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DETERMINATION OF THE STEREOCHEMISTRY OF C-2' AND C-3' POSITIONS OF TAXINE NA-1 (2'-HYDROXYTAXINE II) BY THE ASYMMETRIC SYNTHESIS OF THE REDUCTIVE DEGRADATION PRODUCT OF ITS SIDE CHAIN MOIETY

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Abstract – The reductive degradation of taxine NA-1 (2'-hydroxytaxine II) with *n*-Bu_4NBH_4 gave taxinine A and (–)-3-dimethylamino-3-phenylpropane-1,2-diol (**1**) in addition to 11,12-dihydrotaxinine A. The relative stereochemistry of (–)-**1** was identical with *syn*-3-dimethylamino-3-phenylpropane-1,2-diol, (±)-**1b**, which was synthesized from *cis*-2,3-epoxy-3-phenylpropan-1-ol, (±)-**7**. The absolute configuration of (–)-**1** was certified by comparison of the specific optical rotation and the spectroscopic data of (–)-**1** with those of (+)-**1b** and (–)-**1b**, which were enantioselectively synthesized by Sharpless asymmetric epoxidation reaction of *cis*-cinnamyl alcohol (**6**), respectively. As the result, the relative and absolute configuration of (–)-**1** was same with that of (–)-**1b** possessing (2*R*, 3*S*) configuration. Thus, the absolute configuration of the side chain of taxine NA-1 (2'-hydroxytaxine II) at C-2' and C-3' positions was determined to be (2'*R*, 3'*S*).

Paclitaxel (taxol®) was originally isolated from the stem bark of *Taxus brevifolia* Nutt.[1] Because of its excellent anticancer activity[2] and low content in natural plant resources, numerous attempts of its

synthesis were reported until now.[3] Because of the difficulty of stereo- and enantio-selective construction of taxane ring and the side chain moiety, the total synthesis of paclitaxel and its analogs needed complex steps and their overall yields were very low. Thus, the partial syntheses of the biologically active taxoids from naturally abundant taxoids are more practical method. In the course of our study to find new biologically active taxoids and the precursors for the syntheses of biologically active taxoids from *Taxus cuspidata*, taxine NA-1 (2'-hydoxytaxine II, **A**) was isolated in 0.043% from the fresh needles of this plant as the most abundant basic taxoid.[4] The stereochemistry of the *N*,*N*-dimethyl-3-phenylisoseryl side chain at C-5 of **A** was deduced to be *syn* by the coupling constant between H-2′ and H-3′ (J = 9.5 Hz) in its ^{1}H NMR spectrum, which was good agreement with the dihedral angle between H-2′ and H-3′ (180°) of the most stable conformation of *syn*-*N*,*N*-dimethyl-3-phenylisoseryl side chain based on MM 2 calculation. Considering the co-occurrence of **A** and paclitaxel in the same plant and their common biosynthetic pathway, the C-5 side chain moiety of **A** was deduced to be (2'*R*,3'*S*)-*N*,*N*-dimethyl-3-phenylisoseryl.[4]

In general, it is difficult to decide the relative- and absolute-stereochemistry of the vicinal substituents of acyclic compounds according to the spectroscopic analysis. In this manuscript, we want to report the determination of the stereochemistry at C-2' and C-3' of **A** through enantioselective synthesis of the side chain derivative (**1**), which will be derived by reductive cleavage[5] of the ester bonding between taxinine A[6] and *N*,*N*-dimethyl-3-phenylisoseryl moiety as shown in Figure 1.

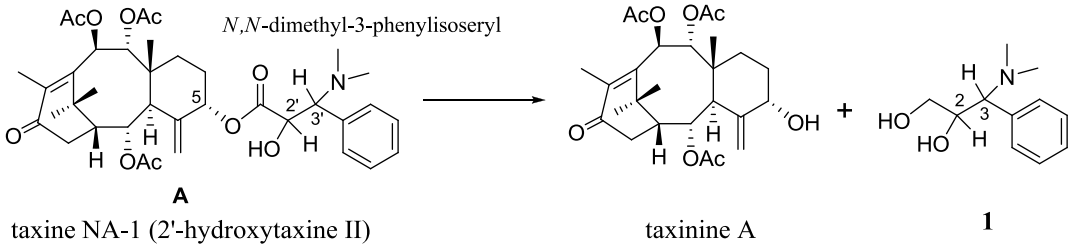
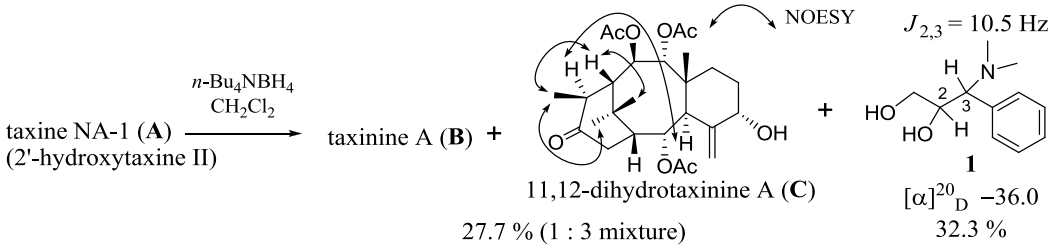


Figure 1. Reductive cleavage of taxine NA-1 (2′-hydroxytaxine II, **A**)

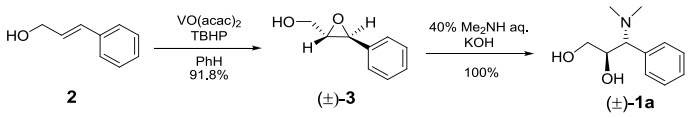
Reduction of taxine NA-1 (2′-hydroxytaxine II) (**A**) with *n*-Bu_4NBH_4 in CH_2Cl_2 at room temperature gave (–)-3-dimethylamino-3-phenylpropane-1,2-diol (**1**) ($[\alpha]^{20}_D$ –36.0) in 32.3% yield together with taxinine A (**B**) and 11,12-dihydrotaxinine A (**C**) as a 1:3 mixture in 27.7% yield (Scheme 1).



Scheme 1

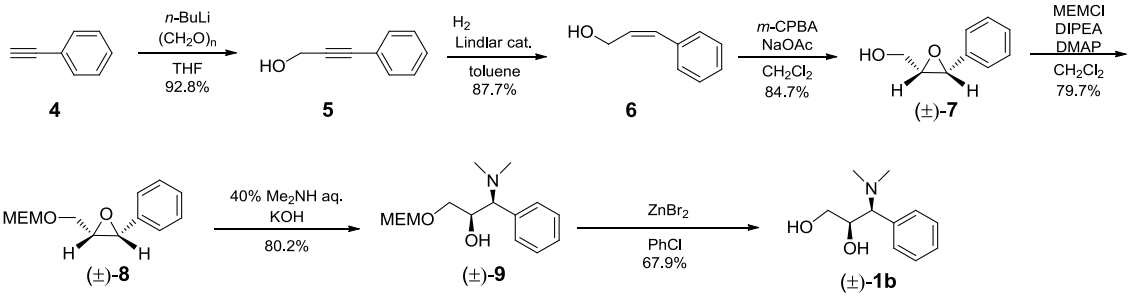
The structure of compound **B** was confirmed to be taxinine A by the comparison of the physical and spectral data with those reported in the literature.[6] The structure of compound **C** was deduced to be spectral data with those reported in the literature.[6] The structure of compound **C** was deduced to be 11,12-dihydrotaxinine A by the analyses of the ^{1}H and ^{13}C NMR spectra of **C**. The stereochemistry of H-11 and H-12 was determined to be β- and α-configurations, respectively by NOESY correlations as shown on the structure **C** (Scheme 1). Detailed spectral data of compounds of **B** and **C** were shown in experimental section.

The structure of (–)-**1** was deduced to be 3-dimethylamino-3-phenylpropane-1,2-diol (**1**) by the analyses of spectral data as shown in experimental section. In ^{1}H NMR spectra, the coupling constant between H-2 and H-3 ($J_{2,3}$ =10.5 Hz) of (–)-**1** was in good accordance with that of H-2' and H-3' ($J_{2',3'}$ = 9.5 Hz) of taxine NA-1 (**A**). Thus, the stereochemical relationship at C-2' and C-3' of **A** was kept in that of C-2 and C-3 in (–)-**1**. In order to determine the stereochemistry at C-2' and C-3' positions of **A**, we decided to synthesize (–)-**1** by the stereo- and enantio-selective manner. First of all, we attempted the synthesis of *anti*-stereoisomer, (±)-**1a** (Scheme 2). Epoxidation of cinnamyl alcohol **2** with *t*-BuO_2H (TBHP) in the presence of VO(acac)$_2$ in benzene[7] gave *trans*-epoxide (±)-**3** in 91.8% yield. Treatment of (±)-**3** with aqueous 40% Me_2NH in the presence of KOH afforded *anti*-isomer, (±)-**1a** in a quantitative yield. ^{1}H and ^{13}C NMR spectral data of (±)-**1a** was different from (–)-**1**. The coupling constant between H-2 and H-3 in ^{1}H NMR spectra of (±)-**1a** was $J_{2,3}$ = 8.1 Hz, which was different from $J_{2,3}$ = 10.5 Hz of (–)-**1**.



Scheme 2

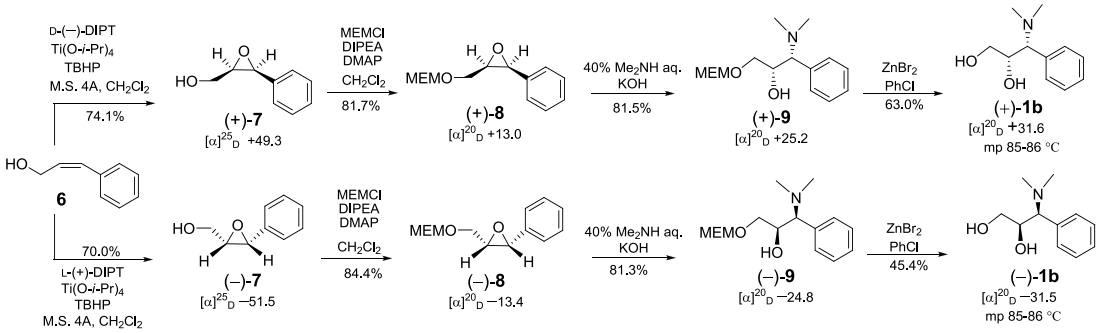
Subsequently, we attempted the synthesis of *syn*-stereoisomer, (±)-**1b** (Scheme 3). Phenylacetylene **4** was treated with paraformaldehyde in the presence of *n*-BuLi in THF to give 3-phenyl-2-propyn-1-ol (**5**) in 92.8% yield. The selective hydrogenation of triple bond of **5** in the presence of Lindlar catalyst afforded *cis*-cinnamyl alcohol (**6**) in 87.7% yield.[8] Epoxidation of **6** with *m*-chloroperoxybenzoic acid (*m*-CPBA) in the presence of sodium acetate in dichloromethane gave *cis*-epoxide (±)-**7** in 84.7% yield. Protection of the hydroxyl group of (±)-**7** by treatment with 2-methoxyethoxymethyl chloride (MEMCl) in the presence of *N*,*N*-diisopropylethylamine (DIPEA) and 4-dimethylaminopyridine (DMAP)[9] gave (±)-**8** in 79.7% yield. Treatment of (±)-**8** with aqueous 40% Me_2NH in the presence of KOH afforded 1-(MEM)oxy-3-dimethylamino-3-phenylpropan-2-ol, (±)-**9** in 80.2% yield. The *syn*-stereochemistry of hydroxyl group at C-2 and dimethylamino group at C-3 in (±)-**9** is apparent considering the reaction



Scheme 3

mechanism of (±)-**8** to (±)-**9** in reaction conditions. 2-Methoxyethoxymethyl (MEM) protecting group of (±)-**9** was removed by treatment with $ZnBr_2$ in boiling chlorobenzene to give *syn*-isomer, (±)-**1b** 67.9% yield. The ^1H and ^{13}C NMR, IR, and HRMS data of (±)-**1b** were identical with those of (−)-**1**, which was obtained from taxine NA-1 (2′-hydroxytaxine II) (**A**). The coupling constant of H-2 and H-3 in ^1H NMR spectrum of (±)-**1b** ($J_{2,3}$ = 10.5 Hz) was in good accordance with that of (−)-**1**. Thus, the stereochemistry at C-2 and C-3 of (−)-**1** is *syn*.

Then, we decided to synthesize the (−)-**1b** and (+)-**1b** by Sharpless asymmetric epoxidation reaction of **6** in order to determine the absolute configuration of (−)-**1** (Scheme 4).



Scheme 4

cis-Cinnamyl alcohol (**6**) was subjected to Sharpless asymmetric epoxidation.[10] Epoxidation of **6** with *ter*-Butyl hydroperoxide (TBHP) in the presence of (−)-diisopropyl D-tartrate [D-(−)-DIPT], titanium isopropoxide [Ti(O-*i*-Pr)$_4$], and molecular sieves (MS) 4A gave optical active epoxyalcohol, (+)-**7** in 74.1% yield. Similarly, enantiomeric epoxyalcohol (−)-**7** was produced from **6** with the participation of L-(+)-DIPT in 70.0% yield. Protection of the primary hydroxyl groups of (+)-**7** and (−)-**7** by MEMCl in the presence of DIPEA and DMAP gave MEM protected epoxides, (+)-**8** and (−)-**8**, respectively. Ring-opening reaction of (+)-**8** and (−)-**8** with aqueous solution of 40% Me_2NH in the presence of KOH gave MEM protected optically active dimethylaminoalcohols, (+)-**9** and (−)-**9**, respectively. Deprotection of MEM protecting group of (+)-**9** and (−)-**9** with $ZnBr_2$ in boiling chlorobenzene gave (+)-**1b** ($[\alpha]^{20}_D$ +31.6) and (−)-**1b** ($[\alpha]^{20}_D$ −31.5), respectively. Judging from the reaction modes of Sharpless

asymmetric epoxidation of **6** and the following ring-opening reaction of resulting optically active epoxides, (+)-**8** and (−)-**8**, the absolute configuration of (+)-**1b** is (2*S*, 3*R*) and that of (−)-**1b** is (2*R*, 3*S*). The ^{1}H NMR, ^{13}C NMR, IR, and HRMS spectra and melting points of (+)-**1b** and (−)-**1b** are superimposable with those of (−)-**1** that was obtained from taxine NA-1 (2′-hydroxytaxine II) (**A**) by reductive cleavage. The sign of the specific rotation of (−)-**1** was identical with that of (−)-**1b** but was opposite with that of (+)-**1b**. Thus, the absolute configuration of (−)-**1** is (2*R*, 3*S*). Therefore, the absolute configuration of C-2′ and C-3′ positions of taxin NA-1 (2′-hydroxytaxine II) (**A**) was determined to be (2′*R*, 3′*S*). The synthetic methodology employed in this report may be applicable to the preparation of C-13 chain modified taxol analogs and the study of their structure-activity relationship.

EXPERIMENTAL

General Experimental Procedures. Melting points were determined by Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured using a Horiba Polarimeter SEPA-200. IR spectra were recorded on a Hitachi 270-30 spectrometer. ^{1}H NMR (200 or 500 MHz) and ^{13}C NMR (50 or 125 MHz) spectra were run on Varian Gemini 200 or Varian UNITY-PS 500 spectrometer in $CDCl_3$. ^{1}H NMR assignments were determined by ^{1}H-^{1}H COSY experiments. ^{13}C NMR assignments were determined using DEPT, HMQC, and HMBC experiments. HREIMS was recorded on a JEOL JMS HX-110 spectrometer. Silica gel (200–400) was employed for flash column chromatography. To describe flash column chromatography conditions, we designated column inside diameter (i.d.), silica gel weight, and solvent in this order. HPLC separations were performed on a Hitachi L-6200 HPLC instrument monitored by Hitachi L-7400 UV detector and a Shodex SE-61 RI detector. To describe HPLC conditions, we designated column, solvent, flow rate (mL/min), detector, and retention time (t_R) in this order. Reactions were run under an atmosphere of N_2 or Ar. THF was distilled from sodium benzophenone ketyl. Benzene was dried over $CaCl_2$, distilled, and stored in a bottle with Na wire equipped with a mercury seal. CH_2Cl_2 was washed with water, dried over $CaCl_2$, and ditilled from CaH_2. Toluene and chlorobenzene were refluxed over CaH_2 for 3 h, distilled, and kept in sealed bottles in the presence of molecular sieves (MS) 4A. 4.71 M CH_2Cl_2 solution of *ter*-butyl hydroperoxide (TBHP) was prepared from commercially available 70% aqueous solution of TBHP as following. 70% Aqueous solution of TBHP (300 mL) was extracted with CH_2Cl_2 (3×100 mL). The CH_2Cl_2 solution of TBHP was refluxed for 10 h in a flask equipped with a Dean-Stark column packed with MS 3A.

Reductive Cleavage of Taxine NA-1 (2′-Hydroxytaxine II) (A). A mixture of taxine NA-1 (2′-hydroxytaxine II) (**A**, 41.4 mg, 0.062 mmol), *n*-Bu_4NBH_4 (26.0 mg, 0.101 mmol) and CH_2Cl_2 (0.7 mL) was stirred at room temperature for 7 h. The reaction was quenched by addition of EtOAc (350 μL)

and the solution was concentrated under reduced pressure to give a pale yellow oily residue (147.4 mg), which was separated by reversed-phase HPLC [Inertsil prep-ODS 250 × 10 mm i.d. stainless column (column A), MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:1:2), 5.0 mL/min, UV (254 nm)]. The first fraction (t_R 2.3 min, 7.5 mg) was further purified by reversed-phase HPLC [colum A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:16:2), 5.0 mL/min, UV (254 nm)] to give spectroscopically pure **(–)-1** (t_R 4.4 min, 3.9 mg, 32.3%) as colorless needles: mp 85–86 °C; $[\alpha]^{20}_D$ –36.0 ($CHCl_3$, *c* 0.30); ^{1}H NMR (500 MHz) δ 7.30–7.40 (3H, m, C_6H_5), 7.10–7.20 (2H, m, C_6H_5), 4.09 (1H, ddd, *J* = 10.5, 3.9, 2.9 Hz, H-2), 3.66 (1H, dd, *J* = 11.7, 2.9 Hz, H-1), 3.59 (1H, d, *J* = 10.5 Hz, H-3), 3.24 (1H, dd, *J* = 11.7, 3.9 Hz, H-1), 2.18 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 132.4 (s, C_6H_5), 129.8 (d, C_6H_5), 128.2 (d, C_6H_5), 128.0 (d, C_6H_5), 69.1 (d, C-3), 68.6 (d, C-2), 63.0 (t, C-1), 40.7 (q, NMe_2); IR ($CHCl_3$) ν_{max} 3396, 1498, 1458 cm^{-1}; HREIMS *m/z* 195.1280 ([M]$^+$, calcd for $C_{11}H_{17}NO_2$ 195.1259). The second fraction [t_R 4.6 min, yellow oil, 8.2 mg (27.7%)] was deduced to be 1:3 mixture of taxinine A (**B**) and 11,12-dihydrotaxinine A (**C**) by the analyses of ^{1}H NMR spectra. The 1:3 mixture of **B** and **C** was separated with normal-phase HPLC [Inertsil prep-sil 250 × 10 mm i.d. stainless column (column B), EtOAc–hexane (3:7), 5.0 mL/min, UV (254 nm) detector]. The first peak (t_R 26 min) gave spectroscopically pure **C** (5.8 mg) as colorless prisms: mp 196–198 °C; $[\alpha]^{20}_D$ –9.1 ($CHCl_3$, *c* 0.15); ^{1}H NMR (500 MHz) δ 5.87 (1H, d, *J* = 10.5 Hz, H-9), 5.74 (1H, br d, *J* = 2.4 Hz, H-2), 5.45 (1H, t, *J* = 1.6 Hz, H-20), 5.25 (1H, dd, *J*= 10.5, 1.2 Hz, H-10), 5.20 (1H, br s, H-20), 4.21 (1H, br t, *J* = 2.7 Hz, H-5), 3.06 (1H, br s, H-3), 2.93 (1H, qd, *J* = 6.84, 4.20 Hz, H-12), 2.55 (1H, dd, *J* = 20.3, 8.1 Hz, H-14), 2.45 (1H, d, *J* = 20.3 Hz, H-14), 2.08 (3H, s, OAc), 2.03 (3H, s, OAc), 2.02 (3H, s, OAc), 1.96 (1H, dd, *J* = 13.5, 4.5 Hz, H-7), 1.86 (1H, br d, *J* = 8.1 Hz, H-1), 1.80 (1H, d, *J* = 4.2 Hz, H-11), 1.80 (1H, m, H-6), 1.66 (1H, m, H-6), 1.57 (1H, m, H-7), 1.53 (3H, s, H-16), 1.35 (3H, d, *J* = 6.8 Hz, H-18), 0.95 (3H, s, H-17), 0.90 (3H, s, H-19); ^{13}C NMR (125 MHz) δ 214.7 (s, C-13), 169.7 (s, OAc), 169.4 (s, OAc), 169.3 (s, OAc), 146.4 (s, C-4), 115.5 (t, C-20), 76.8 (d, C-10), 76.6 (d, C-5), 72.4 (d, C-9), 71.2 (d, C-2), 56.7 (d, C-11), 50.9 (d, C-1), 45.7 (d, C-12), 42.8 (s, C-8), 40.4 (d, C-3), 37.3 (t, C-14), 35.6 (s, C-15), 33.0 (q, C-17), 29.6 (t, C-6), 25.9 (q, C-16), 25.7 (t, C-7), 21.4 (q, OAc), 21.2 (q, OAc), 21.1 (q, OAc), 20.8 (q, C-18), 17.7 (q, C-19); IR ($CHCl_3$) ν_{max} 3480, 1742, 1698 cm^{-1}; HREIMS *m/z* 478.2573 ([M]$^+$, calcd for $C_{26}H_{38}O_8$ 478.2567). The second peak (t_R 44 min) gave spectroscopically pure **B** (1.9 mg) as colorless prisms, mp 255–257 °C; $[\alpha]^{20}_D$ +82.5 ($CHCl_3$, *c* 0.87); ^{1}H NMR (500 MHz) δ 6.09 (1H, d, *J* = 10.2 Hz, H-10), 5.86 (1H, d, *J* = 10.2 Hz, H-9), 5.54 (1H, dd, *J* = 6.2, 2.0 Hz, H-2), 5.15 (1H, br s, H-20), 4.78 (1H, br d, *J* = 1.5 Hz, H-20), 4.19 (1H, br t, *J* = 2.0 Hz, H-5), 3.59 (1H, br d, *J* = 6.2 Hz, H-3), 2.77 (1H, dd, *J* = 20.0, 6.9 Hz, H-14), 2.36 (1H, d, *J* = 20.0 Hz, H-14), 2.23 (3H, s, H-18), 2.18 (1H, dd, *J* = 6.9, 2.0 Hz, H-1), 2.073 (3H, s, OAc), 2.067 (3H, s, OAc), 2.05 (3H, s, OAc), 1.85 (1H, m, H-7), 1.79 (1H, m, H-6),

1.76 (3H, s, H-17), 1.68 (1H, m, H-7), 1.60 (1H, m, H-6), 1.13 (3H, s, H-16), 0.88 (3H, s, H-19); ^{13}C NMR (125 MHz) δ 199.7 (s, C-13), 170. 0 (s, OAc), 169.7 (s,OAc), 169.4 (s, OAc), 149.6 (s, C-11), 147.0 (s, C-4), 138.6 (s, C-12), 114.1 (t, C-20), 76.1 (d, C-9), 76.0 (d, C-5), 73.3 (d, C-10), 70.1 (d, C-2), 48.5 (d, C-1), 44.7 (s, C-8), 40.9 (d, C-3), 37.7 (s, C-15), 37.3 (q, C-16), 36.1 (t, C-14), 30.5 (t, C-6), 26.6 (t, C-7), 25.2 (q, C-17), 21.4 (q, OAc), 20.9 (q, OAc), 20.7 (q, OAc), 17.3 (q, C-19), 14.0 (q, C-18); IR ($CHCl_3$) ν_{max} 3616, 1744, 1676 cm^{-1}.

***trans*-2,3-Epoxy-3-phenylpropan-1-ol (±)-(3).** Into a solution of cinnamyl alcohol (499.3 mg, 3.721 mmol) in benzene (37.2 mL) was added $VO(acac)_2$ (99.8 mg, 0.372 mmol). After $VO(acac)_2$ was dissolved completely, 4.71 M CH_2Cl_2 solution of TBHP (869.0 μL, 4.093 mmol) was added. The mixture was stirred at rt for 140 min. The reaction was terminated by addition of 0.1 M KI (81 mL) and a saturated aqueous solution of $NaHCO_3$ (81 mL). The mixture was extracted with EtOAc (4 × 30 mL). The combined extracts were washed with 0.1 M $Na_2S_2O_3$ (4 × 30 mL), a saturated aqueous solution of $NaHCO_3$ (3 × 30 mL), and a saturated aqueous solution of NaCl (3 × 30 mL), dried (Na_2SO_4), and concentrated to give yellow oil (565.7 mg), which was purified by flash column chromatography [3.0 cm i.d., 27 g, EtOAc–Hexane (3:7)] to give (±)-**3** (513.2 mg, 91.8%) as a yellow oil: ^{1}H NMR (200 MHz) δ 7.20–7.40 (5H, m, C_6H_5), 4.03 (1H, ddd, J = 12.8, 6.3, 2.2 Hz, H-1), 3.92 (1H, d, J = 2.2 Hz, H-3), 3.77 (1H, ddd, J = 12.8, 6.3, 4.1 Hz, H-1), 3.22 (1H, ddd, J = 6.3, 4.1, 2.2 Hz, H-2), 2.50–2.80 (1H, br s, OH); ^{13}C NMR (50 MHz) δ 136.6 (s, C_6H_5), 128.4 (d, C_6H_5), 128.2 (d, C_6H_5), 125.66 (d, C_6H_5), 62.5 (d, C-2), 61.2 (t, C-1), 55.6 (d, C-3); IR (neat) ν_{max} 3428, 1502, 1466 cm^{-1}; HREIMS *m/z* 150.0677 ([M]$^+$, calcd for $C_9H_{10}O_2$ 150.0681).

***anti*-3-Dimethylamino-3-phenylpropane-1,2-diol (±)-(1a).** A solution of (±)-**3** (10.0 mg, 0.067 mmol) in Me_2NH/KOH solution [40% Me_2NH (479 μL), KOH (6.72 mg)] was stirred at rt for 1.5 h. The reaction was quenched by adding a saturated aqueous solution of NaCl (2 mL). The solution was saturated with NaCl by further addition of solid NaCl, and extracted continuously for 12 h with $CHCl_3$. The extract was dried (Na_2SO_4) and concentrated to give yellow crystalline residue (15.3 mg), which was purified by reversed-phase HPLC [column A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:16:2), 5.0 mL/min, UV (254 nm) , t_R 4.7 min] to give (±)-**1a** (13.0 mg, 100%) as colorless needles: mp 99–101 °C; ^{1}H NMR (500 MHz) δ 7.20–7.40 (5H, m, C_6H_5), 4.31 (1H, ddd, J = 8.1, 6.4, 5.6 Hz, H-2), 3.68 (1H, dd, J = 10.5, 5.6 Hz, H-1), 3.66 (1H, dd, J = 10.5, 6.4 Hz, H-1), 3.49 (1H, d, J = 8.1 Hz, H-3), 2.21 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 133.6 (s, C_6H_5), 130.9 (d, C_6H_5), 128.4 (d, C_6H_5), 128.2 (d, C_6H_5), 74.3 (d, C-3), 68.3 (d, C-2), 67.0 (t, C-1), 42.4 (q, NMe_2); IR ($CHCl_3$) ν_{max} 3384, 1498, 1458 cm^{-1}; HREIMS *m/z* 195.1250 ([M]$^+$, calcd for $C_{11}H_{17}O_2N$ 195.1259).

3-Phenyl-2-propyn-1-ol (5). Into a solution of phenylacetylene (4.0 mL, 36.421 mmol) in THF (18.0

mL) was added 1.51 M hexane solution of BuLi (24.1 mL, 36.421 mmol) at −78 °C. The mixture was stirred at −78 °C for 2 h and then warmed to 0 °C. Paraformaldehyde (2.19 g, 72.84 mmol) was added into the mixture, which was stirred at 0 °C for 5 min and at rt for 2.5 h, quenched by adding water, kept for 30 min at rt, and extracted with ether (4 × 30 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ (2 × 30 mL) and a saturated aqueous solution of NaCl (2 × 30 mL), dried (Na_2SO_4), and concentrated to give yellow oily residue (4.832 g), which was purified by flash column chromatography [5.5 cm i.d., 150 g, EtOAc–Hexane (2:8)] to give **5** (4.466 g, 92.8%) as a pale yellow oil: ^{1}H NMR (200 MHz) δ 7.20–7.50 (5H, m, C_6H_5), 4.49 (2H, d, J = 5.2 Hz, H-1), 2.21 (1H, br s, OH); ^{13}C NMR (50 MHz) δ 131.6 (d, C_6H_5), 128.4 (d, C_6H_5), 128.2 (d, C_6H_5), 122.4 (s, C_6H_5), 87.2 (s, C-2 or C-3), 85.6 (s, C-2 or C-3), 51.5 (t, C-1); IR (neat) ν_{max} 3368, 2196, 1496, 1446 cm^{-1}; HREIMS *m/z* 132.0590 ([M]$^+$, calcd for C_9H_8O 132.0575).

***cis*-Cinnamyl Alcohol (6).** Into Lindlar catalyst which was prepared from 5% Pd/$BaSO_4$ (100.7 mg) and quinoline (500 μL) by stirring overnight, **5** (1.001 g, 7.57 mmol) and toluene (75.7 mL) was added. The mixture was stirred under an atmosphere of H_2 for 40 min and filtered through Celite. The filtrate was washed with 2 M HCl (3 × 30 mL), a saturated aqueous solution of NaCl (2 × 30 mL), dried (Na_2SO_4) and concentrated to give an oily crude product (1.040 g), which was subsequently purified by flash column chromatography [4.0 cm i.d., 50 g, EtOAc–hexane (3:7)] to give pale yellow oil (948.1 mg). This was further separated by normal-phase HPLC [Inertsil prep-sil 250 × 10 mm i.d. stainless column (column B), EtOAc–hexane (2:8), 5.0 mL/min, UV (254 nm)]. The peak (t_R 11.3 min) gave spectroscopically pure **6** (890.6 mg, 87.7%) as a pale yellow oil: ^{1}H NMR (200 MHz) δ 7.10–7.40 (5H, m, C_6H_5), 6.58 (1H, br d, J = 11.7 Hz, H-3), 5.88 (1H, dt, J = 11.7, 6.4 Hz, H-2), 4.44 (2H, dd, J = 6.4, 1.6 Hz, H-1), 1.56 (1H, br s, OH); ^{13}C NMR (50 MHz) δ 136.5 (s, C_6H_5), 131.08 (d, C-2), 131.05 (d, C-3), 128.8 (d, C_6H_5), 128.2 (d, C_6H_5), 127.2 (d, C_6H_5), 59.7 (t, C-1); IR (neat) ν_{max} 3344, 1498, 1452 cm^{-1}; HREIMS *m/z* 134.0741 ([M]$^+$, calcd for $C_9H_{10}O$ 134.0732).

***cis*-2,3-Epoxy-3-phenylpropan-1-ol (±)-(7).** Into a solution of **6** (158.3 mg, 1.180 mmol) in CH_2Cl_2 (11.8 mL) was added *m*-CPBA (307.9 mg, 1.420 mmol) at 0 °C. The mixture was stirred for 4 h, quenched by adding a mixture of 0.1 M KI (28.4 mL) and a saturated aqueous solution of $NaHCO_3$ (28.4 mL), and extracted with EtOAc (4 × 40 mL). The combined extracts were washed with 0.1 M $Na_2S_2O_3$ (4 × 40 mL), a saturated aqueous solution of $NaHCO_3$ (3 × 40 mL), and a saturated aqueous solution of NaCl (3 × 40 mL), dried (Na_2SO_4), and concentrated to give an oily crude product (176.5 mg), which was purified by flash column chromatography [2.0 cm i.d., 9.0 g, EtOAc–Hexane (3:7)] to give (±)-**7** (150.2 mg, 84.7%) as a pale yellow oil: ^{1}H NMR (500 MHz) δ 7.20–7.40 (5H, m, C_6H_5), 4.19 (1H, d, J = 4.0 Hz,

H-3), 3.50–3.60 (1H, m, H-1), 3.40–3.50 (2H, m, H-1, H-2), 1.70 (1H, br s, OH); ^{13}C NMR (125 MHz) δ 134.6 (s, C_6H_5), 128.3 (d, C_6H_5), 127.9 (d, C_6H_5), 126.2 (d, C_6H_5), 60.5 (t, C-1), 58.5 (d, C-2), 57.0 (d, C-3); IR (neat) ν_{max} 3412, 1502, 1458 cm^{-1}; HREIMS *m/z* 150.0673 ([M]$^+$, calcd for $C_9H_{10}O_2$ 150.0681).

1-(MEM)oxy-3-phenylpropane-*cis*-2,3-epoxide (±)-(8). Into a solution of (±)-**7** (110.8 mg, 0.738 mmol) in CH_2Cl_2 (7.4 mL) was added *N,N*-diisopropylethylamine (1005 μL, 5.909 mmol), 4-dimethylaminopyridine (DMAP, 9.1 mg, 0.0745 mmol), and MEMCl (336.1 μL, 2.944 mmol). The mixture was stirred for 24.5 h at rt and quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (15 mL). The mixture was extracted by EtOAc (3 × 15 mL). The combined extracts were treated in the usual manner to give a crude oily product (217.7 mg), which was purified by flash column chromatography [2.0 cm i.d., 13.6 g, EtOAc–Hexane (2:8)] to give (±)-**8** (140.2 mg, 79.7%) as a pale yellow oil: ^{1}H NMR (500 MHz) δ 7.30–7.40 (5H, m, C_6H_5), 4.65 (1H, d, J = 6.8 Hz, H-1′), 4.61 (1H, d, J = 6.8 Hz, H-1′), 4.15 (1H, d, J =3.9 Hz, H-3), 3.40–3.60 (7H, m, H-1, H-2, H-2′, H-3′), 3.35 (3H, s, H-4′); ^{13}C NMR (125 MHz) δ 134.6 (s, C_6H_5), 128.1 (d, C_6H_5), 127.7 (d, C_6H_5), 126.2 (d, C_6H_5), 95.5 (t, C-1′), 71.6 (t, C-3′), 66.6 (t, C-1), 65.2 (t, C-2′), 58.9 (q, C-4′), 56.9 (d, C-2), 56.3 (d, C-3); IR (neat) ν_{max} 1502, 1458 cm^{-1}; HREIMS *m/z* 238.1200 ([M]$^+$, calcd for $C_{13}H_{18}O_4$ 238.1205). Numbering of (MEM)oxy group for assignment of ^{1}H and ^{13}C NMR spectra: [$C^{4'}H_3OC^{3'}H_2C^{2'}H_2OC^{1'}H_2O$-].

***syn*-1-(MEM)oxy-3-dimethylamino-3-phenylpropan-2-ol (±)-(9).** A solution of (±)-**8** (6.5 mg, 0.0273 mmol) in Me_2NH/KOH solution [40% Me_2NH (212 μL), KOH (2.97 mg)] was stirred at rt for 20 h. The reaction was quenched by the addition of a saturated aqueous solution of NaCl (1 mL). The aqueous layer was extracted continuously for 6 h with $CHCl_3$. The organic layer was dried (Na_2SO_4) and concentrated to give an oily residue (7.3 mg), which was purified by reversed-phase HPLC [column A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:5:2), 5.0 mL/min, UV (254 nm), t_R 3.5 min] to give (±)-**9** (6.2 mg, 80.2%) as a pale yellow oil: ^{1}H NMR (500 MHz) δ 7.30–7.40 (3H, m, C_6H_5), 7.10–7.20 (2H, m, C_6H_5), 4.66 (1H, d, J = 6.6 Hz, H-1′), 4.62 (1H, d, J = 6.6 Hz, H-1′), 4.19 (1H, ddd, J = 10.7, 4.9, 2.2 Hz, H-2), 3.58 (1H, d, J = 10.7 Hz, H-3), 3.30–3.60 (6H, m, H-1, H-2′, H-3′), 3.30 (3H, s, H-4′), 2.18 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 132.6 (s, C_6H_5), 129.6 (d, C_6H_5), 128.1 (d, C_6H_5), 127.9 (d, C_6H_5), 95.6 (t, C-1′), 71.6 (t, C-2′ or C-3′), 69.5 (d, C-3), 68.7 (t, C-1), 67.9 (d, C-2), 66.4 (t, C-2′ or C-3′), 58.8 (q, C-4′), 40.6 (q, NMe_2); IR (neat) ν_{max} 3420, 1498, 1458 cm^{-1}; HREIMS *m/z* 283.1775 ([M]$^+$, calcd for $C_{15}H_{25}NO_4$ 283.1784).

***syn*-3-Dimethylamino-3-phenylpropane-1,2-diol (±)-(1b).** Into a solution of (±)-**9** (11.1 mg, 0.0392 mmol) in chlorobenzene (400 μL) was added $ZnBr_2$ (48.3 mg, 0.214 mmol). The mixture was stirred at 130 °C for 40 h and quenched by addition of a saturated aqueous solution of $NaHCO_3$ (5 mL). The

obtained solution was saturated with NaCl by adding solid NaCl and then extracted continuously for 4 h with $CHCl_3$. The organic layer was dried (Na_2SO_4) and concentrated to give a yellow oil, which was purified by reversed-phase HPLC [column A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)– MeCN (1:16:2), 5.0 mL/min, UV (254 nm) detector, t_R 4.3 min] to give (±)-**1b** (5.2 mg, 67.9%) as colorless microcrystals, mp 84–85 °C; ^{1}H NMR (500 MHz) δ 7.30–7.40 (3H, m, C_6H_5), 7.10–7.20 (2H, m, C_6H_5), 4.09 (1H, ddd, J = 10.5, 3.9, 2.9 Hz, H-2), 3.67 (1H, dd, J = 11.7, 2.9 Hz, H-1), 3.64 (1H, d, J = 10.5 Hz, H-3), 3.24 (1H, dd, J = 11.7, 3.9 Hz, H-1), 2.21 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 132.3 (s, C_6H_5), 129.8 (d, C_6H_5), 128.24 (d, C_6H_5), 128.16 (d, C_6H_5), 69.2 (d, C-3), 68.7 (d, C-2), 62.0 (t, C-1), 40.7 (q, NMe_2); IR ($CHCl_3$) ν_{max} 3392, 1498, 1458 cm^{-1}; HREIMS *m/z* 195.1252 ([M]$^+$, calcd for $C_{11}H_{17}NO_2$ 195.1259).

(2*R*,3*S*)-2,3-Epoxy-3-phenylpropan-1-ol (+)-(7). Into a mixture of MS 4A (290.2 mg) and CH_2Cl_2 (10.0 mL) were added Ti(O-*i*-Pr)$_4$ (320.9 μL, 1.087 mmol) and (–)-diisopropyl D-tartrate (D-(–)-DIPT, 277.0 μL, 1.304 mmol) at –23 °C. The mixture was stirred for 40 min and **6** (145.9 mg, 1.087 mmol) in CH_2Cl_2 (2.0 mL) and 4.71 M CH_2Cl_2 solution of TBHP (461.6 μL, 2.174 mmol) were added. The reaction mixture was stirred at –23 °C for 2 h and kept in freezer at –23 °C for 47.5 h. The reaction mixture was quenched by stirring in water for 1 h, extracted with $CHCl_3$ (3 × 10 mL), and worked up as usual to give a yellow oil (449.3 mg), which was passed through flash column chromatography [3.5 cm i.d., 28.6 g, EtOAc–Hexane (2:8)] to give a pale yellow oil (148.3 mg). This was further purified by normal-phase HPLC [column B, EtOAc–Hexane (2:8), 5.0 mL/min, RI, t_R 19.9 min] to give (+)-**7** (121.1 mg, 74.1%) as a colorless oil: $[\alpha]^{25}_D$ +49.3 ($CHCl_3$, *c* 1.63); ^{1}H NMR (500 MHz) δ 7.20–7.40 (5H, m, C_6H_5), 4.19 (1H, d, J = 3.9 Hz, H-3), 3.50–3.60 (1H, m, H-1), 3.40–3.50 (2H, m, H-1, H-2), 1.85 (1H, br s, OH); ^{13}C NMR (125 MHz) δ 134.6 (s, C_6H_5), 128.3 (d, C_6H_5), 127.9 (d, C_6H_5), 126.1 (d, C_6H_5), 60.5 (t, C-1), 58.6 (d, C-2), 57.0 (d, C-3); IR (neat) ν_{max} 3416, 1502, 1458 cm^{-1}; HREIMS *m/z* 150.0685 ([M]$^+$, calcd for $C_9H_{10}O_2$ 150.0681).

(2*R*,3*S*)-1-(MEM)oxy-3-phenylpropan-2,3-epoxide (+)-(8). Into a solution of (+)-**7** (96.3 mg, 0.641 mmol) in CH_2Cl_2 (6.4 mL) were added *N,N*-diisopropylethylamine (872.1 μL, 5.128 mmol), DMAP (8.2 mg, 0.0671 mmol), and MEMCl (292.8 μL, 2.564 mmol). The mixture was stirred at rt for 4.7 h, quenched by adding a saturated aqueous solution of $NaHCO_3$ (5 mL), and extracted with EtOAc (3 × 5 mL). The combined extracts were worked up as usual to give an oily crude product (221.8 mg), which was purified by flash column chromatography [2.2 cm i.d., 9.5 g, EtOAC–Hexane (2:8)] to give (+)-**8** (124.8 mg, 81.7%) as a pale yellow oil: $[\alpha]^{20}_D$ +13.0 ($CHCl_3$, *c* 1.69); ^{1}H NMR (500 MHz) δ 7.30–7.40 (5H, m, C_6H_5), 4.65 (1H, d, J = 6.8 Hz, H-1′), 4.61 (1H, d, J = 6.8 Hz, H-1′), 4.16 (1H, d, J = 3.9 Hz,

H-3), 3.40–3.60 (7H, m, H-1, H-2, H-2′, H-3′), 3.35 (3H, s, H-4′); ^{13}C NMR (125 MHz) δ 134.7 (s, C_6H_5), 128.2 (d, C_6H_5), 127.8 (d, C_6H_5), 126.2 (d, C_6H_5), 95.5 (t, C-1′), 71.6 (t, C-3′), 66.6 (t, C-1), 65.2 (t, C-2′), 58.9 (q, C-4′), 57.0 (d, C-2), 56.3 (d, C-3); IR (neat) ν_{max} 1502, 1458 cm^{-1}; HREIMS *m/z* 238.1203 ([M]$^+$, calcd for $C_{13}H_{18}O_4$ 238.1205).

(2*S*,3*R*)-1-(MEM)oxy-3-dimethylamino-3-phenylpropan-2-ol (+)-(9). A solution of (+)-**8** (101.8 mg, 0.427 mmol) in Me_2NH/KOH solution [40% Me_2NH (3.1 mL), KOH (43.5 mg, 0.78 mmol)] was stirred at rt for 35 h. The reaction was quenched by adding a saturated aqueous solution of NaCl (10 mL) and solid NaCl was further added to saturate the aqueous solution. The aqueous solution was extracted continuously for 5 h with $CHCl_3$. The organic layer was dried (Na_2SO_4) and concentrated to give an oily crude product (138.5 mg), which was purified by reversed-phase HPLC [column A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:16:2), 5.0 mL/min, UV (254 nm), t_R 8.6 min] to give (+)-**9** (98.7 mg, 81.5%) as a pale yellow oil: $[\alpha]^{20}_D$ +25.2 ($CHCl_3$, *c* 2.12); ^{1}H NMR (500 MHz) δ 7.30–7.40 (3H, m, C_6H_5), 7.10–7.20 (2H, m, C_6H_5), 4.65 (1H, d, *J* = 6.6 Hz, H-1′), 4.61 (1H, d, *J* = 6.6 Hz, H-1′), 4.18 (1H, ddd, *J* = 10.5, 4.9, 2.2 Hz, H-2), 3.56 (1H, d, *J* = 10.5 Hz, H-3), 3.30–3.60 (6H, m, H-1, H-2′, H-3′), 3.29 (3H, s, H-4′), 2.16 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 132.6 (s, C_6H_5), 129.6 (d, C_6H_5), 128.1 (d, C_6H_5), 127.9 (d, C_6H_5), 95.6 (t, C-1′), 71.5 (t, C-2′ or C-3′), 69.6 (d, C-3), 68.6 (t, C-1), 67.8 (d, C-2), 66.4 (t, C-2′ or C-3′), 58.8 (q, C-4′), 40.6 (q, NMe_2); IR (neat) ν_{max} 3420, 1498, 1458 cm^{-1}; HREIMS *m/z* 283.1789 ([M]$^+$, calcd for $C_{15}H_{25}NO_4$ 283.1784).

(2*S*,3*R*)-3-Dimethylamino-3-phenylpropane-1,2-diol (+)-(1b). Into a solution of (+)-**9** (69.6 mg, 0.246 mmol) in chlorobenzene (2.5 mL) was added $ZnBr_2$ (285.0 mg, 1.266 mmol). The mixture was stirred at 130 °C for 24 h and quenched by adding saturate aqueous solution of $NaHCO_3$ (5 mL). The solution was saturated by adding solid NaCl and extracted continuously for 5 h with $CHCl_3$. The organic layer was dried (Na_2SO_4) and concentrated to give a yellow oily residue (49.9 mg), which was purified by reversed-phase HPLC [column A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:16:2), 5.0 mL/min, UV (254 nm) , t_R 6.8 min] to give (+)-**1b** (30.2 mg, 63.0%) as colorless needles: mp 85–86 °C; $[\alpha]^{20}_D$ +31.6 ($CHCl_3$, *c* 2.23); ^{1}H NMR (500 MHz) δ 7.30–7.40 (3H, m, C_6H_5), 7.10–7.20 (2H, m, C_6H_5), 4.09 (1H, ddd, *J* = 10.5, 3.9, 2.9 Hz, H-2), 3.67 (1H, dd, *J* = 11.7, 2.9 Hz, H-1), 3.64 (1H, d, *J* = 10.5 Hz, H-3), 3.24 (1H, dd, *J* = 11.7, 3.9 Hz, H-1), 2.21 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 132.3 (s, C_6H_5), 129.8 (d, C_6H_5), 128.24 (d, C_6H_5), 128.16 (d, C_6H_5), 69.2 (d, C-3), 68.7 (d, C-2), 62.0 (t, C-1), 40.7 (q, NMe_2); IR ($CHCl_3$) ν_{max} 3384, 1498, 1458 cm^{-1}; HREIMS *m/z* 195.1252 ([M]$^+$, calcd for $C_{11}H_{17}NO_2$ 195.1259).

(2*S*,3*R*)-2,3-Epoxy-3-phenylpropan-1-ol (–)-(7). Into a stirring mixture of MS 4A (300 mg) and dry

CH_2Cl_2 (10.0 mL) were added Ti(O-*i*-Pr)$_4$ (330.0 μL, 1.118 mmol) and (+)-diisopropyl L-tartrate (L-(+)-DIPT, 285.0 μL, 1.342 mmol) at –23 °C. After stirring for 40 min at this temperature, **6** (150.0 mg, 1.118 mmol) in CH_2Cl_2 (2 mL) and 4.71 M CH_2Cl_2 solution of TBHP (475.0 μL, 2.236 mmol) were added to the mixture. The reaction mixture was stirred at –23 °C for 2 h and kept in freezer at –23 °C for 28 h. The reaction was quenched by water and stirred for 1h and extracted with $CHCl_3$ (3 × 10 mL). The extracts were worked up as usual to give yellow oily residue (546.3 mg), which was purified by flash column chromatography [3.5 cm i.d., 31.7 g, EtOAc–Hexane (2:8)] and normal-phase HPLC [column B, EtOAc–Hexane (2:8), 5.0 mL/min, RI detector, t_R 19.0 min] to give (–)-**7** (112.5 mg, 70.0%) as a yellow oil: $[\alpha]^{25}_D$ –51.5 ($CHCl_3$, *c* 1.45); ^{1}H NMR (500 MHz) δ 7.20–7.40 (5H, m, C_6H_5), 4.19 (1H, d, *J* = 3.7 Hz, H-3), 3.50–3.60 (1H, m, H-1), 3.40–3.50 (2H, m, H-1, H-2), 1.77 (1H, br s, OH); ^{13}C NMR (125 MHz) δ 134.6 (s, C_6H_5), 128.3 (d, C_6H_5), 127.9 (d, C_6H_5), 126.1 (d, C_6H_5), 60.5 (t, C-1), 58.6 (d, C-2), 57.0 (d, C-3); IR (neat) ν_{max} 3424, 1502, 1458 cm^{-1}; HREIMS *m/z* 150.0677 ([M]$^+$, calcd for $C_9H_{10}O_2$ 150.0681).

(2*S*,3*R*)-1-(MEM)oxy-3-phenylpropan-2,3-epoxide (–)-(8). DIPEA (843.5 μL, 4.960 mmol), DMAP (8.0 mg, 0.0655 mmol), and MEMCl (292.8 μL, 2.480 mmol) were added dropwise to a solution of (–)-**7** (93.1 mg, 0.620 mmol) in CH_2Cl_2 (6.2 mL). The mixture was stirred at rt for 5.8 h, quenched by adding a saturate aqueous solution of $NaHCO_3$ (5 mL), and extracted with EtOAc (3 × 5 mL). The combined extracts were worked up as usual to give yellow oily residue (177.7 mg), which was purified by flash column chromatography [2.2 cm i.d., 9.5 g, EtOAC–Hexane (2:8)] to give (–)-**8** (124.7 mg, 84.4%) as a pale yellow oil: $[\alpha]^{20}_D$ –13.4 ($CHCl_3$, *c* 1.92); ^{1}H NMR (500 MHz) δ 7.30–7.40 (5H, m, C_6H_5), 4.66 (1H, d, *J* = 6.8 Hz, H-1′), 4.61 (1H, d, *J* = 6.8 Hz, H-1′), 4.16 (1H, d, *J* = 3.9 Hz, H-3), 3.40–3.60 (7H, m, H-1, H-2, H-2′, H-3′), 3.35 (3H, s, H-4′); ^{13}C NMR (125 MHz) δ 134.6 (s, C_6H_5), 128.1 (d, C_6H_5), 127.8 (d, C_6H_5), 126.2 (d, C_6H_5), 95.5 (t, C-1′), 71.6 (t, C-3′), 66.6 (t, C-1), 65.2 (t, C-2′), 58.9 (q, C-4′), 56.9 (d, C-2), 56.3 (d, C-3); IR (neat) ν_{max} 1502, 1458 cm^{-1}; HREIMS *m/z* 238.1207 ([M]$^+$, calcd for $C_{13}H_{18}O_4$ 238.1205).

(2*R*,3*S*)-1-(MEM)oxy-3-dimethylamino-3-phenylpropan-2-ol (–)-(9). A solution of (–)-**8** (92.9 mg, 0.390 mmol) in Me_2NH/KOH solution [40% Me_2NH (2.8 mL), KOH (39.3 mg, 0.70 mmol)] was stirred at rt for 27 h. The reaction was quenched by adding a saturated NaCl solution (10 mL). The aqueous solution was saturated by further addition of solid NaCl and extracted continuously for 9 h with $CHCl_3$. The $CHCl_3$ layer was dried (Na_2SO_4) and concentrated to give yellow oily residue (115.3 mg), which was purified by reversed-phase HPLC [column A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:16:2), 5.0 mL/min; UV (254 nm), t_R 8.2 min] to give (–)-**9** (89.9 mg, 81.3%) as a pale yellow oil:

$[\alpha]^{20}_{D}$ –24.8 ($CHCl_3$, *c* 1.63); ^{1}H NMR (500 MHz) δ 7.30–7.40 (3H, m, C_6H_5), 7.10–7.20 (2H, m, C_6H_5), 4.66 (1H, d, *J* = 6.6 Hz, H-1′), 4.62 (1H, d, *J* = 6.6 Hz, H-1′), 4.19 (1H, ddd, *J* = 10.5, 5.1, 2.2 Hz, H-2), 3.58 (1H, d, *J* = 10.5 Hz, H-3), 3.30–3.60 (6H, m, H-1, H-2′, H-3′), 3.30 (3H, s, H-4′), 2.17 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 132.6 (s, C_6H_5), 129.6 (d, C_6H_5), 128.1 (d, C_6H_5), 127.9 (d, C_6H_5), 95.6 (t, C-1′), 71.5 (t, C-2′ or C-3′), 69.6 (d, C-3), 68.6 (t, C-1), 67.8 (d, C-2), 66.4 (t, C-2′ or C-3′), 58.8 (q, C-4′), 40.6 (q, NMe_2); IR (neat) ν_{max} 3428, 1498, 1458 cm^{-1}; HREIMS *m/z* 283.1783 ($[M]^+$, calcd for $C_{15}H_{25}NO_4$ 283.1784).

(2*R*,3*S*)-3-Dimethylamino-3-phenylpropane-1,2-diol (–)-(1b). Into a solution of (–)-**9** (66.1 mg, 0.233 mmol) in chlorobenzene (2.3 mL) was added $ZnBr_2$ (263.0 mg, 1.168 mmol). The mixture was stirred at 130 °C for 19 h. The reaction was quenched by adding a saturate aqueous solution of $NaHCO_3$ (5 mL) and worked up as usual to give a yellow oily residue (46.0 mg), which was purified by reversed-phase HPLC [column A, MeOH–0.05 M NH_4OAc buffer solution (pH 4.8)–MeCN (1:16:2), 5.0 mL/min, UV (254 nm), t_R 6.8 min] to give (–)-**1b** (20.7 mg, 45.4%) as colorless needles: mp 85–86 °C; $[\alpha]^{20}_{D}$ –31.5 ($CHCl_3$, *c* 1.59); ^{1}H NMR (500 MHz) δ 7.30–7.40 (3H, m, C_6H_5), 7.10–7.20 (2H, m, C_6H_5), 4.09 (1H, ddd, *J* = 10.5, 3.9, 2.9 Hz, H-2), 3.65 (1H, dd, *J* = 11.7, 2.9 Hz, H-1), 3.60 (1H, d, *J* = 10.5 Hz, H-3), 3.24 (1H, dd, *J* = 11.7, 3.9 Hz, H-1), 2.18 (6H, s, NMe_2); ^{13}C NMR (125 MHz) δ 132.4 (s, C_6H_5), 129.7 (d, C_6H_5), 128.1 (d, C_6H_5), 128.0 (d, C_6H_5), 69.1 (d, C-3), 68.6 (d, C-2), 63.0 (t, C-1), 40.7 (q, NMe_2); IR ($CHCl_3$) ν_{max} 3400, 1498, 1458 cm^{-1}; HREIMS *m/z* 195.1274 ($[M]^+$, calcd for $C_{11}H_{17}NO_2$ 195.1259).

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