* **1954**, *76*, 3632.
(10) Woodward, R. B.; Kohman, T. T.; Harris, G. C. *J. Am. Chem. Soc.* **1941**, *63*, 120.
(11) In a previous paper,[3] cis,cis-isomer **7** was erroneously assigned as cis,trans-isomer.

Table I. Bond Lengths (Å) and Bond Angles (deg) for Non-Hydrogen Atoms[a]

Br(1)–C(15)	1.895 (3)	Br(1)–C(15)–C(14)	118.8 (1)
C(1)–C(2)	1.513 (3)	Br(1)–C(15)–C(16)	119.9 (2)
C(1)–C(10)	1.532 (3)	C(2)–C(1)–C(10)	111.3 (1)
C(2)–C(3)	1.521 (3)	C(1)–C(2)–C(3)	111.4 (1)
C(2)–O(1)	1.459 (3)	C(1)–C(2)–O(1)	106.0 (1)
C(3)–C(4)	1.522 (4)	C(3)–C(2)–O(1)	110.1 (1)
C(4)–C(5)	1.526 (4)	C(2)–C(3)–C(4)	109.2 (2)
C(5)–C(6)	1.528 (4)	C(3)–C(4)–C(5)	113.0 (2)
C(5)–C(10)	1.539 (3)	C(4)–C(5)–C(6)	112.8 (2)
C(6)–C(7)	1.510 (4)	C(4)–C(5)–C(10)	111.1 (2)
C(7)–C(8)	1.526 (4)	C(6)–C(5)–C(10)	111.3 (2)
C(8)–C(9)	1.529 (4)	C(5)–C(6)–C(7)	111.9 (2)
C(9)–C(10)	1.515 (4)	C(6)–C(7)–C(8)	111.0 (2)
C(11)–C(12)	1.460 (3)	C(7)–C(8)–C(9)	110.9 (2)
C(11)–O(1)	1.336 (3)	C(8)–C(9)–C(10)	113.1 (2)
C(11)–O(2)	1.226 (3)	C(1)–C(10)–C(5)	111.7 (1)
C(12)–C(13)	1.398 (3)	C(1)–C(10)–C(9)	111.6 (2)
C(12)–C(17)	1.395 (3)	C(5)–C(10)–C(9)	112.3 (2)
C(13)–C(14)	1.382 (4)	C(12)–C(11)–O(1)	112.7 (2)
C(14)–C(15)	1.375 (4)	C(12)–C(11)–O(2)	124.5 (2)
C(15)–C(16)	1.380 (4)	O(1)–C(11)–O(2)	122.8 (2)
C(16)–C(17)	1.353 (4)	C(11)–C(12)–C(13)	122.3 (2)
		C(11)–C(12)–C(17)	119.7 (2)
		C(13)–C(12)–C(17)	118.0 (2)
		C(12)–C(13)–C(14)	120.6 (2)
		C(13)–C(14)–C(15)	119.1 (2)
		C(14)–C(15)–C(16)	121.2 (2)
		C(15)–C(16)–C(17)	119.5 (2)
		C(12)–C(17)–C(16)	121.6 (2)
		C(2)–O(1)–C(11)	118.0 (1)

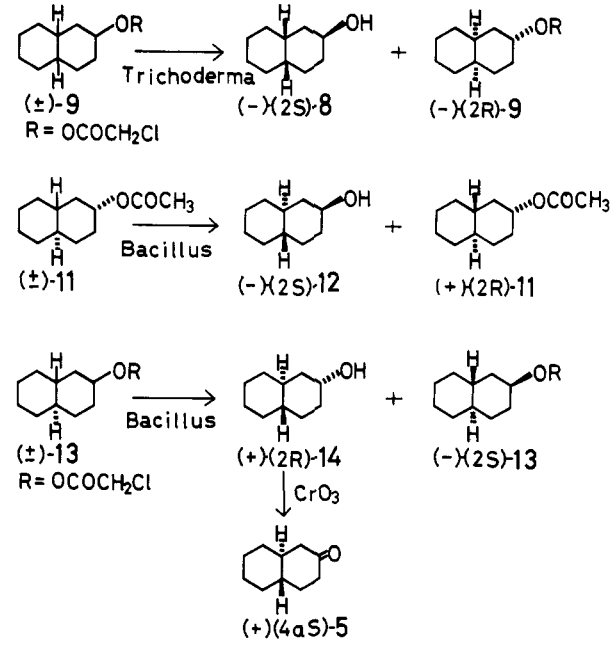
[a] Estimated standard deviations are in parentheses.

benzoate. X-ray analysis of the crystal showed that the absolute structure of (−)-7 is correct as shown in Figure 1 and Table I.

We already found out that chloroacetates of (±)-axial-alcohols (neomenthol and *trans,cis*-decahydro-1-naphthol) could be asymmetrically hydrolyzed by microorganisms, in spite of the difficulty of microbial hydrolysis for (±)-axial-acetates.[2] But the hydrolysis of (±)-*cis,trans*-decahydro-2-naphthyl chloroacetate (**9**) by *Trichoderma koningi* gave (−)-*cis,trans*-decahydro-2-naphthol (**8**) of a low enantiomeric excess (12%) and its absolute configuration was still uncertain. Inversion of the configuration of C-2 of (−)-*cis,cis*-2-alcohol **7** by the method of Mitsunobu[12] using triphenylphosphine–diethyl azodicarboxylate and benzoic acid in tetrahydrofuran, followed by alkaline hydrolysis, gave (+)-*cis,trans*-decahydro-2-naphthol (**8**). This means that (−)-**8** has the 2*S*,4a*S*,8a*R* configuration.

As substrates for microbial hydrolysis, (±)-*trans,cis*-decahydro-2-naphthyl acetate (**11**) and (±)-*trans,trans*-decahydro-2-naphthyl chloroacetate (**13**) were prepared. Reduction of (±)-trans-ketone **5** with lithium aluminum hydride gave mainly (±)-*trans,cis*-decahydro-2-naphthol (**12**), which was acetylated with acetic anhydride to give (±)-trans,cis-2-acetate **11**. Catalytic reduction of (±)-**5** using Adam's catalyst with a small amount of hydrochloric acid in acetic acid gave an axial-alcohol, (±)-*trans,trans*-decahydro-2-naphthol (**14**). Acetylation of (±)-**14** with chloroacetyl chloride gave (±)-2-chloroacetate **13**. Microbial hydrolysis of (±)-**11** with *Bacillus subtilis* var. *niger* gave (−)-(2*S*)-*trans,cis*-decahydro-2-naphthol (**12**) (43% ee) with (+)-(2*R*)-*trans,cis*-2-acetate **11** (92% ee) at 68% hydrolysis. Reductive deacetylation of (+)-**11** with lithium aluminum hydride in ether, followed by crystallization from hexane, gave almost optically pure (+)-**12**. Further, the hydrolysis of (±)-*trans,trans*-2-chloroacetate **13** with *B. subtilis* var. *niger* afforded (+)-*trans,trans*-decahydro-2-naphthol (**14**) with (−)-2-chloroacetate **13** at 45% hydrolysis. As oxidation of (+)-**14** with chromic acid gave (+)-(4a*S*)-trans-ketone **5** of 46% enantiomeric excess, it is obvious that the released alcohol (+)-**14** has the 2*R*,4a*S*,8a*S* configuration and the same enantiomeric excess.

Scheme III



In conclusion, it became apparent that 2*S* enantiomers of decahydro-2-naphthyl acetates, **6** and **12**, and chloroacetate, **9**, can be hydrolyzed faster than their 2*R* enantiomers by the selected microorganisms like the case of acetates of (±)-3-methylcyclohexanols,[1] but (±)-*trans,trans*-2-chloroacetate **13** showed the opposite enantioselectivity as shown in Table II. However, acetates of (±)-decahydro-1-naphthols, (±)-2-methylcyclohexanols, and (±)-2,5-dialkylcyclohexanols can be generally hydrolyzed by the microorganisms to give 1*R* alcohols with their enantiomeric 1*S* acetates.[1,3] The irregularity of the microbial hydrolysis of **13** may be caused by the 1,4-interaction between the 5-methyene and the 2-acetoxyl group at attacking the microbial esterase.

Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were recorded on a JASCO IRA-1 spectrometer. Optical rotations were measured on a JASCO DIP-4 spectrometer. NMR spectra were recorded in a JEOL JNM-FX-100 spectrometer (100 MHz) with Me_4Si as an internal standard. GLC analyses were performed on a JEOL JGC-20K gas chromatograph with a flame ionization detector equipped with a stainless steel column (2 m × 3 mm) packed with 5% SE-30 on Chromosorb W or 10% Hyprose SP-80 on Chromosorb W. ORD were recorded with a JASCO ORD/UV-5 instrument. Mass spectra were taken on a Hitachi M-52 mass spectrometer. Thin-layer chromatography (TLC) was performed on silica gel (Merck H, 0.25 mm thick) with a solvent system, C_6H_6–EtOAc (4:1).

(±)-2-Oxo-2,3,4,4a,5,6,7,8-octahydro-4-naphthalenecarboxylic Acid (1a). (±)-Ethyl ester **1b** (22.2 g, 0.1 mol) was stirred with 100 mL of 15% methanolic KOH under nitrogen at 5 °C for 4 days. The solution was poured into cold aqueous NaCl and extracted with ether to give the recovered ester **1b** (5.0 g). The aqueous layer was acidified with dilute HCl and extracted with ether twice. The combined organic layer was dried over $MgSO_4$. Evaporation of the solvent gave (±)-carboxylic acid **1a**, mp 130–131 °C dec[6], recrystallized from CH_2Cl_2–C_6H_6.

Optical Resolution of (±)-Carboxylic Acid 1a with (−)-(*S*)-α-Methylbenzylamine. To a solution of 6.6 g (34 mmol)

(12) Mitsunobu, O. *Synthesis* **1981**, *1*, 1.

Table II. Chiral Decahydro-2-naphthols Obtained by Microbial Hydrolysis of the Corresponding Racemic Acetates (A) and Chloroacetates (Cl)

racemic substrate	microorganism	% hydrolysis (% recovd crude)	specific rotation, deg (% ee)[a] acetate	alcohol	absolute stereochem[b]
cis,cis-**6** (A)	*Bacillus subtilis* var. *niger* IFO 3108	43 (98)	+30.4 (*c* 6.9, hexane)	−21.4 (*c* 5.6, EtOH) (54% ee)	2*S*,4a*R*,8a*S*
cis,trans-**9** (Cl)	*Trichoderma koningi*	20 (99)		−1.5 (*c* 2.0, EtOH) (12% ee)	2*S*,4a*S*,8a*R*
		79 (99)	−0.3 (*c* 6.0, $CHCl_3$) (26% ee)	−0.6 (*c* 3.0, EtOH) (5% ee)	2*S*,4a*S*,8a*R*
trans,cis-**11** (A)	*B. subtilis* var. *niger*	68 (100)	+10.3 (*c* 5.2, hexane) (92% ee)	−0.6 (*c* 3.0, EtOH) (43% ee)	2*S*,4a*S*,8a*S*
trans,trans-**13** (Cl)	*B. subtilis* var. *niger*	45 (100)	−2.0 (*c* 8.2, $CHCl_3$)	+2.4 (*c* 4.5, $CHCl_3$) (46% ee)	2*R*,4a*S*,8a*S*
	T. koningi	25 (99)	−0.2 (*c* 1.2, $CHCl_3$)	+1.2 (*c* 1.1, $CHCl_3$) (22% ee)	2*R*,4a*S*,8a*S*

[a] Enantiomeric excess. [b] Absolute stereochemistry of alcohol formed.

of **1a** in 60 mL of benzene–acetone (1:2) was added 4.2 g (35 mmol) of (−)-α-methylbenzylamine. Evaporation of the solvent to about a half volume under reduced pressure at 30 °C gave the levorotatory crystalline salt: mp 127–128 °C dec; 4.5 g; $[\alpha]^{17}_D$ −54.0° (*c* 2.0, MeOH). Treatment of the salt with dilute HCl gave (−)-carboxylic acid **1a**: mp 132 °C dec; $[\alpha]^{17}_D$ −21.9° (*c* 1.8, CH_2Cl_2). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.24; H, 7.29. The mother liquor was evaporated after standing for 1 day at room temperature and the residue was extracted with ether. The ethereal layer was washed with dilute HCl and aqueous $NaHCO_3$ and concentrated to give the decomposed product (2.5 g), bp 148–150 °C (20 mmHg), which consisted of 94% of α,β-unsaturated ketone **3** and 6% of β,γ-unsaturated ketone **2** by GLC analysis with 5% SE-30 (column temperature 170 °C, N_2 pressure 0.99 kg/cm², retention time (t_R), 3.8 min for **3** and 3.2 min for **2**). TLC analysis, R_f was 0.48 for **3** and 0.73 for **2**. The product was chromatographed on silica gel with C_6H_6–EtOAc (9:1) to give 3,4,5,6,7,8-hexahydro-2(1*H*)-naphthalenone (**2**), IR (neat) 1720, 1450, 1200 cm⁻¹, and then (−)-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (**3**): $[\alpha]^{20}_D$ −3.9° (*c* 10.0, $CHCl_3$); IR (neat) 1670, 1620, 1330, 1260, 1160 cm⁻¹. The levorotatory salt (4.5 g) was recrystallized from acetone–benzene to give the decomposed neutral product **3** (2.0 g) and a small amount of the crystal, which was treated with dilute HCl to give the (−)-acid **1a**, mp 134–135 °C dec, with the higher rotation: $[\alpha]^{19}_D$ −30.8° (*c* 1.0, CH_2Cl_2); ORD (*c* 0.38 in dioxane, 22 °C) $[\phi]_{260}$ −510°, $[\phi]_{298}$ −130°, $[\phi]_{316}$ −190°. The neutral product was chromatographed on silica gel to give (+)-α,β-unsaturated ketone **3**: bp 108 (7 mmHg); $[\alpha]^{20}_D$ +8.6° (*c* 2.8, $CHCl_3$); ORD (*c* 0.42 in dioxane, 22 °C) $[\phi]_{260}$ +750°, $[\phi]_{300}$ +320°; MS, *m/e* (relative intensity) 150 (M^+, 53), 122 (100), 108 (33), 94 (37), 93 (23), 79 (27).

(+)-(4a*S*,8a*S*)-Octahydro-2(1*H*)-naphthalenone, Trans Form (5). To a solution of (+)-**3** (600 mg, 4 mmol) in 50 mL of liquid ammonia and 5 mL of dry ether was added 416 mg (60 mmol) of lithium for 5 min at −40 °C. After the solution had stirred for 15 min, 4.24 g (80 mmol) of NH_4Cl was added and then the solution was warmed to room temperature. The residue was dissolved in water and extracted with ether. The ethereal layer was washed with dilute HCl and aqueous $NaHCO_3$ and dried over $MgSO_4$. Evaporation of the solvent gave a residual oil, which was treated with CrO_3 in acetic acid to give (+)-trans-ketone **5** (500 mg, 82%): bp 241 °C; $[\alpha]^{20}_D$ +3.9° (*c* 4.6, EtOH); ORD (*c* 0.85 in dioxane, 22 °C) $[\phi]_{274}$ −300°; $[\phi]_{295}$ 0°, $[\phi]_{316}$ +310°; IR(neat) 1720, 1450, 1220, 1170 cm⁻¹; GLC analysis with 5% SE-30 (column temperature 170 °C, N_2 1.10 kg/cm²) t_R 2.3 min, one peak (2.7 min for cis-ketone **4**); MS, *m/e* (relative intensity) 152 (M^+, 65), 108 (100), 82 (80), 65 (57), 55 (82). Anal. Calcd for $C_{10}H_{16}O_1$: C, 78.89; H, 10.59. Found: C, 78.80; H, 10.62.

(−)-(4a*R*,8a*S*)-Octahydro-2(1*H*)-naphthalenone, Cis Form (4). (−)-α,β-Unsaturated ketone **3** (525 mg, 3.5 mmol), $[\alpha]_D$ −3.9° ($CHCl_3$), was hydrogenated by using 60 mg of 5% Pd on charcoal with a small amount of concentrated HCl in 10 mL of EtOH at atmospheric pressure and room temperature. The product was chromatographed on silica gel. Elution with benzene gave (−)-cis-ketone **4** (520 mg, 98%): bp 113 °C (20 mmHg); $[\alpha]^{20}_D$ −0.5° (*c* 5.0 $CHCl_3$); IR(neat) 1720, 1450, 1195, 1160 cm⁻¹, MS, *m/e* (relative intensity) 152 (M^+, 82), 108 (100), 82 (68), 67 (46), 55 (84). Anal. Calcd for $C_{10}H_{16}O_1$: C, 78.89; H, 10.59. Found: C, 79.11; H, 10.60. The product **4** was contaminated with 4% of trans-ketone **5** by CLC analysis. Semicarbazone of (−)-**4**: mp 182–184 °C; $[\alpha]^{20}_D$ −2.4° (*c* 1.7, $CHCl_3$).

Optical Resolution of (4a*RS*,8a*SR*)-Octahydro-2(1*H*)-naphthalenone, Cis Form (4). A solution of (±)-cis-ketone **4** (15.2 g, 0.1 mol) and 21.4 g (0.1 mol) of (−)-menthyl *N*-aminocarbamate in 50 mL of EtOH, which contained 1.0 g of NaOAc and 0.5 mL of acetic acid, was refluxed for 6 h. After evaporation of the ethanol, a residual oil was recrystallized from benzene–ether twice to give a crystalline hydrazone derivative: mp 160 °C; $[\alpha]^{21}_D$ −32.0° (*c* 1.0, $CHCl_3$). Treatment of the hydrazone with phthalic anhydride under steam distillation gave (−)-cis-ketone **4**, which was not contaminated with trans-ketone **5** by GLC analysis: $[\alpha]^{21}_D$ −1.8° (*c* 5.0, $CHCl_3$), −1.9° (*c* 5.0, hexane). Semicarbazone: mp 182–183 °C (from EtOH twice); $[\alpha]^{21}_D$ − 6.2° (*c* 2.0, $CHCl_3$). Anal. Calcd for $C_{11}H_{19}O_1N_3$: C, 63.12; H, 9.15: N, 20.08. Found: C, 63.08; H, 9.18; N, 20.05.

Decarboxylation of Carboxylic Acid 1a to β,γ-Unsaturated Ketone 2. (a) Thermal Decarboxylation. Heating of (−)-carboxylic acid **1a**, $[\alpha]^{21}_D$ −10.2° (CH_2Cl_2), on an oil bath (150–160 °C) under nitrogen for 5 min gave β,γ-unsaturated ketone **2**, which was contaminated with 1.8% of α,β-unsaturated ketone **3** by GLC analysis.

(b) Decarboxylation of Quinine Salt of (±)-Carboxylic Acid 1a. (±)-Carboxylic acid **1a** (582 mg, 30 mmol) and 1.006 g (30 mmol) of quinine hydrate were dissolved in methanol–acetone (1:1) and then 20 mL of benzene was added. Evaporation of the solvent to about 20 mL of the volume deposited a salt as a precipitate. The salt was decarboxylated in acetone–benzene on warming to give an oily product, which was chromatographed on silica gel to give β,γ-unsaturated ketone **2** (95%) 2,4-dinitrophenylhydrazone: mp 176 °C.[8]

Alkaline Decarboxylation of (±)-Ethyl Ester 1b.[7] (±)-Ethyl ester **1b** (2.22 g, 10 mmol) was refluxed with 2.0 g of KOH in 10 mL of water for 7.5 h. The reaction mixture was diluted with water and extracted with ether. Evaporation of the solvent, followed by distillation, gave 1.07 g of the decarboxylated ketone and 400 mg of the recovered ester **1b**. The ketone consisted of 8.8% of β,γ-unsaturated ketone **2** and 91.2% of α,β-unsaturated ketone **3** by GLC analysis.

(±)-*trans,cis*-Decahydro-2-naphthyl Acetate (11). To a stirred suspension of $LiAlH_4$ (380 mg, 10 mmol) in 50 mL of dry ether was added dropwise 3.05 g (20 mmol) of (±)-trans-ketone **5** dissolved in 5 mL of dry ether, and the stirring was continued for 3 h at room temperature. The reaction mixture was poured into dilute HCl and extracted with ether. Evaporation of the solvent gave (±)-decahydro-2-naphthols (3.05 g, 99%), which consisted of 12% of trans,trans-isomer **14** (t_R 7.7 min) and 88% of trans,cis-isomer **11** (t_R 9.8 min) by GLC analysis with 10% Hyprose SP-80 (column temperature 170 °C, N_2 pressure 0.99 kg/cm²). Recrystallization of the alcohol from hexane gave pure (±)-*trans,cis*-decahydro-2-naphthol (**12**): mp 75 °C. Acetylation of (±)-**12** (2.50 g) with acetic anhydride in pyridine for 12 h at room temperature gave (±)-*trans,cis*-2-acetate **11** (3.10 g, 98%): bp 122–123 °C (13 mmHg); IR(neat) 1745, 1240, 1030 cm⁻¹; ^{13}C NMR ($CDCl_3$) δ 21.3, 26.3, 26.6, 31.8, 31.9, 33.3, 33.8, 39.3, 41.1, 42.4, 73.1 (C-O), 170.2 (CO). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.46; H, 10.30.

(±)-*trans,trans*-Decahydro-2-naphthyl Chloroacetate (13). (±)-Trans-ketone **5** (5.6 g, 37 mmol) was hydrogenated by using 550 mg of Adam's catalyst with 0.2 mL of concentrated HCl in 10 mL of acetic acid to give 5.6 g (99%) of (±)-decahydro-2-naphthols, which consisted of 96% of trans,trans-isomer **14** and 4% of trans,cis-isomer **12** by GLC analysis. The reaction of the

alcohols with *p*-nitrobenzoyl chloride in pyridine, followed by recrystallization from ethanol gave pure (±)-*trans,trans*-decahydro-2-naphthyl *p*-nitrobenzoate: mp 112 °C (89%). Alkaline hydrolysis of the *p*-nitrobenzoate with 5% ethanolic NaOH gave pure (±)-trans,trans-2-alcohol **14**, mp 53 °C. A solution of (±)-**14** (3.08 g, 20 mmol) and 3.39 g (30 mmol) of chloroacetyl chloride in 40 mL of CH_2Cl_2 was refluxed for 7 h to give 4.40 g (96%) of (±)-trans,trans-2-chloroacetate **13**: bp 155–156 °C (13 mmHg); IR (neat) 1760, 1315, 1190, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90–2.00 (16 H), 4.07 (2 H, s), 5.15 (1 H, s, $W_{1/2}$ = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 26.6, 28.1, 30.0, 33.7, 37.2, 41.3, 42.7, 72.8 (C-O), 166.7 (CO). Anal. Calcd for $C_{12}H_{19}O_2Cl_1$: C, 62.47; H, 8.30; Cl, 15.37. Found: C, 62.60; H, 8.35; Cl, 15.40.

Microbial Hydrolysis of Substrates. Microbial Hydrolysis of (±)-*cis,cis*-Decahydro-2-naphthyl Acetate (6). As described in the previous paper,[3] microbial hydrolysis of (±)-*cis,cis*-2-acetate **6** (1.5 g) with the cultured broth (100 mL) of *B. subtilis* var. *niger* IFO 3108 under shaking for 2 days at 27 °C afforded (−)-*cis,cis*-decahydro-2-naphthol (**7**), $[\alpha]^{13}_D$ −21.4° (EtOH), at 43% hydrolysis. Crystallization of (−)-**7** from hexane–benzene gave optically impure (−)-**7**, mp 95–98 °C, $[\alpha]^{17}_D$ −2.0° (*c* 2.0, EtOH), as the first crop. Recrystallization of the second crop from the mother liquor (from hexane twice) gave optically pure (−)-**7**: mp 67 °C; $[\alpha]^{17}_D$ −40.0° (*c* 2.0, EtOH); IR (KBr) 3250, 1465, 1445, 1140, 1050, 1025, 950, 815 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 21.2, 26.0, 26.8, 30.1, 31.9, 34.9, 35.1, 35.6, 71.7 (C-O); MS, *m/e* (relative intensity) 136 ($M^+ - H_2O$, 100), 121 (36), 107 (29), 95 (49), 94 (98). Anal. Calcd for $C_{10}H_{18}O_1$: C, 77.86; H, 11.76. Found: C, 78.04; H, 11.78. The optically pure (−)-**7** reacted with (−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA chloride) in pyridine for 12 h at room temperature gave the (−)-MTPA ester of (−)-**7**: ^1H NMR (23 mg in $CDCl_3$ with the presence of 7.0 mg of $Eu(fod)_3$) showed a signal (100% ee) due to (*S*)-OCH_3 protons (δ 4.82). ^1H NMR of the (−)-MTPA ester of (±)-**7** (24 mg in $CDCl_3$ with the presence of 8.0 mg of $Eu(fod)_3$) showed two signals due to (*S*)-OCH_3 and (*R*)-OCH_3 protons (δ 4.89 and 4.99). The reaction of optically pure (−)-**7** with *p*-bromobenzoyl chloride in pyridine gave single crystals of the *p*-bromobenzoate: mp 120 °C (from EtOH); IR (KBr) 1710, 1590, 1480, 1395, 1280, 1120, 840, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20–1.90 (16 H), 4.98 (1 H, m, $W_{1/2}$ = 19 Hz), 7.56 (2 H, d, *J* = 9 Hz), 7.90 (2 H, d, *J* = 9 Hz); ^{13}C NMR ($CDCl_3$) δ 21.5, 26.3, 27.0, 29.3, 31.4, 31.9, 34.6, 35.0, 75.0 (C-O), 127.8, 130.0, 131.1, 131.6, 165.3 (CO). Anal. Calcd for $C_{17}H_{21}O_2Br_1$: C, 60.55; H, 6.28; Br, 23.69. Found: C, 60.50; H, 6.29; Br, 23.75.

X-ray Analysis of the *p*-Bromobenzoate of (−)-*cis,cis*-Decahydro-2-naphthol (−)-7. The crystal data are as follow: orthrhombic, a = 16.980 (2) Å, b = 13.967 (2) Å, c = 6.517 (1) Å, space group $p2_12_12_1$, z = 4, ρ_{calcd} = 1.40 g/cm^3. Two sets of independent reflections, *hkl* and *hkl̄*, with 2θ < 120 were measured at 10 °C on a Rigaku automated four-circle four-circle diffracometer (AFC-5) using Cu Kα radiation (λ 1.5418 Å), θ − 2θ scan mode of width (1.0 + 0.15 tan θ), a scan speed of 4° in 2θ. Intensities of three standard reflections monitored every 50 reflections did not change significantly during data collection. A total 2703 reflections were obtained as observed and corrected for Lorenz and polarization effects, no absorption correction being made.

The structure was solved by a heavy atom method and refined in a usual way by the block-diagonal least-squares method. Including all hydrogen atoms with isotopic temperature factors, the refinement converged to give the *R* factor of 0.038 and 0.037 for each set of *hkl* and *hkl̄*. The final weighting scheme was employed; $w = (\sigma(F_o) + \alpha(F_o) + b(F_o)^2)^{-1}$ with a = −0.077 and b = 0.0037. No peaks heigher than 0.30 $eÅ^{-3}$, except for the peaks of 0.50 $eÅ^{-1}$ around the Br atom, were found on the difference map. The atomic scattering factors applied from "International Tables for X-Ray Crystallography".[13]

When the anomalous dispersion of the bromine atom was included and two sets of reflections were added in the calculations, the refinements terminated to give the values of 0.031 vs. 0.043 (r_w = 0.030 vs. 0.042) for each enantiomorph. Although the difference was significantly beyond the 99.5% level, the comparison between the Bijoet pairs was examined in order to enlarge the determinatiation. The ratios of F values larger than 10 on an absolute scale were calculated for both enantiomorphs. A total of 64 Bijvoet pairs, for which the dispersion effect ($\Delta Fc/Fc$) exceeds 5%, gave all the correct relationships for the sign of nonequality between the calculated and observed F values.

Figure 1 shows a perspective drawing of the moleucle, drawn with the correct absolute configuration, corresponding to the (−)-form. There are no intermolecular contacts less than 3.4 Å in the crystal structures. The bond lengths and angles are given in Table I. Both cyclohexane rings are, as expected, in a chair conformation and the observed bond lengths and angles are quite normal compared with the previous X-ray structural data of similar compounds.

S_N2 Displacement of (−)-*cis,cis*-Decahydro-2-naphthol (7). By the same treatment[2] described for the racemic form (±)-**7**, the configuration of C-2 of (−)-*cis,cis*-2-alcohol **7**, $[\alpha]_D$ −2.0° (EtOH), was inverted with benzoic acid using triphenylphosphine–diethyl azodicarboxylate in THF to give *cis,trans*-decahydro-2-naphthyl benzoate (25%), which was hydrolyzed with 5% ethanolic NaOH to afford (+)-*cis,trans*-decahydro-2-naphthol (**8**) as an oil: $[\alpha]^{21}_D$ +2.6° (*c* 1.56, EtOH). The ^{13}C NMR spectrum of (+)-**8** was identical with those[2] of (±)-**8**.

Microbial Hydrolysis of (±)-*trans,cis*-Decahydro-2-naphthyl Acetate (11). The (±)-acetate **11** (1.70 g) was added to the cultured broth of *B. subtilis* var. *niger*, previously grown for 2 days at 28 °C in 200 mL of a nutrient medium. After incubation for 48 h, steam distillation of the broth, followed by ethereal extraction, gave 1.45 g of an oil, which was chromatographed on silica gel. Elution with benzene gave (+)-*trans,cis*-2-acetate **11** (522 mg): $[\alpha]^{21}_D$ +10.3° (*c* 5.2, hexane). Further elution with benzene–EtOAc (4:1) gave 878 mg of (−)-*trans,cis*-2-alcohol **12**: mp 73–74 °C; $[\alpha]^{21}_D$ −0.55° (*c* 3.0, EtOH) (43% ee, lit[2] mp 72 °C; $[\alpha]^{23}_D$ +1.35° (*c* 2.6, EtOH) for (+)-**12** at 68% hydrolysis). Acetylation of (−)-**2** with acetic anhydride in pyridine gave (−)-*trans,cis*-2-acetate **11**: $[\alpha]^{21}_D$ −4.8° (*c* 3.0, hexane). This rotational value means that (+)-**11** has the 92% enantiomeric excess. Reduction of (+)-**11** with $LiAlH_4$ in ether for 2 h at 20 °C gave almost optically pure (+)-*trans,cis*-decahydro-2-naphthol (**12**): mp 72 °C (from hexane); $[\alpha]^{21}_D$ +1.33° (*c* 1.35, EtOH). Anal. Calcd for $C_{10}H_{18}O_1$: C, 77.86; H, 11.76. Found: C, 77.97; H, 11.79.

Microbial Hydrolysis of (±)-*trans,trans*-Decahydro-2-naphthyl Chloroacetate (13). The (±)-Chloroacetate **13** (1.5 g) was incubated with 100 mL of the cultured broth of *B. subtilis* var. *niger* for 2 days at 28 °C. Steam distillation of the broth, followed by ethereal extraction, gave 1.28 g of an oil, which was chromatographed on silica gel. Elution with benzene gave (−)-*trans,trans*-2-chloroacetate **13** (820 mg): $[\alpha]^{19}_D$ −1.98° (*c* 8.2, $CHCl_3$). Further elution with benzene–EtOAc (4:1) afforded 453 mg of (+)-*trans,trans*-2-alcohol **14**: mp 47–48 °C; $[\alpha]^{19}_D$ +2.39° (*c* 4.5, $CHCl_3$) at 45% hydrolysis. Oxidation of (+)-**14** with CrO_3 in acetic acid for 15 h at 20 °C gave (+)-(4a*S*,8a*S*)-*trans*-ketone **5** (95%): $[\alpha]^{19}_D$ +12.5° (*c* 3.5, EtOH) [46% ee, lit[2] $[\pm]_D$ +27° (*c* 2.04, EtOH)]. This means that (+)-**14** has the 2*R*,4a*S*,8a*S* configuration. Reaction of (+)-**14** with *p*-nitrobenzoyl chloride in pyridine gave the *p*-nitrobenzoate, which was crystallized from ethanol to give racemic product: mp 111 °C; $[\pm]^{20}_D$ 0° (*c* 3.0, $CHCl_3$) as the first crop. Recrystallization of the second crop from ethanol twice geen (−)-*trans,trans*-decahydro-2-naphthyl *p*-nitrobenzoate: mp 108 °C; $[\alpha]^{20}_D$ −10.8° (*c* 0.3, $CHCl_3$). Anal. Calcd for $C_{17}H_{21}O_4N_1$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.43; H, 6.96; N, 4.62. Similarly, microbial hydrolysis of (±)-**13** (500 mg) with the cultured broth of *Trichoderma koningi*, previously grown in 100 mL of a glucose phosphate peptone medium,[3] gave (−)-**13**, $[\alpha]^{21}_D$ −0.23° (*c* 3.5, $CHCl_3$), and (+)-*trans,trans*-2-alcohol **14**: $[\alpha]^{21}_D$ +1.16° (*c* 1.1, $CHCl_3$) (22% ee) at 25% hydrolysis.

Registry No. (±)-**1a**, 91586-50-4; (±)-**1a**·quinine, 91586-52-6; (−)-(*R*)-**1a**, 91684-28-5; (−)-(*R*)-**1a**·(*S*)-α-methylbenzylamine, 91738-49-7; (±)-**1b**, 91684-27-4; **2**, 13837-12-2; **2** (dinitrophenylhydrazone), 1532-46-3; (+)-(*S*)-**3**, 38772-79-1; (−)-(*R*)-**3**, 38772-78-0; (±)-**4**, 5779-29-3; (−)-(4a*R*)-**4**, 91684-30-9; (4a*R*)-**4** (semicarbazone), 91684-31-0; (4a*R*)-**4** ((−)-menthyloxycarbonylhydrazone), 91586-51-5; (±)-**5**, 5779-29-3; (+)-(4a*S*)-**5**, 91684-29-6; (±)-**6**, 91684-32-1; (−)-(2*S*)-**7**, 54324-61-7; (2*S*)-**7** (*p*-bromobenzoate), 91586-57-1; (2*S*)-**7** (MTPA ester), 91586-55-9; (2*R*)-**7** (MTPA ester), 91586-

(13) "International Tables for X-Ray Crystallography"; Kynoch Press: Birmingham, 1962; Vol. 3, p 202.

56-0; (+)-(2R)-8, 91684-37-6; (-)-(2S)-8, 84276-31-3; (2R)-8 (benzoate), 91684-38-7; (±)-9, 88598-49-6; (-)-(2R)-9, 91684-39-8; (±)-11, 36667-75-1; (+)-(2R)-11, 54656-99-4; (-)-(2S)-11, 91684-33-2; (±)-12, 36667-73-9; (+)-(2R)-12, 91684-34-3; (-)-(2S)-12, 52079-66-0; (±)-13, 91586-53-7; (±)-13 (p-nitrobenzoate), 91586-54-8; (-)-(2S)-13, 91684-40-1; (±)-14, 5746-69-0; (±)-14 (p-nitrobenzoate), 91586-54-8; (+)-(2R)-14, 91684-35-4; (2R)-14 (p-nitrobenzoate), 91684-36-5; (-)-MTPA chloride, 39637-99-5; $ClCOCH_2Cl$, 79-04-9; (-)-menthyl N-aminocarbamate, 21391-40-2; phthalic anhydride, 85-44-9; p-nitrobenzoyl chloride, 122-04-3; p-bromobenzoyl chloride, 586-75-4.

Supplementary Material Available: Table III, atomic parameters for anisotropic and isotropic atoms of (-)-*cis,cis*-decahydro-2-naphthyl p-bromobenzoate (1 page). Ordering information is given on any current masthead page.

α-Methoxy-o-xylylene:† Formation by $LiNR_2$-Induced 1,4-Elimination of o-Tolualdehyde Dimethyl Acetal

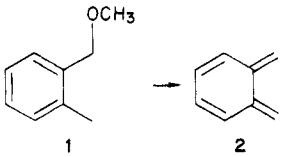
Randall J. Moss and Bruce Rickborn*

Department of Chemistry, University of California, Santa Barbara, California 93106

Received January 23, 1984

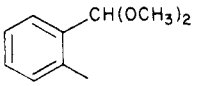
o-Tolualdehyde dimethyl acetal (3) undergoes 1,4-elimination on treatment with $LiNR_2$, generating α-methoxy-o-xylylene (6), as shown by trapping with various olefinic dienophiles. Norbornene gives two isomeric cycloadducts, one of which (trans) undergoes further elimination; the new o-xylylene formed in this step reacts with a second norbornene to form a symmetrical bis(norbornene) adduct. Similarly, the trans cycloadduct of 6 and norbornadiene undergo further elimination, yielding naphthalene by subsequent retro-Diels–Alder reaction. Cycloadducts of 6 with cyclopentene, isoprene, and 1-hexene are formed in moderate to low yields. The reaction with cyclopentene provides a single isomer (cis) which is resistant to further elimination. Isoprene and 1-hexene give complex mixtures of cycloadducts. Control reactions demonstrate that, in the absence of a reactive dienophile, 6 partitions between dimer formation and electrocyclic closure to α-methoxybenzocyclobutene (7); 7 undergoes rapid elimination with LDA to generate benzocyclobutadiene, as shown by trapping with 1,3-diphenylisobenzofuran. Thermal reactions of 7 with norbornene and cyclopentene give the same cycloadducts as formed in the base-induced reactions of 3, suggesting that these arise from the *E* isomer of 6.

The unique propensity of allylic ethers to undergo 1,4-elimination on treatment with lithium dialkylamides has been shown to extend to analogous benzylic ethers. These substrates experience disruption of benzene aromaticity in order to follow this pathway, and hence represent severe tests of the generality of this reaction. The preparation of isobenzofuran (moderately stable in solution) in this manner is quite straightforward,[1] and the procedure has been used to form some substituted derivatives.[2,3] A modification using alkyllithium reagents and catalytic $LiNR_2$ has recently been developed for these materials.[4] The finding that o-xylylene (2) is generated on similar treatment of methyl o-methylbenzyl ether (1) with $LiNR_2$ is particularly strong evidence for the general preference for 1,4-elimination.[5]



1 2

In this paper, results obtained with the analogous acetal 3 are presented. This work was undertaken with the goal

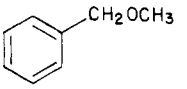


3

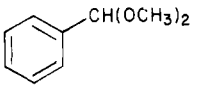
of determining whether the base-induced elimination would in fact occur with this substrate, and if so, to examine some properties of the methoxy-substituted o-xylylene, the stereochemistry of cycloadducts formed on reaction with dienophiles, and the potential of these cycloadducts for further elimination or other reactions.

Results and Discussion

Wittig ether rearrangement and α-elimination processes are the most obvious alternatives to 1,4-elimination in the systems examined in this work. Indeed, reexamination of the simple ether 4 with lithium tetramethylpiperidide



4



5

(LTMP) in hexane showed that Wittig rearrangement occurs, leading to 1-phenylethanol (isolated in moderate yield); the reaction is, however, slower than the 1,4-elimination of the o-methylbenzyl ether 1. The dimethyl acetal of benzaldehyde (5) also reacts with this strong base, giving viscous and presumably polymeric material which has not been characterized. These observations show that α-proton abstraction pathways are likely alternatives for ethers and acetals where 1,4-elimination is either slow or precluded.

A competition kinetics experiment was carried out to explore this point. When an equimolar mixture of 3 and 5 was refluxed for 2.5 h in hexane containing 6 equiv of lithium diisopropylamide (LDA), all of 3 was consumed

† A more systematic name for α-methoxy-o-xylylene is 5-(methoxymethylene)-6-methylene-1,3-cyclohexadiene.

(1) Naito, K.; Rickborn, B. *J. Org. Chem.* **1980**, *45*, 4061.
(2) Makhlouf, M. A.; Rickborn, B. *J. Org. Chem.* **1981**, *46*, 2734.
(3) Cornejo, J.; Ghodsi, S.; Johnson, R. D.; Woodling, R.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 3869.
(4) Crump, S.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 304.
(5) Tuschka, T.; Naito, K.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 70.

0022-3263/84/1949-3694$01.50/0