ASYMMETRIC SYNTHESIS OF (*S*)-1-(5-HYDROXY-2-METHOXY-BENZYL)-7-HYDROXY-6-METHOXY-2-METHYL-1,2,3,4-TETRAHYDROISOQUINOLINE (SO-CALLED "DEHASSILINE")

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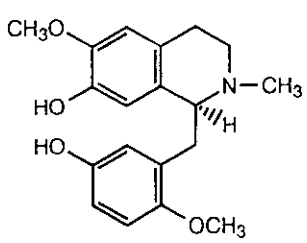
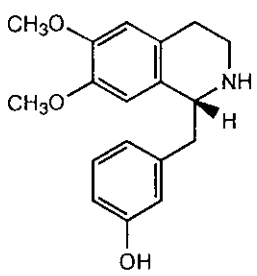
Abstract — Optically active, (*S*)-1-(5-hydroxy-2-methoxybenzyl)-7-hydroxy-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (so-called "dehassiline") (1) was synthesized *via* highly stereoselective reduction of the 3,4-dihydroisoquinolinium ion possessing a chiral auxiliary by Polniaszek's method. The synthetic compound (1) was shown to be different from natural dehassiline, the structure of which should be revised.

The asymmetric synthesis of optically active isoquinoline alkaloids has previously been reported.[1] Among them, the synthetic method *via* reduction of the 1-substituted 3,4-dihydroisoquinolinium ion possessing a chiral auxiliary by Polniaszek,[2] is very concise and highly stereoselective. Recently, we reported the synthesis of (*R*)-noranicanine (2)[3] and so-called "fumarizine" (3)[4] by this method. Herein, we describe the asymmetric



(1)



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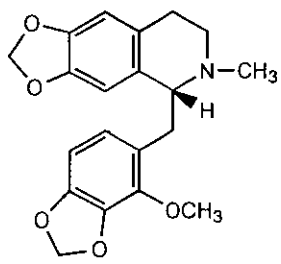

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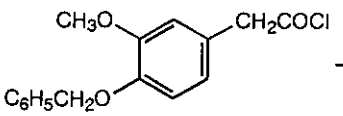

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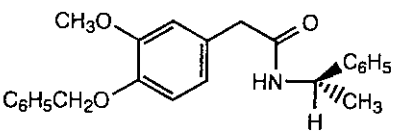

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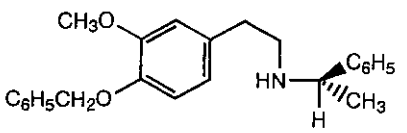

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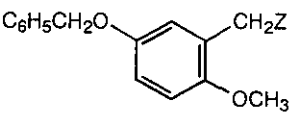
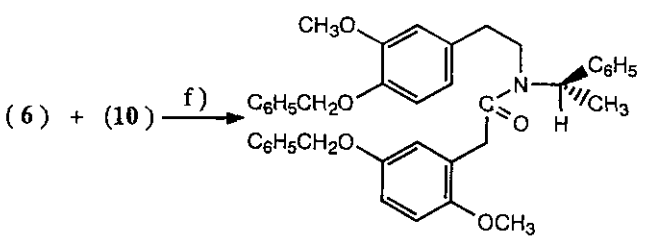


(7) Z = Cl → (8) Z = CN → (9) Z = COOH → (10) Z = COCl



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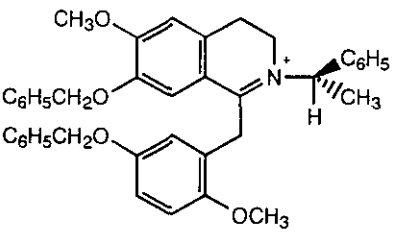

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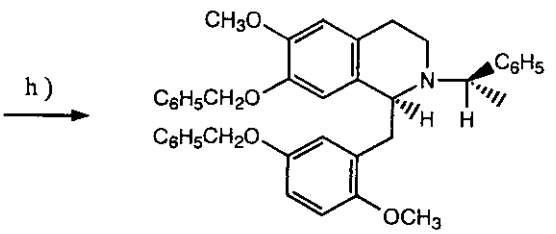

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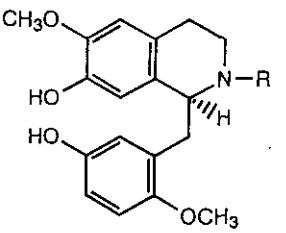

(14) R = H → (15) R = $COOCH_3$

→ (1)

a) (*S*)-1-phenylethylamine/Na_2CO_3 *b)* BF_3-ether, BH_3-THF
c) NaCN/DMSO *d)* KOH/diethylene glycol *e)* $SOCl_2$/benzene
f) Na_2CO_3 *g)* $POCl_3$/toluene *h)* $NaBH_4/CH_3OH$
i) Pd-C/C_2H_5OH-HCl *j)* CH_3OCOCl/CH_2Cl_2 *k)* $LiAlH_4$/THF

synthesis of (*S*)-(+)-dehassiline [(*S*)-(+)-1-(5-hydroxy-2-methoxybenzyl)-7-hydroxy-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline] (1),[5] which was isolated from *Dehassia kurzii* (Lauraceae), by a synthetic route similar to that used for 2 or 3 as shown in scheme.

One of the starting materials, *N*-[(*S*)-1-phenylethyl]-2-(4-benzyloxy-3-methoxyphenyl)ethylamine (6), was obtained by reduction using BH_3-THF of the amide (5), which was prepared by condensation with acid chloride (4) derived from 4-benzyloxy-3-methoxyphenylacetic acid[6] and (*S*)-1-phenylethylamine. As starting material, 5-benzyloxy-2-methoxy-phenylacetic acid (9), mp 148~150°C, was obtained in good yield *via* the benzyl alcohol,[7] the benzyl chloride (7), and the benzyl cyanide (8), from *O*-benzyl derivative[8] of 5-hydroxy-2-methoxybenzaldehyde.[9]

The Schotten-Baumann reaction of the (*S*)-chiral amine (6) with the acid chloride (10) derived from the carboxylic acid (9) afforded the amide (11) as a pale yellow oily substance. The Bischler-Napieralski reaction of the amide (11) with $POCl_3$ in dry toluene afforded the iminium ion (12), which was stereoselectively reduced with sodium borohydride in MeOH at -78°C by Polniaszek's method[2] afforded (*S*)-1-(5-benzyloxy-2-methoxybenzyl)-2-[(*S*)-1-phenylethyl]-7-benzyloxy-6-methoxy-1,2,3,4-tetrahydro-isoquinoline (13) as a pale yellow oily substance, $[\alpha]_D$ +72.2° (c = 0.55, $CHCl_3$), in 74.0% total yield from 11. The optical purity was determined to be 99.5% ee by HPLC with a chiral stationary phase based on a derivatized amylose, CHIRALPAK AD. The deletion of chiral auxiliary and *O*-debenzylation by catalytic hydrogenation of the optical active substituted 1,2,3,4-tetrahydoisoquinoline (13) gave (*S*)-1-(5-hydroxy-2-methoxy-benzyl)-7-hydroxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline (14) as colorless needles, mp 177~179°C, $[\alpha]_D$ +72.1° (c = 0.51, $CHCl_3$). Finally, reduction of *N*-methoxycarbonyl derivative (15) of 14 with $LiAlH_4$ in THF produced (*S*)-1-(5-hydroxy-2-methoxybenzyl)-7-hydroxy-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (1), $[\alpha]_D$ +63.9° (c = 1.00, $CHCl_3$) as a colorless oil showing a single spot on TLC.

All spectral data (UV, IR, ^{1}H-NMR ^{13}C- NMR and MS) of synthetic product were appreciably different with those of the naturally occurring (+)-dehessiline (1)[5] as shown in Table. Therefore, the structure of (+)-dehassiline must be re-examined.

EXPERIMENTAL

Melting points were determined using a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H- and ^{13}C-NMR spectra were measured on a JEOL FX-200 spectrometer in $CDCl_3$ solution with tetramethylsilane as a

Table ^{1}H- and ^{13}C-NMR Chemical Shift Assignments of Synthetic Compound (1) and (+)-Dehassiline

	synthetic compound		natural product	
	$\delta^{13}C$	$\delta^{1}H$	$\delta^{13}C$	$\delta^{1}H$
C-1	62.88	3.77(m)	65.98	3.42(dd, J_1=5.0 Hz, J_2=7.8 Hz)
C-3	45.27	2.77(ddd,J_1=12.8 Hz, J_2=3.9 Hz, J_3=5.8 Hz) 3.25(ddd,J_1=12.6 Hz, J_2=9.4 Hz, J_3=4.9 Hz)	47.34	2.81(dd, J_1=13.4 Hz, J_2=7.0 Hz) 3.14(ddd,J_1=13.4 Hz, J_2=7.8 Hz,J_3=3.5 Hz)
C-4	23.94	2.59(ddd,J_1=16.3 Hz, J_2=4.3 Hz, J_3=4.3 Hz) 2.86(ddd,J_1=15.4 Hz, J_2=9.4 Hz, J_3=6.0 Hz	25.05	2.58(dd, J_1=12.5 Hz, J_2=7.8 Hz) 2.73(dd, J_1=12.5 Hz, J_2=5.0 Hz)
C-5a	124.20		133.04	
C-5	110.74	6.54(s)	121.96	6.67(s)
C-6	151.14[a]		145.52	
C-7	145.60[b]		148.22	
C-8	114.21	6.43(s)	112.61	6.14(s)
C-8a	128.75		124.82	
C-α	36.06	2.83(dd, J_1=13.7 Hz, J_2=5.6 Hz) 3.00(ddd,J_1=13.9 Hz, J_2=6.8 Hz, J_3=3.0 Hz)	40.82	2.67(dd, J_1=13.7 Hz, J_2=5.0 Hz) 3.00(dd, J_1=13.7 Hz, J_2=7.8 Hz)
C-1'	130.21		129.48	
C-2'	150.16[a]		145.46	
C-3'	113.85	6.71(d, J=8.6 Hz)	117.68	6.82(d, J=8.1 Hz)
C-4'	118.88	6.63(dd, J_1=8.6 Hz, J_2=3.0 Hz)	115.60	6.52(dd, J_1=8.1 Hz, J_2=2.1 Hz)
C-5'	143.56[b]		147.76	
C-6'	111.80	6.60(d, J=3.0 Hz)	112.81	6.62(d, J=2.1 Hz)
OCH_3	55.81[c]	3.76(s)	54.4	3.81(s)
OCH_3	55.96[d]	3.85(s)	56.3	3.82(s)
NCH_3	41.66	2.43(s)	41.9	2.61(s)

*Assignments of a,b or c,d on ^{13}C-NMR(δ value) may be interchangeable.

standard. UV and IR spectra were taken on a Shimadzu UV-160 and Shimadzu IR-435 spectrophotomer, respectively. MS spectra were obtained by using JEOL JMS DX-303 EIMS spectrometer. Optical rotations were measured on a JASCO DIP-360 polarimeter. Column chromatography and preparative TLC were carried out on Wakogel C-200 (100~200 mesh) and with silica gel $60F_{254}$, Merck. Most organic extracts were dried over anhyd. $MgSO_4$.

***N*-[(*S*)-1-Phenylethyl]-2-(4-benzyloxy-3-methoxyphenyl)acetamide (5)** To an ether (90 mL) solution of (*S*)-1-phenylethylamine (3.10 mL, 0.024 mol) and 5% aq. Na_2CO_3 (90 mL) solution was slowly added dropwise an anhyd. ether (90 mL) solution of 4-benzyloxy-3-methoxyphenylacetyl chloride (4) prepared from 4-benzyloxy-3-methoxyphenylacetic acid[6] (5.44 g, 0.02 mol) and excess thionyl chloride (10 mL, 0.138 mol) by the usual method. Stirring was continued for 1 h at 0~5°C, and precipitates were filtrated and dissolved in CH_2Cl_2. The organic layer was washed successively with 5% aq. *HCl* solution, 5% aq. *NaOH* solution and water. *Removal of the solvent by* evaporation left a solid, which was recrystallized from ethanol-hexane to furnish the corresponding optically active acetamide (5), colorless needles, mp 115~118°C (6.21 g, 82.8%), $[\alpha]_D^{27}$ +16.5° (c = 0.3, $CHCl_3$). UV λ_{max}^{EtOH} nm(log ε): 204(4.78), 230(sh, 3.98), 280(3.49); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680(C=O); ^{1}H-NMR δ: 1.39(3H, d, J = 7.0 Hz, CH_3), 3.51(2H, s, CH_2CO), 3.84(3H, s, OCH_3), 5.15(1H, q, J = 7.6 Hz, CH), 5.15(2H, s, OCH_2Ph), 5.60(1H, br, NH), 6.68~6.87(3H, m, arom.H×3), 7.15~7.46(10H, m, arom.H×10); EIMS (70 eV) $^m/_z$(rel. intensity): 375(M^+, 83.1), 271(12.2), 227(13.5), 137(70.8), 105(68.6), 91(100); Anal. Calcd for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.73. Found: C, 76.70; H, 6.76; N, 3.81.

***N*-[(*S*)-1-Phenylethyl]-2-(4-benzyloxy-3-methoxyphenyl)ethylamine (6)** To the above amide (5) (3.75 g, 0.01 mol) in anhyd. THF (60 mL) were carefully added dropwise BF_3 ether complex (abt. 47 %, 1.5 mL, 0.05 mol) and 1.0 M BH_3 THF complex (30 mL, 0.03 mol) under argon at rt, and further heated for 2.5 h at 70°C. After the reaction was complete, the excess reagent was decomposed with 5 N aq. HCl solution (90 mL) and the organic solvent was evaporated off *in vacuo*. The aqueous solution was made alkaline with 10% aq. NaOH solution and extracted three times with CH_2Cl_2. The extract was washed with water, and solvent was evaporated off to give a pale yellow oil (6) (3.14 g, 87.0%) showing a single spot on TLC. $[\alpha]_D^{26}$ -22.0° (c = 0.41, $CHCl_3$); UV λ_{max}^{EtOH} nm(log ε): 204(4.73), 229(sh, 3.97), 279(3.43); ^{1}H-NMR δ: 1.32(3H, d, J = 6.6 Hz, CH_3), 1.55(1H, br, NH), 2.70, 2.71(2H×2, m, CH_2×2), 3.75(1H, q, J = 6.6 Hz, CH), 3.84(3H, s, OCH_3), 5.12(2H, s, OCH_2Ph), 6.60~6.81(3H, m,

arom.H×3), 7.18~7.46(10H, m, arom.H×10); EIMS (70 eV) $^{m}/_{z}$ (rel. intensity): 361(M^+, 6.2), 228(68.5), 134(84.3), 105(100). The hyrdochloride was obtained as colorless needles, mp 212~214°C (from MeOH-Me_2CO). Anal. Calcd for $C_{24}H_{27}NO_2 \cdot HCl$: C, 72.44; H, 6.84; N, 3.52. Found: C, 72.31; H, 7.08; N, 3.59.

5-Benzyloxy-2-methoxybenzyl chloride (7) The anhydrous benzene (100 mL) solution of thionyl chloride (40 mL, 0.54 mol) was added to the benzyl alcohol[7] (48.8 g, 0.20 mol) and *N,N*-dimethylaniline (48.1 mL, 0.38 mol) in anhydrous benzene (200 mL) with stirring at 0~5°C. The reaction mixture was stirred continuously at 100°C for 1 h, then washed with 10% aq. HCl and water. The benzene layer dried over anhyd. $CaCl_2$ and treated in the usual manner to give the residue, which was recrystallized from ether-petroleum ether mixture to afford the benzyl chloride (7) (45.9 g, 87.4%), colorless needles, mp 65~67°C. UV λ_{max}^{EtOH} nm(log ε): 205(4.56), 228(sh, 3.95); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 615(C-Cl); ^{1}H-NMR δ: 3.83(3H, s, OCH_3), 4.62(2H, s, CH_2Cl), 5.02(2H, s, OCH_2Ph), 6.79~7.04(3H, m, arom.H×3), 7.25~7.45(5H, m, arom. H×5); EIMS (70 eV) $^{m}/_{z}$ (rel. intensity): 264(19.0), 262(M^+, 50.4), 227(M^+-Cl, 7.4), 171(9.4), 91(100); Anal. Calcd for $C_{15}H_{15}O_2Cl$: C, 68.57; H, 5.75. Found: C, 68.37; H, 5.78.

5-Benzyloxy-2-methoxyphenylacetonitrile (8) To a suspension of sodium cyanide (14.7 g, 0.30 mol) in dimethyl sulfoxide (DMSO, 50 mL) was added dropwise the benzyl chloride (7) (39.3 g, 0.15 mol) in DMSO (120 mL) at rt with stirring. After further stirring at 40~50°C for 1 h, the resultant reaction mixture was poured into ice water (500 mL), and the precipitate was removed by filtration. The precipitate was recrystallized from dil. EtOH to afford the phenylacetonitrile (8), colorless needles, mp 56~58°C (36.1 g, 95.1%). UV λ_{max}^{EtOH} nm(log ε); 202(4.55), 228(4.02); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250(C≡N); ^{1}H-NMR δ: 3.66(2H, s, CH_2CN), 3.81(3H, s, OCH_3), 5.03(2H, s, OCH_2Ph), 6.77~7.05(3H, m, arom.H×3), 7.26~7.46(5H, m, arom. H×5); EIMS (70 eV) $^{m}/_{z}$ (rel. intensity): 253(M^+, 37.8), 161(3.7), 91(100); Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.59; H, 5.96; N, 5.49.

5-Benzyloxy-2-methoxyphenylacetic acid (9) The phenylacetonitrile (8) (25.3 g, 0.10 mol) with 25% ethanolic KOH solution (250 mL) and diethylene glycol (100 mL) was refluxed until the evolution of ammonia ceased (21 h). Then the reaction mixture was acidified with 10% aq. HCl to yield a solid.

The solid collected by filtration was recrystallized from benzene to afford colorless needles (9), mp 148~150°C (23.1 g, 84.9%). UV λ_{max}^{EtOH} nm(log ε): 203(4.57), 226(sh, 3.97); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710(C=O); ^{1}H-NMR δ: 3.64(2H, s, CH_2COOH), 3.79(3H, s, OCH_3), 5.00(2H, s, OCH_2Ph), 6.77~6.88(3H, m, arom.H×3), 7.25~7.44(5H, m, arom.H×5); EIMS (70 eV) $^m/_z$ (rel. intensity): 272(M^+, 60.2), 181(M^+-$C_6H_5CH_2$, 10.6), 149(20.6), 121(10.2), 91(100); Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.79; H, 6.04.

***N*-[2-(4-Benzyloxy-3-methoxyphenyl)ethyl]-*N*-[(*S*)-1-phenylethyl]-2-(5-benzyloxy-2-methoxyphenyl]acetamide (11)** An anhydrous ether solution of 5-benzyloxy-2-methoxyphenylacetyl chloride (10), which formed from the carboxylic acid (9) (2.72 g, 10.0 mmol) and excess $SOCl_2$ in the usual way, was added dropwise to an ether (100 mL) solution of the amine (6) (3.79 g, 10.5 mmol) and 5% aq. Na_2CO_3 (100 mL, 46.7 mmol) solution with stirring at 0~5°C. After further stirring for 2 h at the same temperature, the organic layer was separated, the ether layer was washed successively with 5% aq. HCl solution and water. Removal of the solvent by evaporation left a residue, which was chromatographed with hexane/CH_2Cl_2 (4:1) to give the amide (11) (5.47 g, 88.9%) as a pale yellow oily substance showing a single spot on TLC. $[\alpha]_D$ -32.9° (c = 0.15, $CHCl_3$); UV λ_{max}^{EtOH} nm(log ε): 204(5.00), 229(sh, 4.41), 283(3.81); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630(C=O); ^{1}H-NMR δ: 1.50(3H, d, J = 6.9 Hz, CH_3), 2.12~2.76, 3.11~3.28, 3.71~3.86(2H×3, m, CH_2×3), 3.76, 3.80(3H×2, s, OCH_3×2), 5.01, 5.08(2H×2, s, OCH_2Ph×2), 5.19~6.13(1H, m, CH), 6.38~7.18(6H, m, arom.H×6), 7.23~7.45(5H×3, m, arom.H×15); EIMS (70 eV) $^m/_z$ (rel. intensity): 615(M^+, 13.2), 525(10.0), 375(55.3), 344(50.3), 240(57.1), 134(65.4), 105(75.5), 91(100).

***(S)*-1-(5-Benzyloxy-2-methoxybenzyl)-*N*-[(*S*)-phenylethyl]-7-benzyloxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline (13)** A mixture of the amide (11) (5.25 g, 0.01 mol) and $POCl_3$ (20.0 mL, 0.22 mol) in dry toluene (50.0 mL) was refluxed for 3.5 h. Evaporation of excess reagent and solvent left a residue, which was thoroughly washed with petroleum ether. The residue (iminium ion, 12) was used for the following reaction without purification. To a stirred solution of above iminium ion (12) in MeOH (200 mL) was gradually added $NaBH_4$ (5.7 g, 0.15 mol) at -78°C. After the mixture was stirred at the same temperature for 2 h, excess $NaBH_4$ was decomposed with 10% aq. AcOH and most of MeOH was removed by evaporation *in vacuo*. The residual solution was made alkaline with 10% aq. NH_4OH solution and extracted with CH_2Cl_2. Usual work-up of the CH_2Cl_2 layer gave an oily residue, whose column chromatography on silica gel with hexane-CH_2Cl_2

[9:1 ($^{v}/_{v}$)] gave a pale brownish oil (13), (3.58 g, 74.0% from 11) showing a single spot on TLC. $[\alpha]_D^{25}$ +72.2° (c = 0.55, $CHCl_3$); 99.5% ee [CHIRALPAK AD column (4.6 × 250 mm) (Daicel Chemical Industries, Ltd., Tokyo, JAPAN), mobile phase: hexane/2-propanol = 89/11 ($^{v}/_{v}$) including 0.1% diethylamine, flow rate: 0.5 mL/min, detection: 254 nm, k_1' = 21.6, k_2' = 25.3]; UV λ_{max}^{EtOH} nm(log ε); 204(5.07); ^{1}H-NMR δ: 1.32(3H, d, J = 6.4 Hz, CH_3), 2.43(1H, m, C-4), 2.69(1H, dd, J_1 = 12.8 Hz, J_2 = 6.5 Hz, C-α), 2.83(1H, m, C-4), 2.94(1H, m, C-3), 3.17(1H, m, C-α), 3.29(1H, m, C-3), 3.79(3H, s, OCH_3), 3.85(3H, s, OCH_3), 3.92(1H, br, CH), 4.22(1H, br, C-1), 4.80(2H, d, J = 6.4 Hz, OCH_2Ph), 4.94(2H, s, OCH_2Ph), 6.09(1H, s, C-8), 6.55(1H, d, J = 2.9 Hz, C-6'), 6.60(1H, s, C-5), 6.63(1H, d, J = 9.0 Hz, C-3'), 6.80(1H, dd, J_1 = 8.9 Hz, J_2 = 3.0 Hz, C-4'), 6.93~7.11(5H, m, arom.H×5), 7.14~7.34(5H, m, arom.H×5), 7.35~7.42(5H, m, arom.H×5); EIMS (70 eV) $^{m}/_{z}$ (rel. intensity); 599(M^+, 1.0), 372(100), 268(34.2), 178(17.7), 105(54.8), 91(46.3).

(*S*)-1-(5-Hydroxy-2-methoxybenzyl)-7-hydroxy-6-methoxy-1,2,3,4-tetrahydroisoquinoline (14) A mixture of 13 (1.68 g, 2.80 mmol) and 10% Pd-C (*ca.* 200 mg) in EtOH (*ca.* 120 mL) containing conc.HCl (4 mL) was shaken at rt under a hydrogen atmosphere (3.75 $^{kg}/_{cm^2}$) for 23 h using a medium-pressure catalytic hydrogenator. The catalyst was removed by filtration and most EtOH was removed by evaporation *in vacuo*. The residual solution was made alkaline with 10% aq. NH_4OH solution and extracted with CH_2Cl_2. The CH_2Cl_2 solution was treated by the usual method and the residue was subjected to column chromatography. The fraction eluted with Me_2CO gave a solid, which was recrystallized from $CHCl_3$ to afford colorless needles (14), mp 177~179°C (0.75 g, 84.9%). $[\alpha]_D$ +72.1° (c = 0.51, $CHCl_3$); UV λ_{max}^{EtOH} nm(log ε): 204(4.82), 224(sh, 2.30), 289(4.02); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3505(OH); ^{1}H-NMR δ: 2.71(1H, m, C-4), 2.76(1H, m, C-α), 2.81(1H, m, C-4), 3.16(1H, dd, J_1 = 9.3 Hz, J_2 = 3.9 Hz, C-3), 3.21(1H, m, C-α), 3.31(1H, m, C-3), 3.80, 3.81(3H×2, s, OCH_3×2), 4.08(1H, br, C-1), 6.65(1H, s, C-8), 6.66(1H, d, J = 7.1 Hz, C-3'), 6.67(1H, s, C-6'), 6.69(1H, s, C-5), 6.83(1H, dd, J_1 = 7.0 Hz, J_2 = 2.2 Hz, C-4'); EIMS (70 eV) $^{m}/_{z}$ (rel. intensity): 315(M^+, 0.2), 178(100), 163(42.9), 134(23.0), 107(33.2), 94(12.5); Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.25; H, 6.61; N, 4.44.

(*S*)-1-(5-Hydroxy-2-methoxybenzyl)-7-hydroxy-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (1) To the stirred solution of above base (14) (315 mg, 1 mmol) in CH_2Cl_2 (5 mL) was gradually added a solution of methyl

chlorocarbonate (104 mg, 1.1 mmol) in CH_2Cl_2 (3 mL) at rt. After stirring for 1 h, 10% aq. NH_4OH solution (5 mL) was added with further stirring for 1 h. The CH_2Cl_2 layer was washed with water, and was treated by the usual method to give a residue *N*-methoxycarbonyl derivative (15), was used for the following reaction without purification. To a suspension of $LiAlH_4$ (1.0 g, 2.63 mmol) in anhyd. THF (15 mL) was added gradually a solution of compound (15) in anhyd. THF (5 mL). After the reaction mixture was refluxed for 2 h, the excess of reagent was decomposed with water and 10% aq. HCl solution. The filtrate was made alkaline with 10% aq. NH_4OH solution and extracted with CH_2Cl_2. Usual work-up of the CH_2Cl_2 layer gave an oily residue, whose column chromatography with CH_2Cl_2-Me_2CO [7:3 ($^v/_v$)] gave a pale brownish oil (1), showing a single spot on TLC (220 mg, 66.9% from 14). $[\alpha]_D$ +63.9° (c = 1.00, $CHCl_3$); UV λ_{max}^{EtOH} nm (log ε): 288(3.89),225 (4.17), 203(4.78); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520(OH); EIMS (70 eV) $^m/_z$ (rel. intensity): 329(M^+, 0.4), 192(100), 177(12.2); ^{13}C- and ^1H-NMR spectral data are shown in Table.

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