

[Chem. Pharm. Bull.]
33(10)4333—4337(1985)

Stereoselective Reactions. X.¹⁾ Total Synthesis of Optically Pure Antitumor Lignan, Burseran²⁾

KIYOSHI TOMIOKA, TSUNEO ISHIGURO, and KENJI KOGA*

Faculty of Pharmaceutical Sciences, University of Tokyo,
Hongo, Bunkyo-ku, Tokyo 113, Japan

(Received March 12, 1985)

Optically pure *trans*- and *cis*-burseran (**4**, **10**) were stereoselectively synthesized in an unequivocal manner. Comparison of their behaviors on gas chromatography indicated that naturally occurring antitumor lignan, burseran, is the *trans*-isomer.

Keywords—antitumor lignan; relative configuration; absolute configuration; asymmetric synthesis; burseran; isodeoxypodophyllotoxin; deoxypodorhizon

In previous papers^{3,4)} we have reported the development of novel asymmetric reactions on the basis of the novel use of optically pure (*S*)- γ -hydroxymethyl γ -butyrolactone, easily available in quantity from L-glutamic acid, and its successful application to the asymmetric total synthesis of an antitumor lignan lactone steganacin. In the present paper we describe the stereoselective total synthesis of optically pure *trans*- and *cis*-burseran, and the determination of the relative configuration of naturally occurring antitumor lignan burseran as the *trans*-isomer.

Burseran was isolated as an antitumor compound from *Bursera microphylla* (Burseraceae) and has been characterized as a lignan, 3-(3,4-methylenedioxybenzyl)-4-(3,4,5-trimethoxybenzyl)tetrahydrofuran.⁵⁾ Although Trumbull and Cole undertook a synthetic study of burseran in order to determine its stereochemistry, a mixture of *trans*- and *cis*-burseran (**4** and **10**) was obtained. Gas chromatographic analysis, however, showed that naturally occurring burseran had a retention time identical to that of the faster-moving component of the synthetic mixture.⁶⁾ Thus, in order to establish the relative configuration of natural burseran, it is necessary to achieve a stereoselective synthesis of both *trans*- and *cis*-burseran in an unequivocal manner.

($-$)-*trans*-Burseran (($-$)-**4**) was synthesized from ($-$)-deoxypodorhizon (($-$)-**2**), available from (+)-(*R*)-**1**,^{4c,f)} as shown in Chart 1. Reduction of ($-$)-**2** with LiAlH₄ in tetrahydrofuran (THF) afforded the diol (($-$)-**3**) in 84% yield. Treatment of ($-$)-**3** with *para*-toluenesulfonyl chloride (*p*-TsCl) in pyridine resulted in concomitant tetrahydrofuran ring formation to afford *trans*-burseran (($-$)-**4**) in 72% yield. The optical antipode ((+)-**4**) was synthesized starting from (+)-**2**.^{4f,g)} The infrared (IR) and mass spectra (MS) of ($-$)- and (+)-**4** are identical with reported spectra of natural burseran.⁵⁾

(+)-*cis*-Burseran ((+)-**10**) was stereoselectively synthesized from (+)-(*R*)-**1**^{4c,f)} as shown in Chart 1. Lithioenolate derived from (+)-**1** was allowed to react with 3,4,5-trimethoxybenzaldehyde to give a mixture of ($-$)-podorhizol (($-$)-**5a**) and ($-$)-epipodorhizol (($-$)-**5b**).⁷⁾ Attempted dehydration of the mixture (**5a**, **b**) in refluxing xylene in the presence of *para*-toluenesulfonic acid (*p*-TsOH) according to the Matsui's procedure,⁸⁾ however, afforded a cyclization product, ($-$)-isodeoxypodophyllotoxin (($-$)-**6**,⁷⁾ in 76% yield. Successful dehydration of **5** was achieved by tosylation followed by elimination reaction of the tosylate to afford ($-$)-anhydropodorhizol (($-$)-**7**)⁷⁾ in 80% yield. Catalytic hydrogenation of ($-$)-**7** over

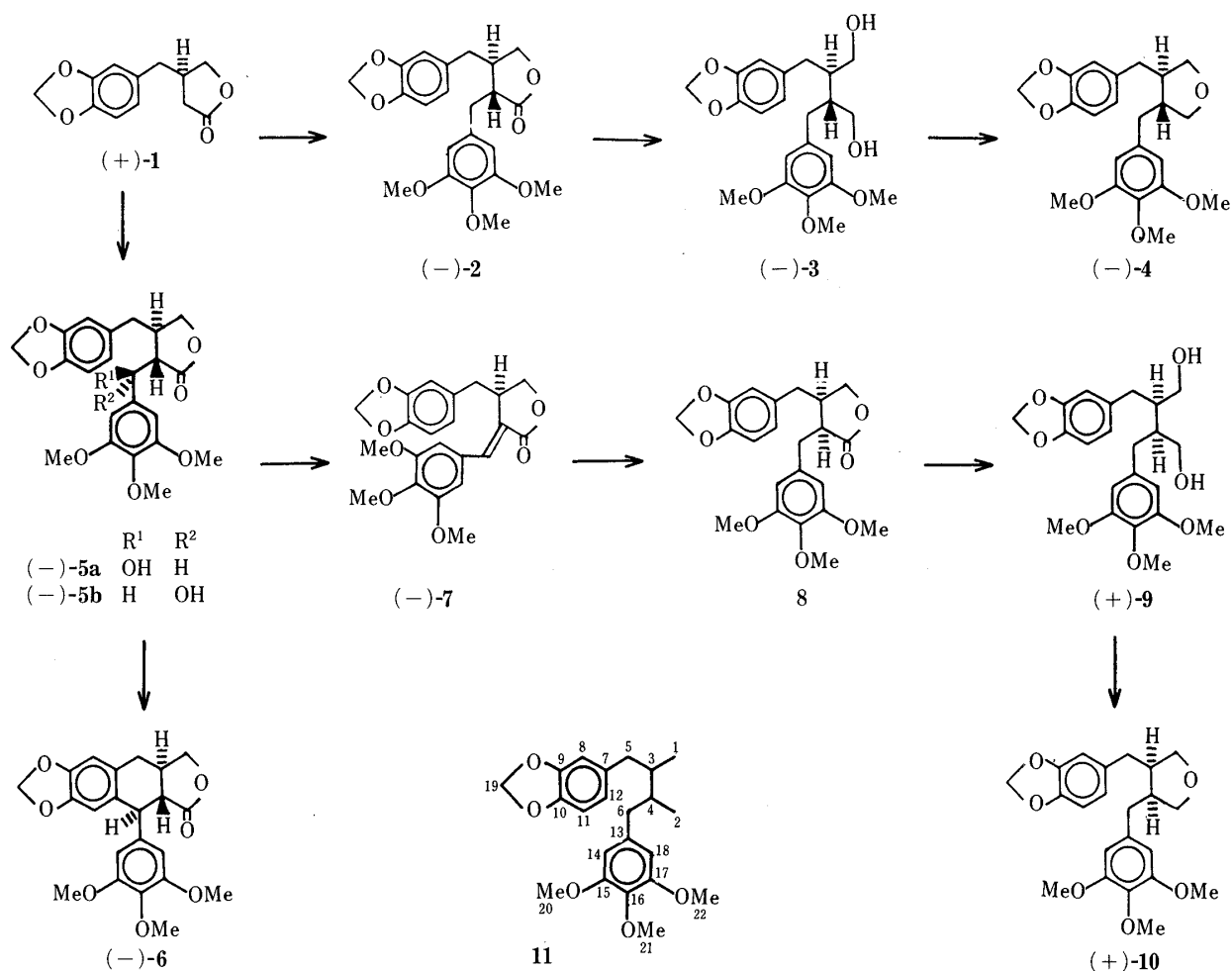


Chart 1

5% Pd-C in AcOH gave a mixture of the expected *cis*-dihydroanhydropodorhizol (**8**)⁷ and (-)-**2** in a ratio of 7:3 (determined by carbon 13 nuclear magnetic resonance (NMR) analysis (Table I)). Reduction of the mixture (**8** and (-)-**2**) with LiAlH₄ in THF gave, after purification by column chromatography, the pure diol ((+)-**9**) and (-)-**3**, in 50 and 15% yields, respectively. In the same way as described for the preparation of the *trans*-isomer ((-)-**4**), the diol ((+)-**9**) was converted to (+)-*cis*-burseran ((+)-**10**). The IR and MS spectra of (+)-**10** were also indistinguishable from those reported for natural burseran.⁵⁾

The relative configurations of (-)-**4** and (+)-**10** were unambiguous on the basis of the stereoselective synthetic pathway, and were also supported by ¹³C-NMR analyses as shown in Table I. It was, as expected, found that the peaks derived from the *cis*-compound ((+)-**10**) appeared at higher field than those of the *trans*-isomer ((-)-**4**).

Finally, gas chromatographic analysis using the same type of column as reported⁵⁾ showed that synthetic *trans*-isomer ((-)-**4**) moved faster (retention time: 1.5 min) than the *cis*-isomer ((+)-**10**) (retention time: 2.2 min). Therefore, it was concluded that naturally occurring antitumor burseran is the *trans*-isomer. The absolute stereochemistry of natural burseran still remains unknown, because the optical rotation of natural burseran is not available.⁹⁾ However, since the novel method for the asymmetric synthesis developed by us has the advantage that either enantiomer is available,^{3,4)} both (-)- and (+)-**4** could be synthesized as described above.

TABLE I. ^{13}C -NMR Data for 2, 3, 4, 8, 9, 10^{a)}

Carbon ^{b)}	2	8	3	9	4	10
1	71.1 t	69.4 t	60.2 t	63.0 t	73.2 t	71.9 t ^{c)}
2	178.4 s	177.7 s	60.2 t	63.0 t	73.2 t	72.0 t ^{c)}
3 or 4	41.0 d	40.2 d	43.7 d	44.8 d	46.3 d	43.6 d
4 or 3	46.4 d	45.3 d	44.1 d	45.3 d	46.6 d	43.8 d
5 or 6	35.2 t	31.2 t	35.9 t	33.7 t	39.2 t	33.3 t
6 or 5	38.3 t	32.8 t	36.6 t	33.7 t	39.9 t	33.9 t
7 or 13	131.6 s	132.0 s	134.3 s	134.1 s	134.1 s	134.3 s
8 or 11	108.2 d	108.4 d	108.0 d	108.1 d	108.0 d	108.2 d
9 or 10	146.3 s	146.3 s	145.7 s	145.8 s	145.8 s	145.9 s
10 or 9	147.8 s	147.9 s	147.6 s	147.7 s	147.6 s	147.7 s
11 or 8	108.8 d	109.0 d	109.3 d	109.3 d	108.9 d	108.9 d
12	121.5 d	121.8 d	121.8 d	121.8 d	121.4 d	121.4 d
13 or 7	133.4 s	134.4 s	136.4 s	136.3 s	136.1 s	136.3 s
14, 18	106.3 d	105.5 d	106.0 d	106.0 d	105.6 d	105.7 d
15, 17	153.2 s	153.3 s	153.0 s	153.0 s	153.1 s	153.2 s
16	136.8 s	136.8 s	136.1 s	136.2 s	136.4 s	136.3 s
19	101.0 t	101.0 t	100.8 t	100.8 t	100.8 t	100.8 t
20, 22	56.0 q	56.2 q	56.0 q	56.0 q	56.0 q	56.1 q
21	60.7 q	60.8 q	60.8 q	60.9 q	60.8 q	60.8 q

a) Taken in CDCl_3 . Tetramethylsilane as an internal standard. b) For numbering, see 11 in Chart 1. c) Assignments may be reversed.

Experimental¹⁰⁾

(-)-(2*R*,3*R*)-2-(3,4-Methylenedioxybenzyl)-3-(3,4,5-trimethoxybenzyl)-1,4-butanediol ((-)-3)—A solution of (-)-2 ($[\alpha]_D^{25} - 22.2^\circ$ ($c = 0.410$, CHCl_3))^{4c,f)} (200 mg, 0.5 mmol) in THF (5 ml) was added to a suspension of LiAlH_4 (38 mg, 1.0 mmol) at room temperature. The whole was stirred for 1 h, then water (0.04 ml), 15% aq. NaOH (0.04 ml), and water (0.12 ml) were added successively. Filtration and concentration *in vacuo* afforded a yellow oil (230 mg). Purification by silica gel column chromatography (ether- CHCl_3 (3:1)) afforded (-)-3 (170 mg, 84%) as colorless fine needles of mp 94–95°C (from ether-*n*-hexane). $[\alpha]_D^{20} - 29.9^\circ$ ($c = 0.976$, CHCl_3). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3420, 3230, 1589. ^1H -NMR (CDCl_3) δ : 1.6–2.0 (2H, m, $\text{ArCH}_2\text{CH} \times 2$), 2.5–2.8 (4H, m, $\text{ArCH}_2 \times 2$), 3.0–3.2 (2H, br s, $\text{OH} \times 2$), 3.3–3.9 (4H, m, $\text{CH}_2\text{OH} \times 2$), 3.80 (9H, s, $\text{OCH}_3 \times 3$), 5.87 (2H, s, OCH_2O), 6.31 (2H, s, aromatic H), 6.5–6.7 (3H, m, aromatic H). ^{13}C -NMR (Table I). MS m/z : 404 (M^+). Anal. Calcd for $\text{C}_{22}\text{H}_{28}\text{O}_7 \cdot 1/3\text{H}_2\text{O}$: C, 64.37; H, 7.04. Found: C, 64.38; H, 7.13.

(+)-3—Reduction of (+)-2 ($[\alpha]_D^{25} + 21.3^\circ$ ($c = 0.400$, CHCl_3))^{4f,g)} afforded (+)-3 as colorless fine needles of mp 93.5–94.5°C (from ether-*n*-hexane). $[\alpha]_D^{20} + 31.6^\circ$ ($c = 0.950$, CHCl_3). Anal. Calcd for $\text{C}_{22}\text{H}_{28}\text{O}_7 \cdot 1/3\text{H}_2\text{O}$: C, 64.37; H, 7.04. Found: C, 64.42; H, 6.93. IR, ^1H -NMR, MS, and thin layer chromatography (TLC) behavior were identical with those for (-)-3.

(-)-(3*R*,4*R*)-3-(3,4-Methylenedioxybenzyl)-4-(3,4,5-trimethoxybenzyl)tetrahydrofuran((-)-trans-Burseran)((-)-4)—A solution of *p*-TsCl (74.3 mg, 0.39 mmol) in pyridine (3 ml) was added to (-)-3 ($[\alpha]_D^{20} - 29.9^\circ$ ($c = 0.976$, CHCl_3)) (150 mg, 0.37 mmol) and the whole was stirred at room temperature for 4 h, then at reflux for 3 h. The mixture was diluted with a mixture of benzene (200 ml) and CHCl_3 (50 ml), then washed with satd. aq. CuSO_4 , water, satd. aq. NaHCO_3 , and brine. The organic layer was dried over MgSO_4 and concentrated *in vacuo* to leave a yellow oil (150 mg). Purification by silica gel column chromatography (ether- CHCl_3 (1:4)) gave (-)-4 (103 mg, 72%) as a pale yellow oil. $[\alpha]_D^{20} - 34.8^\circ$ ($c = 0.926$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1591. ^1H -NMR (CDCl_3) δ : 1.9–2.6 (6H, m, $\text{ArCH}_2\text{CH} \times 2$), 3.3–4.0 (4H, m, CH_2OCH_2), 3.82 (9H, s, $\text{OCH}_3 \times 3$), 5.8–5.9 (2H, m, OCH_2O), 6.28 (2H, s, aromatic H), 6.4–6.7 (3H, m, aromatic H). ^{13}C -NMR (Table I). MS m/z : 386 (M^+), 182, 181, 167, 151, 136, 135, 77, 69. Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{O}_6$: C, 68.38; H, 6.78. Found: C, 68.08; H, 6.72.

(+)-4—Cyclization of (+)-3 ($[\alpha]_D^{20} + 31.6^\circ$ ($c = 0.950$, CHCl_3)) afforded (+)-4 as a pale yellow oil. $[\alpha]_D^{20} + 37.5^\circ$ ($c = 0.982$, CHCl_3). IR, ^1H -NMR, MS, and TLC behavior were identical with those for (-)-4.

(-)-Podorhizol ((-)-5a) and (-)-Epipodorhizol ((-)-5b)—A solution of (+)-1^{4c,f)} ($[\alpha]_D^{20} + 5.22^\circ$ ($c = 1.13$, CHCl_3)) (110 mg, 0.50 mmol) in THF (3 ml) was added to a solution of lithium diisopropylamide (0.55 mmol) in THF (5 ml) at -78°C and the mixture was stirred at -78°C for 25 min. A solution of 3,4,5-trimethoxybenzaldehyde (108 mg, 0.55 mmol) in THF (3 ml) was added, and the whole was stirred at -78°C for 2 h and quenched with AcOH

(0.5 ml). After dilution with AcOEt (150 ml), the organic solution was washed with 10% aq. HCl, 15% aq. NaOH, and brine, then dried over MgSO₄. Concentration *in vacuo* gave a yellow oil (220 mg). Purification by preparative TLC (SiO₂, iso-PrOH-CHCl₃ (0.5 : 99.5)) afforded (–)-**5a** (85.9 mg, 42%) (*R*_f: 0.25) and (–)-**5b** (84.1 mg, 41%) (*R*_f: 0.30).

(–)-**5a**: A yellow glass. $[\alpha]_D^{21} - 51.7^\circ$ ($c = 0.944$, CHCl₃) (lit.,⁷) $[\alpha]_D^{21} - 51.8^\circ$ ($c = 1.046$, CHCl₃). IR $\nu_{\max}^{\text{CH}_2\text{Cl}_2} \text{ cm}^{-1}$: 3600, 3480, 1760, 1598. ¹H-NMR (CDCl₃) δ : 2.0–3.0 (4H, m, CH₂, CH × 2), 3.2 (1H, br s, OH), 3.84 (9H, s, OCH₃ × 3), 3.8–4.5 (2H, m, CH₂O), 5.25 (1H, d, $J = 2$ Hz, CHOH), 5.92 (2H, s, OCH₂O), 6.24 (1H, s, aromatic H), 6.3–6.8 (4H, m, aromatic H). MS m/z : 416 (M^+).

(–)-**5b**: Amorphous powder of mp 49–51 °C (lit.,⁷) 51–53 °C), $[\alpha]_D^{21} - 32.3^\circ$ ($c = 0.600$, CHCl₃) (lit.,⁷) $[\alpha]_D^{21} - 32.6^\circ$ ($c = 0.628$, CHCl₃). IR $\nu_{\max}^{\text{CH}_2\text{Cl}_2} \text{ cm}^{-1}$: 3500, 1760, 1598. ¹H-NMR (CDCl₃) δ : 2.0–2.8 (5H, m, CH₂, CH × 2, OH), 3.81 (3H, s, OCH₃), 3.85 (6H, s, OCH₃ × 2), 4.06 (2H, m, CH₂O), 4.81 (1H, d, $J = 6.6$ Hz, CHOH), 5.89 (2H, s, OCH₂O), 6.0–6.4 (2H, m, aromatic H), 6.4–6.8 (3H, m, aromatic H). MS m/z : 416 (M^+).

Spectroscopic data for (–)-**5a, b** were identical with those reported.⁷ The mixture was directly used for the next step.

(–)-**Isodeoxypodophyllotoxin ((–)-6)**—A solution of the mixture of **5a** and **5b** (460 mg), obtained from (+)-**1** (220 mg, 1.0 mmol) as above, and *p*-TsOH (30 mg) in xylene (60 ml) was stirred at reflux for 2 h.⁸ The whole was washed with satd. aq. NaHCO₃ and brine, then dried over MgSO₄. Concentration *in vacuo* afforded a brown solid (450 mg). Purification by silica gel column chromatography (ether-CHCl₃ (1 : 5)) afforded (–)-**6** (300 mg, 76% from (+)-**1**) as a white solid of mp 250–253 °C (from AcOEt) (lit.,⁷) mp 252–254 °C). $[\alpha]_D^{21} - 80.8^\circ$ ($c = 0.624$, CHCl₃) (lit.,⁷) $[\alpha]_D^{21} - 84.6^\circ$ ($c = 0.614$, CHCl₃). IR $\nu_{\max}^{\text{CH}_2\text{Cl}_2} \text{ cm}^{-1}$: 1783, 1592. ¹H-NMR (*d*₆-DMSO) δ : 3.68 (3H, s, OCH₃), 3.74 (6H, s, OCH₃), 5.90 (2H, s, OCH₂O), 6.20 (1H, s, aromatic H), 6.50 (2H, s, aromatic H), 6.71 (1H, s, aromatic H). MS m/z : 398 (M^+). Anal. Calcd for C₂₂H₂₂O₇: C, 66.32; H, 5.57. Found: C, 66.02; H, 5.59.

(–)-**Anhydropodorhizol ((–)-7)**—A solution of *n*-BuLi (0.70 mmol) in *n*-hexane (0.44 ml) was added to a solution of **5a, b**, obtained from (+)-**1** (110 mg, 0.50 mmol), in THF (4 ml) and the mixture was stirred at –78 °C for 30 min. A solution of *p*-TsCl (133 mg, 0.70 mmol) in THF (1 ml) was added, and the whole was stirred at room temperature for 2.5 h, then poured into satd. aq. NH₄Cl (10 ml) and extracted with AcOEt (50 ml × 2). The organic solution was washed with 10% HCl, satd. aq. NaHCO₃, and brine, then dried over MgSO₄. Concentration *in vacuo* gave a yellow oil (270 mg). A solution of the above yellow oil and *tert*-BuOK (78.4 mg, 0.70 mmol) in MeOH (5 ml) was stirred at room temperature for 12 h and poured into 10% aq. HCl (5 ml). The mixture was extracted with AcOEt (50 ml × 2). The combined extracts were washed with satd. aq. NaHCO₃, and brine, then dried over MgSO₄. Concentration *in vacuo* gave a yellow oil (210 mg). Purification by silica gel column chromatography (ether-CHCl₃ (1 : 99)) afforded (–)-**7** (160 mg, 80%) as a pale yellow oil. $[\alpha]_D^{21} - 54.1^\circ$ ($c = 0.54$, CHCl₃) (lit.,⁷) $[\alpha]_D^{21} - 55.2^\circ$ ($c = 0.598$, CHCl₃). IR $\nu_{\max}^{\text{CH}_2\text{Cl}_2} \text{ cm}^{-1}$: 1755, 1650, 1587. ¹H-NMR (CDCl₃) δ : 2.68 (1H, dd, $J = 10$ and 15 Hz, ArCH₂), 3.11 (1H, dd, $J = 5$ and 15 Hz, ArCH₂), 3.92 (9H, s, OCH₃ × 3), 3.6–4.1 (1H, m, CH), 4.1–4.5 (2H, m, CH₂O), 6.00 (2H, s, OCH₂O), 6.5–6.8 (3H, m, aromatic H), 6.86 (2H, s, aromatic H), 7.60 (1H, d, $J = 2$ Hz, CH). MS m/z : 398 (M^+). IR and ¹H-NMR data were in good agreement with those reported for (–)-**7**.⁷

(+)-**(2R,3S)-2-(3,4-Methylenedioxybenzyl)-3-(3,4,5-trimethoxybenzyl)-1,4-butanediol ((+)-9)**—A mixture of (–)-**7** (240 mg, 0.60 mmol) and 5% Pd-C (100 mg) in AcOH (3 ml) was stirred at room temperature for 12 h under an atmosphere of hydrogen. The mixture was filtered and concentrated to leave a colorless oil. Purification by silica gel column chromatography (ether-CHCl₃ (0.5 : 9.5)) gave *cis*-dihydroanhydropodorhizol (**8**) (150 mg, 63%)⁷ containing deoxypodorhizon ((–)-**2**) (30% by ¹³C-NMR (Table I)). A mixture of **8** and (–)-**2** (120 mg, 0.3 mmol), obtained above, in THF (10 ml) was added to a suspension of LiAlH₄ (23 mg, 0.6 mmol) in THF (5 ml) and the whole was stirred at room temperature for 1 h. Water (0.02 ml), 15% aq. NaOH (0.02 ml), and water (0.06 ml) were added, then the mixture was filtered. The filtrate was concentrated *in vacuo* to give a colorless glass (110 mg). Purification by silica gel TLC (ether-CHCl₃ (4 : 6)) gave (–)-**3** (30 mg, 15%) and (+)-**9** (60 mg, 50%) as a pale yellow oil. $[\alpha]_D^{20} + 9.65^\circ$ ($c = 0.974$, CHCl₃). IR $\nu_{\max}^{\text{film}} \text{ cm}^{-1}$: 3300, 1580. ¹H-NMR (CDCl₃) δ : 1.8–2.4 (2H, m, CH), 2.5–2.9 (4H, m, ArCH₂ × 2), 3.2–4.0 (6H, m, CH₂OH × 2), 3.80 (9H, s, OCH₃ × 3), 5.90 (2H, s, OCH₂O), 6.40 (2H, s, aromatic H), 6.70 (3H, s, aromatic H). ¹³C-NMR (Table I). MS m/z : 404 (M^+).

(+)-**cis-Burseran ((+)-10)**—A solution of (+)-**9** (90 mg, 0.22 mmol) and *p*-TsCl (45 mg, 0.23 mmol) in pyridine (4 ml) was stirred at –18 °C for 4 h and at room temperature for 1 h, then diluted with a mixture of benzene (50 ml) and CHCl₃ (50 ml). The whole was washed with satd. aq. CuSO₄, satd. aq. NaHCO₃, and brine, then dried over MgSO₄. Concentration *in vacuo* gave a yellow oil (80 mg). Purification by silica gel column chromatography (ether-CHCl₃ (1 : 9)) afforded (+)-**9** (60 mg, 67% recovery) and (+)-**10** (28 mg, 33%) as a colorless oil. $[\alpha]_D^{20} + 5.4^\circ$ ($c = 0.558$, CHCl₃). IR $\nu_{\max}^{\text{film}} \text{ cm}^{-1}$: 1580. ¹H-NMR (CDCl₃) δ : 2.4–3.1 (6H, m, ArCH₂CH × 2), 3.6–4.1 (4H, m, CH₂OCH₂), 3.84 (9H, m, OCH₃ × 2), 5.91 (2H, s, OCH₂O), 6.38 (2H, s, aromatic H), 6.68 (3H, s, aromatic H). ¹³C-NMR (Table I). MS m/z : 386 (M^+), 182, 181, 167, 151, 136, 135, 77, 69. Anal. Calcd for C₂₂H₂₆O₆: C, 68.38; H, 6.78. Found: C, 68.18; H, 6.85. IR, ¹H-NMR, and MS were indistinguishable from those reported for burseran,⁵ but were clearly different from those of (–)-**4**.

Gas Chromatography of *trans*- and *cis*-Burseran ((–)-4 and (+)-10)—The retention times of (–)-**4** and (+)-**10** were 1.5 and 2.2 min, respectively (stainless steel column, 1 m, 15% QF-I on Diasolid A, 258 °C, carrier gas N₂ 1 kg/cm²).

Acknowledgment The authors express their thanks to Professor Sansei Nishibe, Faculty of Pharmaceutical Sciences, Higashi Nihon Gakuen University, Japan, for providing spectra of deoxypodorhizon and anhydro-dihydropodorhizon.

References and Notes

- 1) Part IX: N. Ikota, H. Shibata, and K. Koga, *Chem. Pharm. Bull.*, **33**, 3299 (1985).
- 2) A part of this work has been reported. K. Tomioka and K. Koga, *Heterocycles*, **12**, 1523 (1979).
- 3) For reviews, see: a) K. Tomioka, *Yakugaku Zasshi*, **104**, 1009 (1984); b) *Idem*, *Advances in Pharmaceutical Sciences, The Research Foundation For Pharmaceutical Sciences*, **1**, 121 (1985).
- 4) a) K. Tomioka, H. Mizuguchi, and K. Koga, *Tetrahedron Lett.*, **1978**, 4687; b) *Idem, ibid.*, **1979**, 1409; c) K. Tomioka and K. Koga, *ibid.*, **1979**, 3315; d) K. Tomioka, T. Ishiguro, and K. Koga, *J. Chem. Soc., Chem. Commun.*, **1979**, 652; e) *Idem, Tetrahedron Lett.*, **21**, 2973 (1980); f) K. Tomioka, H. Mizuguchi, and K. Koga, *Chem. Pharm. Bull.*, **30**, 4304 (1982); g) K. Tomioka, T. Ishiguro, Y. Iitaka, and K. Koga, *Tetrahedron*, **40**, 1303 (1984); h) K. Tomioka, H. Mizuguchi, T. Ishiguro, and K. Koga, *Chem. Pharm. Bull.*, **33**, 121 (1985); i) T. Ishiguro, H. Mizuguchi, K. Tomioka, and K. Koga, *ibid.*, **33**, 609 (1985).
- 5) J. R. Cole, E. Bianchi, and E. R. Trumbull, *J. Pharm. Sci.*, **58**, 175 (1969).
- 6) E. R. Trumbull and J. R. Cole, *J. Pharm. Sci.*, **58**, 176 (1969).
- 7) M. Kuhn and A. von Wartburg, *Helv. Chim. Acta*, **50**, 1546 (1967).
- 8) K. Yamashita and M. Matsui, *Bull. Agric. Chem. Soc. Jpn.*, **23**, 230 (1959).
- 9) More information on natural burseran was not available from Drs. J. R. Cole and E. R. Trumbull.
- 10) Melting points were measured using Büchi 510 melting point apparatus and are not corrected. Optical rotations were taken with a JASCO DIP-181 automatic polarimeter. IR spectra were taken with a JASCO Infrared Spectrometer Model DS-402 G and a JASCO IRA-I Grating Infrared Spectrometer. ¹H-NMR spectra were taken with a JNM-PS 100 Spectrometer, with a JEOL FX-100 Spectrometer at 100 MHz, or with a Hitachi R-24 Spectrometer at 60 MHz. ¹³C-NMR spectra were taken with a JEOL FX-100 Spectrometer at 25 MHz. Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. MS were taken with a JEOL-01, SG-2 Mass Spectrometer.