Concise Syntheses of Coronarin A, Coronarin E, Austrochaparol and Pacovatinin A

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Total syntheses of (+)-coronarin A (1), (+)-coronarin E (2), (+)-austrochaparol (3) and (+)-pacovatinin A (4) were achieved from the synthetic (+)-albicanyl acetate (6). Dess–Martin oxidation of (+)-albicanol (5) derived from the chemoenzymatic product (6) gave an aldehyde (7), which was subjected to Julia one-pot olefination using β-furylmethyl-heteroaromatic sulfones (8 or 9) gave (+)-*trans* coronarin E (2) and (+)-*cis* coronarin E (12) with high *cis*-selectivity. The synthesis of (+)-coronarin A (1) from (+)-*trans* coronarin E (2) was achieved, while (+)-*cis* coronarin E (12) was converted to the natural products (+)-(5*S*,9*S*,10*S*)-15,16-epoxy-8(17),13(16),14-labdatriene (13) and (+)-austrochaparol (3). By the asymmetric synthesis of (+)-3, the absolute structure of (+)-3 was determined to be 5*S*, 7*R*, 9*R*, 10*S* configurations. Homologation of (+)-albicanol (5) followed by allylic oxidation gave (7α)-hydroxy nitrile (17), which was finally converted to the natural (+)-pacovatinin A (4) in 8 steps from (+)-albicanol (5).

Key words (+)-coronarin A; (+)-coronarin E; (+)-austrochaparol; (+)-pacovatinin A; total synthesis

There are many natural products possessing a labdane skeleton in nature. Among them, (+)-coronarin A (**1**),[1] (+)-coronarin E (**2**),[2] (+)-austrochaparol (**3**)[3] and (+)-pacovatinin A (**4**)[4] are typical compounds (Chart 1). For the synthesis of these compounds, (+)-albicanol (**5**) is the desirable compound as starting material. We reported that lipase-assisted resolution of racemic albicanol (±)-**5** gave (+)-albicanyl acetate (**6**, 56%, 67% ee) and (−)-albicanol (**5**, 38%, >99% ee) in the presence of acylating reagent.[5] Hydrolysis of 67% ee of (+)-**6** gave 67% ee of (+)-albicanol (**5**), which was again subjected to lipase-assisted resolution to obtain the optically pure (+)-**6** in 53% yield. This chemoenzymatic procedure was found to be effective for procurement as starting material for the synthesis of chiral decaline type sesquiterpenoids and diterpenoids. Herein we report the concise synthesis of (+)-coronarin A (**1**), (+)-coronarin E (**2**), (+)-austrochaparol (**3**) and (+)-pacovatinin A (**4**) from (+)-albicanyl acetate (**6**).

Synthesis of (+)-Coronarin A (1), (+)-Coronarin E (2) and (+)-Austrochaparol (3) The furanolabdane diterpenoids, coronarin A (**1**) and coronarin E (**2**), are isolated from rhizomers of the Brazilian antirheumatic medicinal plant, *Hedychium Coronarium* (Zingiberaceae).[1,2] These compounds exhibit a significant cytotoxic effect against Chinese hamster V-79 cells and sarcoma 180 ascites in mice.[1] The structures of these compounds are established by chemical and spectroscopic methods. The absolute structure of **1** was determined based on the allyic benzoate rule, because the *p*-bromobenzoate of **1** showed a positive cotton curve at 245 nm.[1] (+)-Austrochaparol (**3**) is isolated from the aerial parts of *Austroeupatorium chaparense* and its absolute structure has not been determined yet.[3] The synthesis of (+)-**1** was achieved from natural product, (+)-sclareolide in ten steps.[6] For the synthesis of these compounds, carbon–carbon bond formation between an aldehyde (**7**) and β-furylmethyl unit sulfone **A** or phosphonium salt **B** is necessary as shown in Chart 2.

The aldehyde (**7**) could be derived from the present enzymatic product (**6**). Wittig reaction of **7** and phosphonium salt **B** was reported to give **2** in 32% yield.[7] To overcome the low yield of this carbon–carbon bond formation process, one-pot Julia coupling[8] of **7** and heteroaromatic sulfone **A** (**8** or **9**) possessing β-furylmethyl moiety was carried out. The straightforward synthesis of these compounds from (+)-albicanyl acetate (**6**) is shown in Chart 3.

The synthesis of the desired sulfone **A** was shown in Chart 3. The reaction of 3-furylmethanol with 2-mercaptobenzothiazole (BTSH) or 1-phenyl-1*H*-tetrazol-5-thiol (PTSH) in the presence of triphenylphosphine (Ph_3P) and diethylazodicarboxylate (DEAD) gave sulfides (**10**, 91% yield) or (**11**, 91% yield), which was separately oxidized with *m*-chloroperbenzoic acid (*m*-CPBA) to afford sulfones (**8**, 67% yield) or (**9**, 31% yield), respectively. Treatment of (+)-albicanyl acetate (**6**) with K_2CO_3 gave (+)-albicanol (**5**) in quantitative yield, which was treated with Dess–Martin reagent to afford

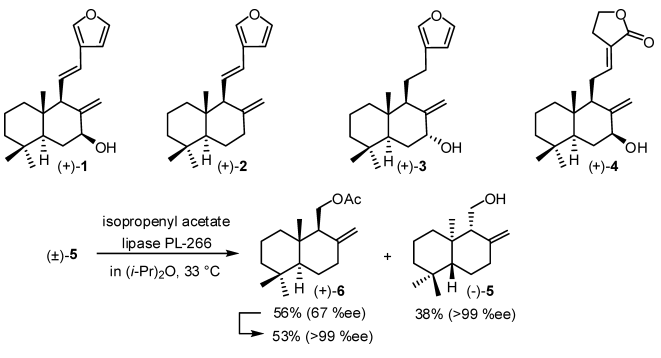

Chart 1

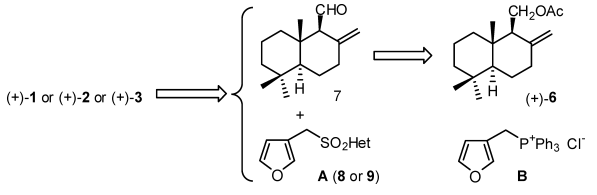

Chart 2

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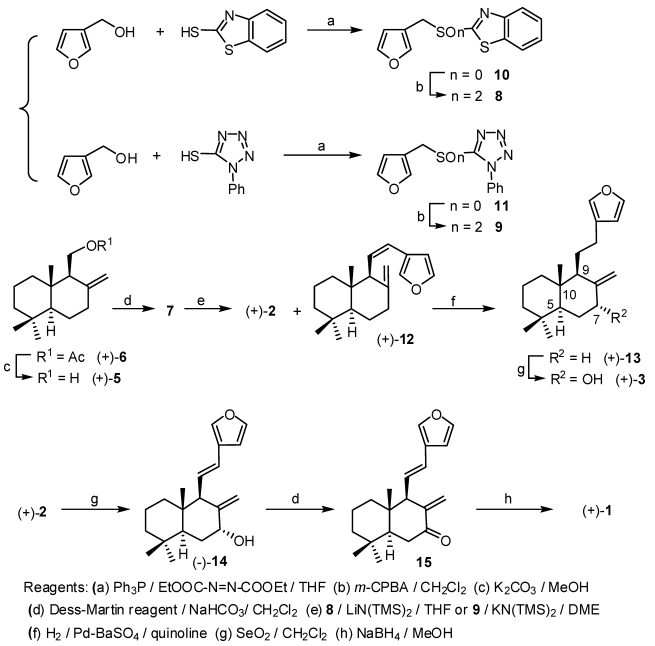

Chart 3

the aldehyde (**7**) in 83% yield. The Julia one-pot olefination between an aldehyde (**7**) and sulfone (**8**) in the presence of lithium bis(trimethylsilylamide) gave (+)-coronarin E (**2**, 11% yield) and (+)-*cis*-coronarin E (**12**, 77% yield, $[\alpha]_D^{23}$ +109.1° (c=0.44, $CHCl_3$)). The physical data ($[\alpha]_D^{20}$ +22.4° (c=1.40, $CHCl_3$) and ^{1}H-NMR) of the synthetic (+)-**2** were identical with those ($[\alpha]_D$ +22.3° (c=0.44, $CHCl_3$) and ^{1}H-NMR)[2] of the natural (+)-**2**. The ^{1}H-NMR data of the synthetic (+)-**12** were in agreement with those of the reported (+)-**12** derived from natural (−)-sclareol.[9] When the reaction conditions (sulfone **8** or **9**, base, solvent) were changed for the purpose of improvement of ratio of *trans*-(+)-**2**, the results were as shown in Table 1 (entries 1—5). High *cis*-selectivity was observed in every case.

Hydrogenation of the main *cis*-(+)-**12** in the presence of quinoline and 5% Pd–$BaSO_4$ gave compound (+)-**13** (86% yield, $[\alpha]_D^{23}$ +44.1° (c=0.59, $CHCl_3$)), which was in accord with the reported natural product (+)-(5*S*,9*S*,10*S*)-15,16-epoxy-8(17),13(16),14-labdatriene (**13**, $[\alpha]_D^{26}$ +49.3° (c=1.00, $CHCl_3$)).[10] Allylic oxidation of (+)-**13** with SeO_2 gave (+)-austrochaparol (**3**, 50% yield, $[\alpha]_D^{27}$ +5.6° (c=0.50, $CHCl_3$)). The physical data ($[\alpha]_D$ and ^{1}H-NMR) of the synthetic (+)-**3** were identical with those ($[\alpha]_D^{24}$ +8.5° (c=6.11, $CHCl_3$) and ^{1}H-NMR) of natural **3**.[3] Consequently, absolute configurations of natural **3** were confirmed to be 5*S*, 7*R*, 9*R*, 10*S*. Generation of 7α-hydroxy compound (**3**) could be explained by an attack of the reagent from the less-hindered α-side. Moreover, allylic oxidation of (+)-**2** with SeO_2 afforded (−)-*epi*-coronarin A (**14**, 47% yield, $[\alpha]_D^{23}$ −13.4° (c=1.16, $CHCl_3$)), which was subjected to oxidation with Dess–Martin reagent to give a α,β-unsaturated ketone (**15**). $NaBH_4$ reduction of **15** gave (+)-coronarin A [(**1**, mp 99—101 °C, $[\alpha]_D^{23}$ +26.9° (c=0.35, $CHCl_3$)] in 78% yield from (+)-**14**. The physical data of the synthetic (+)-**1** were identical with those (mp 100—101 °C, $[\alpha]_D$ +25.4° (c=0.28, $CHCl_3$) and ^{1}H-NMR)[1] of the natural (+)-**1**.

Synthesis of Pacovatinin A (4) Pacovatinin A (**4**) was isolated from seeds of the Brazilian medicinal plant, *Renealmia exaltata* L.f. (Zingiberaceae), and its structure including absolute configurations was elucidated by spectroscopic analysis and a modified Mosher method.[4] On the other hand, hedychilactone A (**4**) was isolated from the methanolic extract of the fresh rhizome of *Hedychium coronarium* KOENG, and found to inhibit the increase of vascular permeability induced by acetic acid in mice and nitric oxide production in lipopolysaccharide-activated mouse peritoneal macrophages.[11,12] Interestingly, hedychilactone A has been already reported under a different name, pacovatinin A (**4**). The straightforward synthesis of (+)-**4** from (+)-**5** is shown in Chart 4.

Table 1. Stereoselectivity by One-Pot Julia Coupling

Entry	Hetero-sulfone (**8** or **9**)	Base	Solvent	Yield (%)	*cis*-**12** : *trans*-**2**
1	**8**	$LiN(TMS)_2$	THF	88	87 : 13
2	**8**	$NaN(TMS)_2$	THF	74	88 : 12
3	**8**	$KN(TMS)_2$	THF	75	91 : 9
4	**8**	$KN(TMS)_2$	DME	86	97 : 3
5	**9**	$KN(TMS)_2$	DME	73	98 : 2

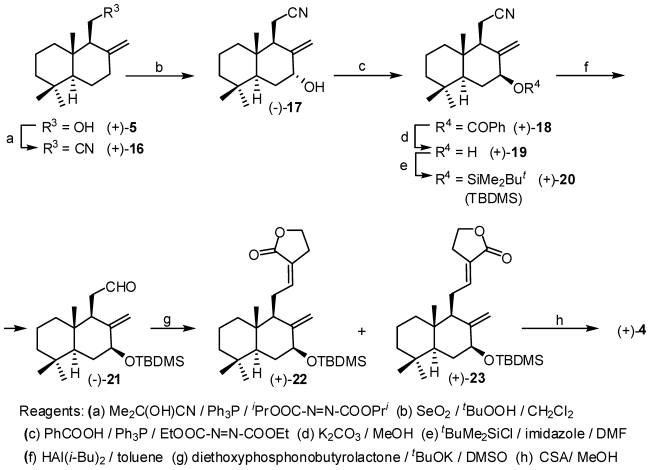

Chart 4

Homologation of (+)-**5** was accomplished by displacement of the hydroxyl group with cyanide under Mitsunobu conditions[13,14] in the presence of acetone cyanohydrin to give nitrile **16** in 64% yield. ^{1}H- and ^{13}C-NMR data of the synthetic **16** were identical with those of the reported (+)-**16** by us.[15] Allylic oxidation of **16** using a combination of SeO_2 and *tert*-BuOOH gave the 7α-hydroxy compound (**17**) in 79% yield. Stereochemical inversion of 7α-configuration to 7β-configuration was achieved by the Mitsunobu method.[16] Treatment of **17** with benzoic acid in the presence of Ph_3P and diethylazodicarboxylate (DEAD) afforded 7β-acyloxy nitrile (**18**, 79% yield), which was treated with K_2CO_3 in MeOH to provide 6β-alcohol (**19**) in 78% yield. Silylation of the secondary alcohol group of **19** followed by Dibal reduction gave an aldehyde (**21**) in overall 84% yield (2 steps from **19**). Horner–Emmons condensation of **21** and diethoxyphosphonobutyrolactone in the presence of *tert*-BuOK gave the less polar compound (**22**, 27% yield) and the more polar one (**23**, 63% yield). Deprotection of silyl group of **23** provided (+)-**4** [$[\alpha]_D^{24}$ +12.8° (c=1.0, $CHCl_3$), 92% yield], of which

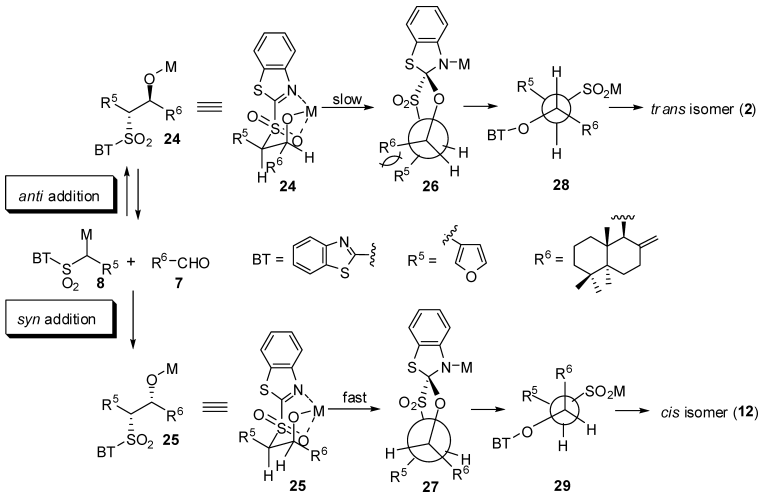

Chart 5. Proposed Mechanism for the One-Pot Julia Olefination

spectral data (^{1}H- and ^{13}C-NMR) were identical with those of the reported (+)-**4** [$[\alpha]_D^{23}$ +10.0° (c=1.00, $CHCl_3$)].[4)]

Discussion

Julia one-pot olefination between aldehyde (**7**) and BT-sulfone (**8**) gave (+)-*cis*-coronain E (**12**) with high *cis*-selectivity. This high selectivity could be explained as shown in Chart 5.

Metallated BT-sulfone (**8**) condenses with aldehyde (**7**) to give *anti* isomer (**24**) and *syn* isomer (**25**), which are converted to intermediates **26** and **27**, respectively. Direct loss of lithio-benzothiazolone and sulfur dioxide from intermediates **26** and **27** may yield *trans* isomer (**2**) *via* **28** and *cis* isomer (**12**) *via* **29**, respectively. The energy barrier to Smiles rearrangement for the *anti* isomer (**24**) is presumably higher than that for the corresponding *syn* isomer (**25**) due to the eclipsed/gauche arrangement of R^5 and R^6 in the appropriate transition state for spirocyclisation. Therefore, the formation rate of **26** from **24** may be slow, while that of **27** from **25** may be fast. The possibility of addition/retroaddition in the reaction of metallated BT-sulfone with aldehyde has been established experimentally.[7)] Equilibration between **24** and **25** together with faster Smiles rearrangement/elimination for the latter provide a reasonable explanation for the high *cis*-selectivity.

Conclusion

Total syntheses of (+)-coronarin A (**1**), (+)-coronarin E (**2**), (+)-austrochaparol (**3**) and (+)-pacovatinin A (**4**) were achieved from (+)-albicanyl acetatel (**6**), which was effectively obtained based on the enzymatic resolution of (±)-**5**. Dess–Martin oxidation of (+)-albicanol (**5**) derived from (+)-**6** gave an aldehyde (**7**), which was subjected to Julia one-pot olefination using β-furylmethyl-heteroaromatic sulfones (**8** or **9**) gave (+)-*trans* coronarin E (**2**) and (+)-*cis* coronarin E (**12**) with high *cis*-selectivity. Allylic oxidation of (+)-*trans* coronarin E (**2**) followed by consecutive oxidation and $NaBH_4$ reduction gave (+)-coronarin A (**1**). Partial reduction of (+)-*cis* coronarin E (**12**) provided (+)-(5*S*, 9*S*,10*S*)-15,16-epoxy-8(17),13(16),14-labdatriene (**13**), which was subjected to allylic oxidation to provide (+)-austrochaparol (**3**). Consequently, absolute configurations of natural **3** were confirmed to be 5*S*, 7*R*, 9*R*, 10*S*. Homologation of albicanol (+)-**5** followed by allylic oxidation gave (7α)-hydroxy nitrile **17**, which was subjected to the Mitsunobu reaction to provide the desired (7β)-acyloxy nitrile **18**. This compound was converted to the (7β)-siloxy aldehyde **21**, which was subjected to the Horner–Emmons reaction to afford the desired *trans* γ-lactone **23**. Deprotection of the silyl group of **23** gave the natural (+)-pacovatinin A (**4**) in 15% overall yield (8 steps) from (+)-albicanol (**5**).

Experimental

All melting points were measured on a Yanaco MP-3S micro melting point apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on a JEOL EX 400 spectrometer. Spectra were taken with 5—10% (w/v) solution in $CDCl_3$ with Me_4Si as an internal reference. The mass spectra, FAB and EI, were obtained with a JEOL JMS-600 H (matrix; glycerol, *m*-nitrobenzyl alcohol) or a JEOL JMS-AM II 50 spectrometer, respectively. IR spectra were recorded on a JASCO FT/IR-300 spectrometer. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.

3-Furylmethyl Benzothiazol-2-yl Sulfide (10) To a solution of 3-furylmethanol (3.01 g, 30.6 mmol) in THF (70 ml) was added 2-mercaptobenzothiazole (10.2 g, 61.2 mmol), Ph_3P (16.0 g, 61.2 mmol) and 2.2 M diethylazodicarboxylate (DEAD) in toluene solution (28 ml, 61.2 mmol) at 0 °C and the whole mixture was stirred under argon atmosphere for 14 h at room temperature (rt). The reaction mixture was diluted with 2 M aqueous NaOH and extracted with Et_2O. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (150 g, *n*-hexane : AcOEt=100 : 1) to afford **10** (6.90 g, 91%) as a pale yellow oil. **10**: IR (neat): 3126, 3062, 1503 cm^{-1}; ^{1}H-NMR δ: 4.42 (2H, br s), 6.44 (1H, br s), 7.28 (1H, ddd, J=9.0, 7.2, 1.2 Hz), 7.35 (1H, br s), 7.41 (1H, ddd, J=8.0, 7.2, 1.2 Hz), 7.47 (1H, m), 7.74 (1H, ddd, J=9.0, 1.2, 0.8 Hz), 7.88 (1H, ddd, J=9.0, 1.2, 0.8 Hz). ^{13}C-NMR δ: 28.0, 111.0, 120.3, 121.0, 121.5, 124.3, 126.1, 135.3, 141.1, 143.3, 153.0, 166.2. *Anal.* Calcd for $C_{12}H_9NOS_2$: C, 58.27; H, 3.67; N, 5.66. Found: C, 58.36; H, 3.86; N, 5.31. HR-MS (EI) Calcd for $C_{12}H_9NOS_2$: 247.0126. Found: 247.0127.

3-Furylmethyl Benzothiazol-2-yl Sulfone (8) To a solution of **10** (10.67 g, 43.1 mmol) in CH_2Cl_2 (200 ml) was added *m*-chloroperbenzoic acid (*m*-CPBA; 27.96 g, 129 mmol) at 0 °C and the whole mixture was stirred for 2 h at rt. The reaction mixture was diluted with 2 M aqueous NaOH and extracted with CH_2Cl_2. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (200 g, *n*-hexane : AcOEt=10 : 1) to afford **8** (8.08 g, 67%) as colorless needles. **8**: mp 134—136 °C (colorless needles from *n*-hexane–AcOEt); IR (KBr): 3141, 1555, 1504 cm^{-1}; ^{1}H-NMR δ: 4.62 (2H, br s), 6.35 (1H, br s), 7.34—7.36 (2H, m), 7.59 (1H, ddd, J=8.0, 7.2, 1.2 Hz), 7.64 (1H, ddd, J=8.0, 7.2, 1.2

Hz), 7.97 (1H, ddd, J=8.0, 1.2, 0.8 Hz), 8.24 (1H, ddd, J=8.0, 1.2, 0.8 Hz). ^{13}C-NMR δ: 51.7, 111.1, 111.5, 122.3, 125.4, 127.7, 128.0, 136.9, 143.4, 143.8, 152.5, 165.0. *Anal.* Calcd for $C_{12}H_9NO_2S_2$: C, 51.60; H, 3.25; N, 5.01. Found: C, 51.73; H, 3.37; N, 4.59.

3-Furylmethyl 1-Phenyl-1*H*-tetrazol-5-yl Sulfide (11) To a solution of 3-furylmethanol (1.00 g, 10.2 mmol) in THF (20 ml) was added 1-phenyl-1*H*-tetrazol-5-thiol (3.65 g, 20.5 mmol), Ph_3P (5.36 g, 20.4 mmol) and 2.2 M diethylazodicarboxylate (DEAD) in toluene solution (7.0 ml, 15.4 mmol) at 0 °C and the whole mixture was stirred under argon atmosphere for 3 h at rt. The reaction mixture was diluted with 2 M aqueous NaOH and extracted with Et_2O. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (100 g, *n*-hexane : AcOEt=30 : 1) to afford **11** (2.38 g, 91%) as a pale yellow oil. **11**: IR (neat): 3137, 3068, 1595, 1499 cm^{-1}; ^{1}H-NMR δ: 4.48 (2H, s), 6.23 (1H, dd, J=1.6, 0.4 Hz), 7.36 (1H, dd, J=1.6, 1.6 Hz), 7.51—7.55 (6H, m). ^{13}C-NMR δ: 27.9, 110.7, 119.4, 123.7 (2C), 129.7 (2C), 130.1, 133.5, 141.4, 143.4, 153.7. HR-MS (EI) Calcd for $C_{12}H_{10}N_4OS$: 258.0565. Found: 258.0575.

3-Furylmethyl 1-Phenyl-1*H*-tetrazol-5-yl Sulfone (9) To a solution of **11** (0.201 g, 0.779 mmol) in CH_2Cl_2 (3.5 ml) was added *m*-chloroperbenzoic acid (*m*-CPBA; 0.836 g, 4.84 mmol) at 0 °C and the whole mixture was stirred for 15 h at rt. The reaction mixture was diluted with 2 M aqueous NaOH and extracted with CH_2Cl_2. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (200 g, *n*-hexane : AcOEt=5 : 1) to afford **9** (0.069 g, 31%) as colorless needles. **9**: mp 138—140 °C (colorless needles from *n*-hexane–AcOEt); IR (KBr): 3121, 3070, 1601, 1497 cm^{-1}; ^{1}H-NMR δ: 4.84 (2H, s), 6.43 (1H, dd, J=2.0, 0.8 Hz), 7.40 (1H, dd, J=1.6, 1.6 Hz), 7.48—7.63 (6H, m). ^{13}C-NMR δ: 53.3, 109.7, 111.7, 125.1 (2C), 129.5 (2C), 131.4, 132.8, 143.9, 144.2, 152.7. *Anal.* Calcd for $C_{12}H_{10}N_4O_3S$: C, 49.65; H, 3.47; N, 19.30. Found: C, 49.85; H, 3.58; N, 19.48.

(+)-*trans*-Coronarin E (2) and (+)-*cis*-Coronarin E (12) 1) A suspension of (+)-**6** (4.50 g, 17.0 mmol) and K_2CO_3 (8.36 g, 60.5 mmol) in MeOH (50.0 ml) was stirred for 12 h at rt. The reaction mixture was evaporated, diluted with saturated brine and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and evaporated to afford a crude product which was chromatographed on silica gel (100.0 g) to give (+)-**5** (3.78 g, 99% yield) from *n*-hexane : AcOEt=30 : 1 eluent. (+)-**5**: mp 71—73 °C (colorless needles from *n*-hexane), $[\alpha]_D^{24}$ +10.8° (c=0.5, $CHCl_3$, corresponds to >98% ee), ^{1}H-NMR data of (+)-**5** were identical with those of the reported (+)-**5**.[10] *Anal*. Calcd for $C_{15}H_{22}O$: C, 81.02; H, 11.79. Found: C, 81.19; H, 11.97. 2) To a solution of (+)-**5** (1.00 g, 4.49 mmol) in CH_2Cl_2 (65.0 ml) was added $NaHCO_3$ (5.89 g, 70.1 mmol) and Dess–Martin reagent (3.15 g, 7.43 mmol) at 0 °C and the reaction mixture was stirred for 2 h at rt. The reaction mixture was directly subjected to chromatography on silica gel (100 g, *n*-hexane : AcOEt=200 : 1) to give **7** (0.823 g, 83% yield) as a colorless oil. **7**; ^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, s), 0.89 (3H, s), 1.03 (1H, dd, J=12.6, 2.8 Hz), 1.15 (3H, s), 1.17—1.28 (2H, m), 1.38—1.50 (3H, m), 1.54—1.66 (2H, m), 1.69—1.75 (1H, m), 2.05—2.13 (1H, m), 2.37—2.49 (2H, m), 4.50 (1H, br s), 4.92 (1H, br s), 9.87 (1H, d, J=4.8 Hz). ^{13}C-NMR δ: 16.0, 18.7, 21.9, 23.1, 33.4, 33.5, 36.7, 39.0, 39.9, 41.9, 54.0, 67.9, 109.2, 145.0, 205.7. 3) To a solution of **8** (1.14 g, 4.09 mmol) in THF (15.0 ml) was added 1.0 M solution of lithium bis(trimethylsilylamide) in toluene (4.10 ml, 4.10 mmol) at −78 °C under argon atmosphere. After being stirred at −78 °C for 20 min, **7** (0.819 g, 3.72 mmol) in THF (5 ml) was slowly added. The mixture was stirred for 0.5 h at −78 °C. The reaction was diluted with brine and extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (100 g, *n*-hexane) to afford (+)-**12** (0.814 g, 77%) and (+)-**2** (0.116 g, 11%) in elution order.

(+)-**12** (Colorless Oil): $[\alpha]_D^{23}$ +109.1° (c=0.44, $CHCl_3$). IR (neat): 1644 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.84 (3H, s), 0.86 (3H, s), 0.87 (3H, s), 0.91—0.95 (1H, m), 1.11 (1H, dd, J=12.5, 2.8 Hz), 1.14—1.22 (1H, m), 1.35—1.42 (3H, m), 1.47—1.54 (1H, m), 1.55—1.57 (1H, m), 1.70—1.72 (1H, m), 2.06—2.14 (1H, m), 2.50 (1H, ddd, J=13.4, 4.4, 2.3 Hz), 2.81 (1H, d, J=10.0 Hz), 4.61 (1H, dd, J=3.7, 2.0 Hz), 4.75 (1H, dd, J=3.7, 2.0 Hz), 5.62 (1H, dd, J=11.8, 9.4 Hz), 6.32 (1H, d, J=12.0 Hz), 6.34 (1H, t, J=1.2 Hz), 7.32 (1H, t, J=1.2 Hz), 7.34 (1H, t, J=1.2 Hz). ^{13}C-NMR δ: 14.3, 19.0, 21.9, 23.4, 33.4 (2C), 36.4, 39.0, 39.9, 42.1, 54.9, 57.0, 108.4, 111.0, 120.7, 122.2, 130.0, 140.7, 142.4, 148.0. HR-MS (EI) Calcd for $C_{20}H_{28}O_2$: 284.2140. Found: 284.2145. (+)-**2**: mp 94—96 °C (colorless needles from *n*-hexane). $[\alpha]_D^{20}$ +22.4° (c=1.4, $CHCl_3$). IR (neat): 1643 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.84 (3H, s), 0.85 (3H, s), 0.90 (3H, s), 1.02—1.07 (1H, m), 1.11 (1H, dd, J=12.4, 2.8 Hz), 1.15—1.24 (1H, m), 1.34—1.44 (3H, m), 1.46—1.53 (2H, m), 1.63—1.74 (1H, m), 2.06—2.14 (1H, m), 2.40 (1H, d, J=10.4 Hz), 2.45 (1H, ddd, J=13.4, 4.4, 2.4 Hz), 4.53 (1H, q, J=2.0 Hz), 4.75 (1H, q, J=2.0 Hz), 5.97 (1H, dd, J=15.8, 10.0 Hz), 6.19 (1H, d, J=15.6 Hz), 6.54 (1H, br s), 7.33—7.36 (2H, m). ^{13}C-NMR δ: 15.0, 19.1, 22.0, 23.4, 33.6 (2C), 36.8, 39.1, 40.8, 42.3, 54.8, 61.5, 107.6, 108.0, 121.7, 124.5, 128.3, 139.6, 143.2, 150.2. HR-MS (EI) Calcd for $C_{20}H_{28}O_2$: 284.2140. Found: 284.2138.

(+)-(5*S*,9*S*,10*S*)-15,16-Epoxy-8(17),13(16),14-labdatriene (13) A mixture of (+)-**12** (0.300 g, 1.05 mmol), quinoline (0.05 g, 0.38 mmol) and 5% Pd–$BaSO_4$ (0.200 g) in MeOH (10.0 ml) was subjected to hydrogenation under hydrogen atmosphere for 3 d at ordinary temperature. The reaction mixture was filtered with the aid of celite and filtrate was condensed to give a residue which was chromatographed on silica gel (20.0 g, *n*-hexane) to provide (+)-**13** (0.259 g, 86%) as a colorless oil. (+)-**13**: $[\alpha]_D^{23}$ +44.1° (c=0.59, $CHCl_3$). IR (neat): 1644, 1564, 1496 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.69 (3H, s), 0.80 (3H, s), 0.86 (3H, s), 0.97 (1H, dd, J=12.6, 4.0 Hz), 1.07 (1H, dd, J=12.8, 2.8 Hz), 1.16 (1H, dd, J=13.2, 4.0 Hz), 1.29—1.53 (3H, m), 1.54—1.66 (3H, m), 1.69—1.79 (3H, m), 1.97 (1H, ddd, J=12.8, 12.8, 5.2 Hz), 2.19—2.28 (1H, m), 2.40 (1H, ddd, J=12.6, 3.8, 2.0 Hz), 2.55 (1H, ddd, J=14.0, 10.0, 2.8 Hz), 4.56 (1H, s), 4.86 (1H, s), 6.26 (1H, br s), 7.19 (1H, br s), 7.34 (1H, br s). ^{13}C-NMR δ: 14.5, 19.4, 21.7, 23.6, 24.0, 24.4, 33.6 (2C), 38.3, 39.0, 39.6, 42.1, 55.5, 56.1, 106.2, 111.0, 125.6, 138.7, 142.6, 148.5. HR-MS (EI) Calcd for $C_{20}H_{30}O_2$: 286.2297. Found: 286.2300.

(+)-Austrochaparol (3) To a solution of (+)-**13** (0.050 g, 0.175 mmol) in CH_2Cl_2 (1.50 ml) was added SeO_2 (0.160 g, 1.43 mmol) at 0 °C and the whole mixture was stirred for 12 h at rt. The reaction mixture was diluted with saturated $Na_2S_2O_3$ and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Removal of the organic solvent gave a crude residue, which was chromatographed on silica gel (5.00 g, *n*-hexane : AcOEt=10 : 1) to afford (+)-**3** (0.026 g, 50%) as a colorless oil. (+)-**3**: $[\alpha]_D^{27}$ +5.6° (c=0.50, $CHCl_3$). IR (KBr): 3330 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.67 (3H, s), 0.80 (3H, s), 0.88 (3H, s), 1.05 (1H, ddd, J=17.0, 13.0, 4.0 Hz), 1.21 (1H, ddd, J=17.0, 13.0, 4.0 Hz), 1.35—1.65 (7H, m), 1.70—1.84 (2H, m), 1.84—1.90 (1H, m), 2.17 (1H, dd, J=10.0, 1.3 Hz), 2.20—2.29 (1H, m), 2.53 (1H, ddd, J=14.2, 10.0, 4.0 Hz), 4.40 (1H, br s), 4.70 (1H, dd, J=1.3, 1.1 Hz), 5.09 (1H, dd, J=1.1, 1.1 Hz), 6.27 (1H, d, J=1.0 Hz), 7.20 (1H, dd, J=1.1, 1.1 Hz), 7.35 (1H, dd, J=1.6, 1.6 Hz). ^{13}C-NMR δ: 13.5, 19.4, 21.5, 23.4, 23.7, 31.0, 33.1, 33.3, 38.8, 39.8, 42.1, 47.6, 50.4, 74.2, 109.7, 110.9, 125.4, 138.7, 142.7, 149.6. HR-MS (EI) Calcd for $C_{20}H_{30}O_2$: 302.2246. Found: 302.2244.

(−)-*epi*-Coronarin A (14) To a solution of (+)-**2** (0.050 g, 0.176 mmol) in CH_2Cl_2 (1.50 ml) was added SeO_2 (0.039 g, 0.252 mmol) at 0 °C and the whole mixture was stirred for 30 min at 0 °C. The reaction mixture was diluted with brine and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$. Removal of the organic solvent gave a crude residue, which was chromatographed on silica gel (5.00 g, *n*-hexane : AcOEt=20 : 1) to afford (−)-**14** (0.025 g, 47%) as a colorless oil. (−)-**14**: $[\alpha]_D^{23}$ −13.4° (c=1.16, $CHCl_3$). IR (neat): 3390, 1647 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.81 (3H, s), 0.83 (3H, s), 0.90 (3H, s), 1.03—1.13 (1H, m), 1.16—1.28 (2H, m), 1.37—1.67 (6H, m), 1.81—1.91 (1H, m), 2.88 (1H, d, J=10.0 Hz), 4.38—4.42 (1H, m), 4.69 (1H, dd, J=1.6, 1.6 Hz), 4.98 (1H, dd, J=1.6, 1.6 Hz), 5.90 (1H, dd, J=15.8, 10.0 Hz), 6.24 (1H, d, J=15.8 Hz), 6.50—6.53 (1H, m), 7.31—7.37 (2H, m). ^{13}C-NMR δ: 14.0, 19.0, 21.7, 30.0, 33.1, 33.2, 39.4, 40.4, 42.2, 46.9, 56.0, 73.4, 107.5, 111.8, 122.4, 124.3, 127.2, 139.7, 143.3, 151.3. HR-MS (EI) Calcd for $C_{20}H_{28}O_2$: 300.2089. Found: 300.2082.

(+)-Coronarin A (1) To a solution of (−)-**14** (0.009 g, 0.03 mmol) in CH_2Cl_2 (1.00 ml) was added Dess–Martin reagent (0.038 g, 0.09 mmol) at 0 °C and the whole mixture was stirred for 1 h at the same temperature. The reaction mixture was filtered and the filtrate was condensed to give a crude **15**, which was used for the next reaction without further purification. To a solution of the above **15** in MeOH (1.00 ml) was added $NaBH_4$ (0.001 g, 0.03 mmol) at 0 °C and the whole mixture was stirred for 20 min at the same temperature. The reaction mixture was diluted with saturated $NaHCO_3$ and extracted with Et_2O. The organic layer was dried over $MgSO_4$. Removal of the organic solvent gave a residue, which was chromatographed on silica gel (3.00 g, *n*-hexane : AcOEt=20 : 1) to provide (+)-**1** (0.007 g, 78%) as a colorless oil. (+)-**1**: mp 99—101 °C (colorless needles from *n*-hexane), $[\alpha]_D^{23}$ +26.9° (c=0.35, $CHCl_3$). IR (neat): 3351, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.85 (3H, s), 0.85 (3H, s), 0.93 (3H, s), 0.93—1.04 (1H, m), 1.13—1.56 (7H, m), 1.82 (1H, br s), 2.10 (1H, ddd, J=12.0, 5.6, 2.4 Hz), 2.35 (1H, d, J=9.6 Hz), 4.10 (1H, dd, J=11.2, 5.6 Hz), 4.74 (1H, s), 5.13 (1H, s), 5.99 (1H, dd, J=15.6, 9.6 Hz), 6.21 (1H, d, J=15.6 Hz), 6.55 (1H, s), 7.37 (2H, m). ^{13}C-NMR δ: 15.0, 19.0, 21.9, 33.1, 33.5 (2C), 39.1, 40.3, 42.0, 52.5,

59.7, 73.3, 104.8, 107.6, 122.2, 124.3, 126.9, 139.8, 143.3, 152.1. HR-MS (EI) Calcd for $C_{20}H_{28}O_2$: 300.2089. Found: 300.2080.

(+)-(1*R*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-2-methylene-1-naphthaleneacetonitrile (16) To a solution of (+)-**5** (0.60 g, 2.7 mmol) in toluene (10 ml) was added acetone cyanohydrin (2.5 ml, 27 mmol), Ph_3P (1.1 g, 4.1 mmol) and diisopropylazodicarboxylate (DIAD, 0.8 ml, 4.1 mmol) and the mixture was stirred for 1 d at 70 °C. The reaction mixture was diluted with water (ice) and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (40 g, *n*-hexane : AcOEt=19 : 1) to afford a nitrile (**16**) (0.400 g, 64%) as colorless plates (*n*-hexane). ^{1}H- and ^{13}C-NMR data of the synthetic **16** were identical with those of the reported (+)-**16**.[15]

(+)-(1*R*,3*S*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-3-hydroxy-2-methylene-1-naphthaleneacetonitrile (17) To a solution of SeO_2 (0.111 g, 1 mmol) in CH_2Cl_2 (5 ml) was added 5.5 M *tert*-BuOOH in decane solution (0.73 ml, 4 mmol) and the mixture was stirred for 1 h at rt. A solution of **16** (0.462 g, 2 mmol) in CH_2Cl_2 (1 ml) was added to the above solution and the whole mixture was stirred for 1 d at rt. The reaction mixture was diluted with saturated $Na_2S_2O_3$ solution and extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (40 g, *n*-hexane : AcOEt=3 : 1) to afford (−)-**17** (0.392 g, 79%). Recrystallization of (−)-**17** from *n*-hexane gave colorless needles. (−)-**17**: mp 149—150 °C; $[\alpha]_D^{23}$ −24.9° (*c*=0.83, $CHCl_3$); IR (KBr): 3445, 2259 cm^{-1}; ^{1}H-NMR δ: 0.67 (3H, s), 0.82 (3H, s), 0.91 (3H, s), 1.18—1.29 (2H, m), 1.38—1.48 (1H, m), 1.51—1.62 (5H, m), 1.71 (1H, dd, *J*=13.6, 3.0 Hz), 1.91 (1H, ddd, *J*=13.6, 2.5, 2.5 Hz), 2.30 (1H, dd, *J*=16.6, 10.8 Hz), 2.58 (1H, dd, *J*=16.6, 3.8 Hz), 2.73 (1H, ddd, *J*=19.9, 1.9, 2.0 Hz), 4.43 (1H, br s), 4.77 (1H, d, *J*=1.8 Hz), 5.18 (1H, d, *J*=1.5 Hz). ^{13}C-NMR δ: 13.0, 13.8, 19.2, 21.6, 30.3, 33.1, 33.3, 38.9, 39.6, 41.8, 47.2, 47.9, 73.2, 110.6, 119.8, 147.8. MS (FAB) *m*/*z*: 248 (M^++1), 230 (M^++1-H_2O).

(+)-(1*R*,3*R*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-3-benzoyloxy-2-methylene-1-naphthaleneacetonitrile (18) To a solution of (−)-**17** (0.209 g, 0.84 mmol) in THF (6 ml) was added benzoic acid (0.642 g, 5.3 mmol), Ph_3P (1.324 g, 5.1 mmol) and 49% diethylazodicarboxylate in toluene solution (2.2 ml, 5.1 mmol) at 0 °C and the whole mixture was stirred for 1 h at 0 °C. The reaction mixture was diluted with 7% aqueous $NaHCO_3$ and extracted with Et_2O. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (40 g, *n*-hexane : AcOEt=5 : 1) to afford (+)-**18** (0.234 g, 79%) as colorless prisms (*n*-hexane/AcOEt). (+)-**18**: mp 150—151 °C; $[\alpha]_D^{25}$ +89.7° (*c*=0.95, $CHCl_3$); IR (KBr): 3349 cm^{-1}; ^{1}H-NMR δ: 0.78 (3H, s), 0.85 (3H, s), 0.94 (3H, s), 1.16—1.29 (3H, m), 1.32 (1H, dd, *J*=13.1, 2.5 Hz), 1.45—1.68 (4H, m), 2.18—2.27 (2H, m), 2.44 (1H, dd, *J*=16.6, 10.0 Hz), 2.61 (1H, dd, *J*=16.6, 4.6 Hz), 4.82 (1H, br s), 5.31 (1H, br s), 5.46 (1H, dd, *J*=16.6, 5.5 Hz), 7.47 (2H, t, *J*=7.6 Hz), 7.59 (1H, t, *J*=7.5 Hz), 8.13 (2H, d, *J*=7.7 Hz). ^{13}C-NMR δ: 13.9, 14.0, 19.1, 21.7, 30.1, 33.5, 33.6, 39.0, 39.2, 41.6, 51.5, 52.4, 74.3, 105.7, 119.3, 128.3 (2C), 129.5 (2C), 130.1, 132.9, 143.8, 165.0. *Anal.* Calcd for $C_{23}H_{29}NO_2$: C, 78.59; H, 8.32; N, 3.98. Found: C, 78.39; H, 8.51; N, 3.50. MS (FAB) *m*/*z*: 352 (M^++1).

(+)-(1*R*,3*R*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-3-hydroxy-2-methylene-1-naphthaleneacetonitrile (19) A mixture of (+)-**18** (0.160 g, 0.46 mmol) and K_2CO_3 (0.077 g, 0.55 mmol) in MeOH (2 ml) was stirred for 3 h at rt. The reaction mixture was diluted with 7% aqueous $NaHCO_3$ and extracted with Et_2O. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (10 g, *n*-hexane : AcOEt=5 : 1) to afford (+)-**19** (0.088 g, 78%) as colorless plates (*n*-hexane/AcOEt). (+)-**19**: mp 107—108 °C; $[\alpha]_D^{23}$ +35.3° (*c*=0.92, $CHCl_3$); IR (KBr): 3425, 2260 cm^{-1}; ^{1}H-NMR δ: 0.68 (3H, s), 0.83 (3H, s), 0.93 (3H, s), 1.07—1.34 (5H, m), 1.43—1.49 (1H, m), 1.51—1.62 (2H, m), 1.79 (1H, d, *J*=5.0 Hz), 2.06—2.17 (2H, m), 2.41 (1H, dd, *J*=16.6, 10.6 Hz), 2.59 (1H, dd, *J*=16.6, 4.0 Hz), 4.07 (1H, dd, *J*=11.0, 5.0 Hz), 4.81 (1H, br s), 5.34 (1H, br s). ^{13}C-NMR δ: 13.8, 13.9, 19.1, 21.6, 33.1, 33.4 (2C), 38.9, 39.0, 41.5, 51.3, 52.4, 72.8, 104.7, 119.7, 148.2. *Anal.* Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.71; H, 10.28; N, 5.33. MS (FAB) *m*/*z*: 270 (M^++Na).

(+)-(1*R*,3*R*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-3-*tert*-butyldimethylsiloxy-2-methylene-naphthaleneacetonitrile (20) A mixture of (+)-**19** (0.131 g, 0.53 mmol), *tert*-butyldimethylsilyl chloride (TBDMSCl; 0.123 g, 0.82 mmol) and imidazole (0.063 g, 0.92 mmol) in DMF (1.5 ml) was stirred for 1 h at rt. The reaction mixture was diluted with brine and extracted with Et_2O. The organic layer was dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (10 g, *n*-hexane : AcOEt=10 : 1) to afford (+)-**20** (0.186 g, 97%) as colorless needles (*n*-hexane). (+)-**20**: mp 69 °C; $[\alpha]_D^{27}$ +20.8° (*c*=0.75, $CHCl_3$); IR (KBr): 2245 cm^{-1}; ^{1}H-NMR δ: 0.09 (3H, s), 0.10 (3H, s), 0.67 (3H, s), 0.82 (3H, s), 0.91 (3H, s), 0.93 (9H, s), 1.13 (1H, dd, *J*=12.9, 2.3 Hz), 1.21 (1H, dd, *J*=11.9, 6.3 Hz), 1.24—1.37 (2H, m), 1.42—1.49 (1H, m), 1.51—1.62 (2H, m), 1.95 (1H, ddd, *J*=12.6, 5.5, 2.5 Hz), 2.03—2.10 (1H, m), 2.39 (1H, dd, *J*=16.9, 10.6 Hz), 2.55 (1H, dd, *J*=16.7, 4.3 Hz), 3.98 (1H, dd, *J*=10.8, 5.3 Hz), 4.73 (1H, br s), 5.37 (1H, br s). ^{13}C-NMR δ: −4.8, −4.7, 13.9, 14.1, 18.6, 19.2, 21.8, 26.0 (3C), 33.4, 33.5, 34.1, 39.1, 39.2, 41.7, 51.6, 52.6, 74.0, 105.6, 119.8, 147.8. *Anal.* Calcd for $C_{22}H_{39}NOSi$: C, 73.07; H, 10.87; N, 3.87. Found: C, 73.04; H, 11.02; N, 3.64. MS (FAB) *m*/*z*: 384 (M^++Na).

(−)-(1*R*,3*R*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-3-*tert*-butyldimethylsiloxy-2-methylene-naphthaleneacetoaldehyde (21) To a solution of (+)-**20** (0.185 g, 0.51 mmol) in toluene (1.5 ml) was added 1 M diisobutylaluminum hydride (Dibal) in toluene solution (0.6 ml, 0.6 mmol) at −78 °C and the reaction mixture was stirred for 30 min at at −78 °C. To the reaction mixture was added acetone (0.2 ml) at 0 °C. The reaction mixture was acidified with 2 M HCl solution and extracted with Et_2O. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (10 g, *n*-hexane : AcOEt=20 : 1) to afford (−)-**21** (0.163 g, 87%) as a colorless oil. (−)-**21**: $[\alpha]_D^{24}$ −14.7° (*c*=1.02, $CHCl_3$); IR (KBr): 1726 cm^{-1}; ^{1}H-NMR δ: 0.069 (3H, s), 0.076 (3H, s), 0.70 (3H, s), 0.82 (3H, s), 0.91 (3H, s), 0.93 (9H, s), 1.00—1.09 (1H, m), 1.14—1.27 (1H, m), 1.28—1.40 (1H, m), 1.40—1.61 (3H, m), 1.96 (1H, ddd, *J*=12.6, 5.5, 2.0 Hz), 2.27 (1H, dd, *J*=10.6, 4.0 Hz), 2.45 (1H, ddd, *J*=16.6, 4.0, 1.0 Hz), 2.55 (1H, ddd, *J*=16.9, 10.6, 3.0 Hz), 3.98 (1H, dd, *J*=11.1, 5.5 Hz), 4.54 (1H, br s), 5.24 (1H, br s), 9.63 (1H, dd, *J*=3.5, 1.0 Hz). ^{13}C-NMR δ: −4.8, −4.7, 14.7, 18.6, 19.4, 21.8, 26.0 (3C), 33.5 (2C), 34.3, 38.7, 39.4, 39.7, 42.0, 49.3, 53.1, 74.4, 105.8, 149.8, 202.7. *Anal.* Calcd for $C_{22}H_{40}O_2Si$: C, 72.46; H, 11.06. Found: C, 72.39; H, 10.99. MS (FAB) *m*/*z*: 387 (M^++Na).

Horner–Emmons Condensation of (−)-21 and Diethoxyphosphonobutyrolactone To a solution of diethoxyphosphonobutyrolactone (0.510 g, 2.3 mmol) in DMSO (2.5 ml) was added *t*-BuOK (0.213 g, 1.9 mmol) and the reaction mixture was stirred for 30 min at rt. To a solution of (−)-**21** (0.163 g, 0.44 mmol) in DMSO (0.5 ml) was added the above ylide solution at rt and the whole mixture was stirred for 30 min at rt. The reaction mixture was diluted with brine and extracted with Et_2O. The organic layer was dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (15 g, *n*-hexane : AcOEt=5 : 1) to afford the less polar (+)-**22** (0.053 g, 27%) as a colorless amorphous solid and the more polar (+)-**23** (0.122 g, 63%) as colorless needles (*n*-hexane). (+)-**22**: mp 104 °C; $[\alpha]_D^{24}$ +21.8° (*c*=1.0, $CHCl_3$); IR (KBr): 1745, 1660 cm^{-1}; ^{1}H-NMR δ: 0.069 (3H, s), 0.082 (3H, s), 0.72 (3H, s), 0.81 (3H, s), 0.88 (3H, s), 0.93 (9H, s), 1.00—1.22 (3H, m), 1.24—1.38 (2H, m), 1.38—1.45 (1H, m), 1.46—1.56 (1H, m), 1.66 (1H, d, *J*=10.6 Hz), 1.74—1.81 (1H, m), 1.93 (1H, ddd, *J*=12.1, 5.0, 2.0 Hz), 2.69—2.79 (1H, m), 2.84—2.91 (2H, m), 2.97—3.07 (1H, m), 3.91 (1H, dd, *J*=11.1, 5.0 Hz), 4.26—4.34 (2H, m), 4.52 (1H, d, *J*=1.5 Hz), 5.25 (1H, d, *J*=1.5 Hz), 6.01—6.18 (1H, m). ^{13}C-NMR δ: −4.7 (2C), 14.5, 18.7, 19.4, 21.8, 22.9, 26.1 (3C), 29.2, 33.5, 33.6, 34.6, 39.0, 39.4, 42.0, 53.2, 55.5, 65.3, 74.9, 105.3, 122.9, 144.6, 149.4, 170.0. *Anal.* Calcd for $C_{26}H_{44}O_3Si$: C, 72.17; H, 10.25. Found: C, 71.74; H, 10.15. HR-MS (EI) *m*/*z*: Calcd for $C_{26}H_{44}O_3Si$: 432.3060. Found: 432.3050. (+)-**23**: mp 97 °C; $[\alpha]_D^{24}$ +7.0° (*c*=1.0, $CHCl_3$); IR (KBr): 1745, 1660 cm^{-1}; ^{1}H-NMR δ: 0.070 (3H, s), 0.083 (3H, s), 0.71 (3H, s), 0.82 (3H, s), 0.90 (3H, s), 0.93 (9H, s), 0.96—1.80 (9H, m), 1.94 (1H, ddd, *J*=12.6, 5.6, 2.5 Hz), 2.22—2.44 (2H, m), 2.80—2.96 (2H, m), 3.92 (1H, dd, *J*=11.1, 5.5 Hz), 4.38 (2H, t-like), 4.52 (1H, d, *J*=1.0 Hz), 5.26 (1H, d, *J*=1.5 Hz), 6.68 (1H, ddd, *J*=9.9, 6.5, 3.0 Hz). ^{13}C-NMR δ: −4.7 (2C), 14.5, 18.6, 19.4, 21.8, 24.4, 25.6, 26.1 (3C), 33.5 (2C), 34.4, 39.2, 39.3, 42.0, 53.0, 54.4, 65.3, 74.5, 105.2, 124.6, 141.6, 149.3, 170.9. *Anal.* Calcd for $C_{26}H_{44}O_3Si$: C, 72.17; H, 10.25. Found: C, 72.10; H, 10.32. MS (FAB) *m*/*z*: 455 (M^++Na).

(+)-Pacovatinin A (4) To a solution of (+)-**23** (0.091 g, 0.21 mmol) in a mixed solvent [MeOH (2 ml)/THF (0.5 ml)] was added 10-camphorsufonic acid (CSA; 0.073 g, 0.32 mmol) at rt and the reaction mixture was stirred for 6 h rt. The reaction mixture was diluted with 7% aqueous $NaHCO_3$ and extracted with Et_2O. The organic layer was washed with brine, and dried over $MgSO_4$. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (5 g, *n*-hexane : AcOEt=2 : 1) to afford (+)-**4** (0.062 g, 92%) as a colorless amorphous solid. (+)-**4**: mp 146—147 °C; $[\alpha]_D^{24}$ +12.8° (*c*=1.0, $CHCl_3$); IR (KBr): 3266, 1747, 1677 cm^{-1};

^{1}H-NMR δ: 0.72 (3H, s), 0.83 (3H, s), 0.92 (3H, s), 1.05 (1H, ddd, J=12.6, 12.6, 4.0 Hz), 1.17 (1H, dd, J=12.6, 2.5 Hz), 1.21—1.35 (2H, m), 1.41—1.48 (1H, m), 1.48—1.64 (2H, m), 1.71 (1H, br d, J=5.0 Hz), 1.80 (1H, br d, J=8.1 Hz), 2.11 (1H, ddd, J=11.6, 5.6, 2.5 Hz), 2.23—2.34 (1H, m), 2.35—2.45 (1H, m), 2.84—2.92 (2H, m), 4.00 (1H, ddd, J=10.8, 5.3, 5.3 Hz), 4.39 (2H, t-like), 4.52 (1H, br s), 5.20 (1H, br s), 6.68 (1H, ddd, J=10.1, 6.8, 3.0 Hz). ^{13}C-NMR δ: 14.3, 19.3, 21.6, 25.2, 25.2, 33.5, 33.5, 33.5, 39.1, 39.2, 41.8, 53.0, 54.4, 65.3, 73.6, 104.2, 124.9, 141.5, 150.1, 171.2. *Anal.* Calcd for $C_{20}H_{30}O_3 \cdot 0.5H_2O$: C, 73.36; H, 9.54. Found: C, 73.87; H, 9.24. HR-MS (EI) *m/z*: Calcd for $C_{20}H_{30}O_3$: 318.2195. Found: 318.2198.

References and Notes

1) Itokawa H., Morita H., Katou I., Takya K., Cavalheiro A. J., de Oliveira R. C. B., Ishige M., Motidome M., *Planta Medica*, **1988**, 311—315 (1988).
2) Itokawa H., Morita H., Takya K., Motidome M., *Chem. Pharm. Bull.*, **36**, 2682—2684 (1988).
3) Bohlmann F., Zdero C., Gupta R. K., King R. M., Robinson H., *Phytochemistry*, **19**, 2695—2705 (1980).
4) Sekiguchi M., Shigenori H., Ohsaki A., Kobayashi J., *J. Nat. Prod*., **64**, 1102—1106 (2001).
5) Amano Y., Kinoshita M., Akita H., *J. Mol. Catalysis B: Enzymatic*, **32**, 141—148 (2005).
6) Oh S., Jeong I. H., Shin W-S., Lee S., *Bioorg. Med. Chem. Lett.*, **13**, 2009—2012 (2003).
7) Review: Blakemore P. R., *J. Chem. Soc. Perkin Trans. 1*, **2002**, 2563—2585 (2002).
8) Maria K., Maria L., Valentine R., *Tetrahedron*, **61**, 2003—2010 (2005).
9) Jung M., Ko I., Lee S., *J. Nat. Prod.*, **61**, 1394—1396 (1998).
10) Akita H., Amano Y., Kato K., Nozawa M., *Tetrahedron: Asymmetry*, **15**, 725—732 (2004).
11) Matsuda H., Morikawa T., Sakamoto Y., Toguchida I., Yoshikawa M., *Heterocycles*, **56**, 45—56 (2002).
12) Morikawa T., Matsuda H., Sakamoto Y., Ueda K., Yoshikawa M., *Chem. Pharm. Bull.*, **50**, 1045—1049 (2002).
13) Tsunoda T., Uemoto K., Nagin C., Kawamura M., Kaku H., Ito S., *Tetrahedron Lett.*, **40**, 7355—7358 (1999).
14) Micheal T. C., Franck C., *J. Am. Chem. Soc.*, **128**, 3128—3129 (2006).
15) Kinoshita M., Ohtsuka M., Nakamura D., Akita H., *Chem. Pharm. Bull.*, **50**, 930—934 (2002).
16) Mitsunobu O., *Synthesis*, **1981**, 1—28 (1981).