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TETRAHEDRON: *ASYMMETRY*

Facile one-pot transformation of 2,3-epoxy alcohols into allylic alcohols: first total synthesis of (−)-4-*O*-(6′-hydroxy-7′(9′)-dehydro-6′,7′-dihydrogeranyl)coniferol

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Abstract

An efficient and practical synthesis of optically active allylic alcohols from 2,3-epoxy alcohols by the in situ formation of the epoxy iodides and their subsequent reduction with phosphine hydroxyiodide has been established. Using this reaction as the key step, we synthesized (−)-4-*O*-(6′-hydroxy-7′(9′)-dehydro-6′,7′-dihydrogeranyl)coniferol.

1. Introduction

Optically active allylic alcohols have been frequently used as chiral building blocks for the preparation of enantiomerically pure compounds.[1] There are at present various methods for the synthesis of optically active allylic alcohols including the kinetic resolution of racemic allylic alcohols,[2] reductive rearrangement of 2,3-epoxy alcohols by metal,[3] halide[4] and tellurium-based chemistry.[5] To our knowledge, one-pot transformation of 2,3-epoxy alcohols into allylic alcohols, especially via epoxy iodides, is limited to Dorta's method[4e] using a Ph_3P, iodine, imidazole, 2,6-lutidine and water system. Dorta's original method can be successfully applied to the formation of tertiary allylic alcohols, but gives unsatisfactory results in the formation of secondary allylic alcohols.

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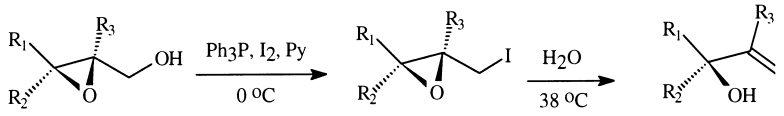
2. Results and discussion

With a view to efficient synthesis, we have developed a facile approach to the synthesis of chiral allylic alcohols, starting from the corresponding 2,3-epoxy alcohol, readily available in one step via Sharpless asymmetric epoxidation[6] (Scheme 1).



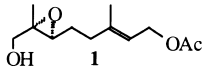
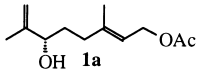
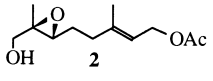
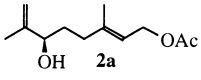
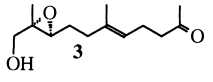
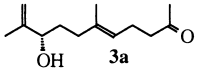
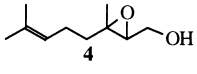
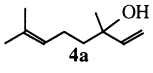
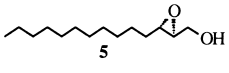
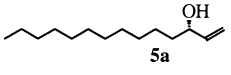
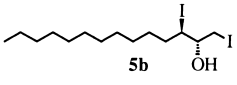
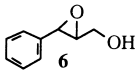
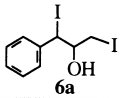
Scheme 1.

In this scheme, the epoxy alcohol is converted in situ into the corresponding epoxy iodide with Ph_3P, iodide and pyridine, which then undergoes reductive elimination by reaction with phosphine hydroxyiodide (prepared in situ by addition of H_2O[7]), to give the allylic alcohol. We have examined this process on a range of substrates (Table 1).

As can be seen from Table 1, the reductive ring opening worked well for trisubstituted 2,3-epoxy alcohol; the allylic alcohols **1a**–**4a** were obtained in excellent yield and good enantiomeric excess (entries 1–4). Entries 1–2 in the Table 1 illustrated that chirality of the epoxides **1**–**2** at C-6 is totally conserved in the allylic alcohols **1a**–**2a**.[8] Under the same conditions (entry 5), the 2,3-disubstituted epoxide **5** gave the rearranged secondary allylic alcohol **5a** in 71% yield and 83% *ee*. In this case, the corresponding iodohydrin **5b** was formed in 28% yield.

To our surprise, 3-phenyloxirane methanol **6** treated under the same conditions (entry 6), gave the

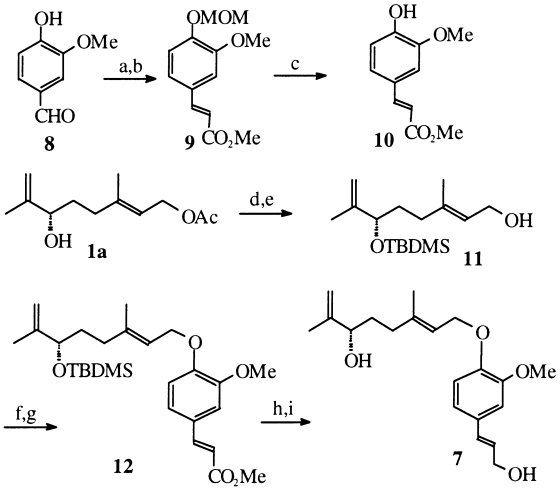
Table 1

Entry	Substrates	Products	Time (h)[a]	Yield (%)[b]	e.e.(%)[c]
1	 **1**	 **1a**	6	91	92
2	 **2**	 **2a**	6	91	91
3	 **3**	 **3a**	6	96	>95
4	 **4**	 **4a**	36	97	-
5	 **5**	 **5a**	30	71	83
		 **5b**		28	-
6	 **6**	 **6a**	4	98	-

a) All the reactions were carried out at 0 °C for 2 h, then 1*eq* H_2O was added into system; b) Isolated yield; c) The enantiomeic excess of the chiral allylic alcohols was measured by 400 MHz ^{1}HNMR analysis of its MTPA ester.

corresponding iodohydrin **6a** in 98% yield. As a consequence of the electronic effect of the phenyl group, the iodine atom reacted at the C-3 position first.

Some Ligularia species have long been used as folk remedies becasue of their antibiotic, antiphlogistic and antitumor activities.[9] Compound **7**,[10] a novel coniferyl alcohol, was isolated from *Ligularia duciformis* (Compoitae). The structure of **7**, determined by spectroscopic techniques, corresponded to 4-*O*-(6′-hydroxy-7′(9′)-dehydro-6′,7′-dihydrogeranyl)-coniferol. However, the absolute configuration at C-6′ was not determined. Herein, we report the total synthesis of (6′*S*)-(−)-**7** from allylic alcohol **1a** (Scheme 2).



Scheme 2. Reagents and conditions: (a) MOMCl, K_2CO_3, acetone, reflux, 1 h, 96%; (b) $Ph_3P{=}CHCO_2CH_3$, PhH, reflux, 2 h, 96%; (c) 3 N HCl, MeOH, reflux, 30 min, 100%; (d) TBDMSCl, imidazole, DMF, rt, 12 h, 97%; (e) K_2CO_3, MeOH, rt, 2 h, 100%; (f) Ph_3P, NCS, THF, rt, 2 h, 89%; (g) **10**, K_2CO_3, acetone, reflux, 8 h, 82%; (h) $LiAlH_4$, Et_2O, 0°C, 12 h, 93%; (i) 1 M n-$Bu_4N^+F^-$/THF, rt, 16 h, 97%

Vanillin **8** was protected with MOMCl, then the Wittig reaction gave the unsaturated ester **9**. Deprotection of the protective group in **9** give the phenol **10**.

Compound **1a** was protected with TBDMSCl, and then the acetyl group was removed. Alcohol **11** was converted to the chloride with NCS/Ph_3P in dry THF.[11] Etherification of chloride was carried out with **10** in K_2CO_3/acetone at reflux. Ether **12** was reduced by $LiAlH_4$ in Et_2O to the corresponding alcohol. Deprotection of silyl ether with 1 M n-$Bu_4N^+F^-$/THF at room temperature[12] gave the title compound **7** in 97% yield as a white solid (mp 83–84°C), $[\alpha]_D^{20}$ −3.93 (*c* 0.89, $CHCl_3$). The spectral data of the title compound **7** was compatible with the assigned structures.

3. Experimental section

^{1}H NMR spectra were recorded on a Varian FT-80A or a Bruker AM-400 spectrometer and ^{13}C NMR spectra were recorded on a 100 MHz spectrometer in $CDCl_3$ solution using TMS as the internal reference. IR spectra were obtained using a FT-170SX (film) spectrophotometer. Mass spectra were measured on a VG ZAB-HS spectrometer by direct inlet at 70 eV, and signals were given in *m/z* with relative intensity (%) in brackets. Optical rotation measurements were carried out on a Perkin–Elmer 141 polarimeter. All solvents were freshly purified and dried by standard techniques prior to use. All reactions were routinely carried out under an inert atmosphere of Ar, and monitored by TLC. Purification of products

was conducted by flash column chromatography (FCG) on silica gel (200–300 mesh) purchased from Qing Dao Marine Chemical Co.

Epoxy alcohols **1**, **2** and **5** were prepared according to the literature;[6a] epoxy alcohol **3** was prepared from (*E*)-geranyl acetone by SeO_2 oxidation, followed by epoxidation with L-(+)-DET, *tert*-butyl hydroperoxide (TBHP) and $Ti(O^iPr_4)$;[6b] (±)-2,3-epoxygeraniol **4** was prepared from the epoxidation of geraniol with $VO(acac)_2$/TBHP;[13] (±)-2,3-epoxy-3-phenylpropan-1-ol **6** was prepared from the epoxidation of cinnamyl alcohol with *m*CPBA.

3.1. General procedure: (2E,6S)-6-hydroxy-7(9)-dehydro-6,7-dihydrogeranyl acetate **1a**

To a stirred solution of epoxy alcohol **1** (228 mg, 1 mmol) in dry Et_2O:CH_3CN (5:3, 8 ml) were added sequentially Ph_3P (786 mg, 3 mmol), pyridine (0.32 ml, 4 mmol) and I_2 (381 mg, 1.5 mmol) at 0°C. After being stirred for 2 h at 0°C, H_2O (18 μl, 1 mmol) was added into the system. The reaction mixture was refluxed for 6 h at 38°C, then 20% $Na_2S_2O_3$ (aq.) (2 ml) and saturated $NaHCO_3$ (aq.) (2 ml) were added to quench the reaction and the organic layer was extracted with ether (3×50 ml). The combined ether extracts were washed with 5% HCl (4×10 ml), saturated $NaHCO_3$ (10 ml), H_2O and brine, then dried. Evaporation of the solvent gave the residue, which was flash chromatographed eluting with pet. ether:ethyl acetate (v/v 6:1) to afford **1a** (194 mg, 91%) as a colorless oil. $[\alpha]_D^{20}$ −26.2 (c 0.6, $CHCl_3$); IR (film): ν_{max}=3472, 3074, 2942, 2861, 1727, 1671, 1650, 1296, 1024, 953, 900 cm^{-1}; EIMS (*m/z*): 213 (0.1%, M+1), 185 (0.1), 152 (1.4), 134 (5), 119 (8), 84 (38), 67 (38), 43 (100), 41 (38); ^{1}H NMR (400 MHz; $CDCl_3$): δ 5.36 (1H, t, J=6.8 Hz, CH=), 4.93, 4.84 (2H, s, CH_2=), 4.57 (2H, d, J=7.0 Hz, CH_2O), 4.04 (1H, t, J=5.6 Hz, CHO), 2.12–2.02 (2H, m, CH_2), 2.04 (3H, s, CH_3), 1.75 (3H, s, CH_3), 1.72 (3H, s, CH_3), 1.68–1.62 (2H, m, CH_2). Anal. calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.54. Found: C, 67.76; H, 9.47.

3.2. Preparation and analysis of Mosher's ester[14]

To a solution of dicyclohexylcarbodiimide (DCC, 17 mg, 83 μmol) and epoxy alcohol **1a** (16 mg, 75 μmol) in 0.5 ml of dry CH_2Cl_2 was added (*S*)-(−)-α-methoxy-β-trifluoromethyl-phenylacetic acid (19 mg, 83 μmol) and a catalytic amount of DMAP. After stirring at room temperature for 24 h, the solution was evaporated in vacuo and the residue was directly chromatographed with pet. ether:ethyl acetate (15:1). The purified Mosher's ester (32 mg, 99%) was analyzed by the 400 MHz ^{1}H NMR spectrum.

3.3. (2E,6R)-6-Hydroxy-7(9)-dehydro-6,7-dihydrogeranyl acetate **2a**

Epoxy alcohol **2** (650 mg, 2.85 mmol) afforded allylic alcohol **2a** (550 mg, 2.59 mmol, 91%) as a colorless oil. $[\alpha]_D^{20}$ +20.8 (c 0.6, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$): δ 5.37 (1H, t, J=6.7 Hz, CH=), 4.94, 4.85 (2H, s, CH_2=), 4.58 (2H, d, J=7.0 Hz, CH_2O), 4.05 (1H, t, J=6.5 Hz, CHO), 2.17–2.02 (2H, m, CH_2), 2.05 (3H, s, CH_3), 1.73 (3H, s, CH_3), 1.72 (3H, s, CH_3), 1.69–1.62 (2H, m, CH_2).

3.4. (5E,9S)-5,10-Dimethyl-9-hydroxy-6,10-undecadienyl-2-one **3a**

Epoxy alcohol **3** (404 mg, 1.79 mmol) afforded allylic alcohol **3a** (361 mg, 1.72 mmol, 96%) as a colorless oil. $[\alpha]_D^{20}$ −14.4 (c 0.9, $CHCl_3$); IR (film): ν_{max}=3451, 3072, 2959, 2861, 1713, 1649, 898 cm^{-1}; EIMS (*m/z*): 210 (0.2%, M), 192 (0.6, M−18), 177 (2), 159 (3), 134 (7), 119 (8), 93 (7), 82 (2), 67 (13), 55 (10), 43 (100); ^{1}H NMR (400 MHz; $CDCl_3$): δ 5.11 (1H, t, J=7.4 Hz, CH=), 4.92, 4.82 (2H, s, CH_2=), 4.02 (1H, t, J=6.4 Hz, CHO), 2.46 (2H, t, J=7.4 Hz, CH_2), 2.28–2.23 (2H, m, CH_2), 2.14 (3H,

s, CH_3), 2.09–1.93 (2H, m, CH_2), 1.71 (3H, s, CH_3), 1.64 (3H, s, CH_3), 1.68–1.55 (2H, m, CH_2). Anal. calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.43; H, 10.48.

3.5. (±)-Linalool **4a**

Epoxy alcohol **4** (340 mg, 2 mmol) afforded linalool **4a** (298 mg, 1.94 mmol, 97%) as a colorless oil. ^{1}H NMR (80 MHz; $CDCl_3$): δ 5.91 (1H, dd, J=17.3, 10.7 Hz, CH=), 5.21 (1H, d, J=17.3 Hz, CH=), 5.11 (1H, t, J=6.7 Hz, CH=), 5.07 (1H, d, J=10.7 Hz, CH=), 2.08–1.94 (2H, m, CH_2), 1.68 (3H, s, CH_3), 1.65 (3H, s, CH_3), 1.58–1.50 (2H, m, CH_2), 1.28 (3H, s, CH_3).

3.6. (3S)-3-Hydroxy-1-tetradecene **5a**

Epoxy alcohol **5** (190 mg, 0.83 mmol) afforded allylic alcohol **5a** (125 mg, 0.59 mmol, 71%) as a colorless oil. $[\alpha]_D^{20}$ +4.5 (c 0.4, $CHCl_3$); IR (film): ν_{max}=3357, 3008, 2925, 1644, 919 cm^{-1}; EIMS (*m/z*): 211 (0.6%, M−1), 194 (0.4, M−18), 183 (13), 166 (2), 109 (12), 85 (33), 57 (100); ^{1}H NMR (400 MHz; $CDCl_3$): δ 5.87 (1H, ddd, J=6.4, 10.4, 17.0 Hz, CH=), 5.22 (1H, d, J=17.2 Hz, CH=), 5.10 (1H, d, J=10.3 Hz, CH=), 4.10 (1H, dt, J=6.34, 6.33 Hz, CHO), 1.55–1.48 (2H, m, CH_2), 1.26 (18H, brs, 9CH_2), 0.88 (3H, t, J=6.6 Hz, CH_3). **5b** (108 mg, 0.23 mmol, 28%). IR (film): ν_{max}=3288, 2921, 2851, 1433, 1179, 1100 cm^{-1}; EIMS (*m/z*): 466 (6%, M), 339 (37), 279 (2), 237 (8), 223 (14), 209 (21), 183 (100), 171 (95), 155 (33), 123 (22), 109 (31), 95 (31), 69 (14), 43 (8); ^{1}H NMR (80 MHz; $CDCl_3$): δ 4.15 (1H, m, CHI), 3.55 (2H, m, CH_2I), 3.34 (1H, m, CHO), 1.55–1.48 (2H, m, CH_2), 1.28 (18H, brs, 9CH_2), 0.89 (3H, t, J=5.8 Hz, CH_3). Anal. calcd for $C_{14}H_{28}OI_2$: C, 36.07; H, 6.05. Found: C, 35.99; H, 6.08.

3.7. 1,3-Diiodo-2-hydroxy-1-phenyl-propane **6a**

Epoxy alcohol **6** (150 mg, 1 mmol) afforded iodohydrin **6a** (382 mg, 0.98 mmol, 98%) as a yellow oil. IR (film): ν_{max}=3520, 3059, 3026, 1599, 1490, 1244, 1117, 1067, 1010, 744, 697 cm^{-1}; EIMS (*m/z*): 388 (0.1%, M), 261 (100, M−127), 253 (2), 183 (8), 133 (18), 105 (36), 91 (51), 77 (18); ^{1}H NMR (80 MHz; $CDCl_3$): δ 7.61–7.28 (5H, m, ArH), 5.26 (1H, t, J=7.8 Hz, CHI), 3.63 (2H, d, J=4.7 Hz, CH_2I), 3.18 (1H, dt, J=4.8, 7.9 Hz, CHO), 2.71 (1H, brs, OH). Anal. calcd for $C_9H_{10}OI_2$: C, 27.86; H, 2.60. Found: C, 27.77; H, 2.56.

3.8. Methyl 4-methoxymethoxy-3-methoxy-cinnamate **9**

A mixture of vanillin **8** (1.54 g, 10 mmol), methoxymethyl chloride (0.81 ml, 11 mmol) and anhydrous K_2CO_3 (3 g) in dry acetone (15 ml) was refluxed for 1 h. The mixture was cooled and filtered. The filtrate was evaporated and the residue was chromatographed on silica gel with pet. ether:ethyl acetate (15:1) to give 4-methoxymethoxy-3-methoxy-benzaldehyde (1.90 g, 9.6 mmol, 96%) as a yellow oil. To a solution of the aldehyde (1 g, 5.05 mmol) in benzene (20 ml) was added (methoxycarbonylmethylene)triphenylphosphorane (2.02 g, 6 mmol), and the mixture was stirred at 80°C for 2 h. The solvent was removed under vacuum and then the residue was chromatographed on silica gel (pet. ether:ethyl acetate 15:1) to give the ester **9** (1.22 g, 4.84 mmol, 96%) as a yellow oil. IR (film): ν_{max}=2977, 1712, 1654, 1598, 1512, 1464, 1257, 1159, 986, 921, 846, 815 cm^{-1}; EIMS (*m/z*): 252 (M, 10%), 222 (11), 206 (2), 176 (4), 147 (3), 119 (2), 89 (3), 77 (4), 45 (100); ^{1}H NMR (80 MHz; $CDCl_3$): δ (ppm) 7.64 (1H, d, J=15.9 Hz, CH=), 7.12 (2H, m, ArH), 7.08 (1H, d, J=1.6 Hz, ArH), 6.33 (1H, d, J=15.9 Hz, CH=), 5.26 (2H, s, OCH_2), 3.91 (3H, s, CH_3), 3.80 (3H, s, CH_3), 3.51 (3H, s, CH_3).

3.9. *Methyl 4-hydroxy-3-methoxy-cinnamate* ***10***

To a solution of compound **9** (504 mg, 2 mmol) in methanol (10 ml) was added 3 N aqueous HCl (2 ml). The mixture was refluxed for 30 min and extracted with Et_2O (50 ml). The organic phase was washed with water, brine and dried over Mg_2SO_4. After evaporation of the solvent, the residue was chromatographed on silica gel (pet. ether:ethyl acetate 6:1) to give the phenol **10** (415 mg, 2 mmol, 100%) as a yellow oil. IR (film): ν_{max}=3484, 3058, 3003, 2950, 1728, 1634, 1595, 1516, 1099, 982, 848, 819 cm^{-1}; EIMS (*m/z*): 208 (M, 100%), 177 (13), 145 (35), 117 (13), 89 (14), 77 (12), 51 (13); ^1H NMR (80 MHz; $CDCl_3$): δ 7.63 (1H, d, J=16.0 Hz, CH=), 7.12 (2H, m, ArH), 6.94 (1H, d, J=1.6 Hz, ArH), 6.30 (1H, d, J=16.0 Hz, CH=), 3.90 (3H, s, CH_3), 3.80 (3H, s, CH_3).

3.10. *(2*E*,6*S*)-6-(*tert*-Butyldimethylsilyloxy)-7(9)-dehydro-6,7-dihydrogreaniol* ***11***

To a solution of alcohol **1a** (228 mg, 1.08 mmol) in dry DMF (1 ml) was added imidazole (82.8 mg, 2.69 mmol) and *tert*-butyldimethylchlorosilane (TBDMSCl, 178.3 mg, 1.18 mmol) at room temperature, and the mixture was stirred at that temperature for 12 h. The reaction mixture was extracted with Et_2O (3×50 ml), the organic phase was washed with H_2O, brine and dried with $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel (pet. ether:ethyl acetate, 20:1) to give silyl ether (341 mg, 1.04 mmol, 97%) as a colorless oil. To a solution of the silyl ether (252 mg, 0.77 mmol) in MeOH (3 ml) was added K_2CO_3 (76 mg, 0.55 mmol) and the reaction mixture was stirred at room temperature for 2 h. After concentration of the MeOH in vacuo, the residue was dissolved in Et_2O (50 ml) and washed with water and brine and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel (pet. ether:ethyl acetate 6:1) to give the alcohol **11** (217 mg, 0.77 mmol, 100%) as a colorless oil. $[\alpha]_D^{20}$ −4.94 (c 1.2, $CHCl_3$); IR (film): ν_{max}=3348, 3072, 2952, 2886, 1669, 1650, 1259, 1081, 1004, 898, 856 cm^{-1}; EIMS (*m/z*): 227 (M−1, 1%), 209 (1), 185 (14), 141 (11), 135 (11), 107 (39), 93 (65), 75 (100), 73 (50), 57 (19), 55 (28), 43 (29), 41 (32); ^1H NMR (400 MHz; $CDCl_3$): δ 5.41 (1H, t, J=6.9 Hz, CH=), 4.86, 4.77 (2H, s, CH_2=), 4.16 (2H, d, J=7.0 Hz, OCH_2), 4.02 (1H, t, J=6.3 Hz, OCH), 2.06–1.93 (2H, m, CH_2), 1.65–1.56 (2H, m, CH_2), 1.67 (6H, s, $2CH_3$), 0.89 (9H, s, $C(CH_3)_3$), 0.04 (3H, s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$). Anal. calcd for $C_{16}H_{32}O_2Si$: C, 67.55; H, 11.34. Found: C, 67.73; H, 11.27.

3.11. *Methyl (2′*E*,6′*S*)-4-*O*-[6′-(*tert*-butyldimethylsilyloxy)-7′(9′)-dehydro-6′,7′-dihydrogeranyl]-coniferate* ***12***

A solution of NCS (117 mg, 0.88 mg) and Ph_3P (231 mg, 0.88 mmol) in anhydrous THF (1 ml) were stirred at room temperature for 30 min. A solution of alcohol **11** (216 mg, 0.76 mmol) in THF (2 ml) was then added dropwise. The reaction mixture was stirred at room temperature for 2 h. The mixture was extracted with Et_2O (50 ml). The organic phase was washed with saturated $NaHCO_3$, water and brine, then dried. The solvent was evaporated and the residue was chromatographed on silica gel (pet. ether:ethyl acetate 15:1) to give the chloride (206 mg, 0.68 mmol, 89%) as a colorless oil. To a mixture of the chloride (206 mg, 0.68 mmol) and phenol **10** (155 mg, 0.75 mmol) in dry acetone (5 ml) was added anhydrous K_2CO_3 (138 mg, 1 mmol) and the mixture was refluxed for 8 h. The mixture was evaporated in vacuo and the residue was chromatographed on silica gel (pet. ether:ethyl acetate 10:1) to give the ester **12** (263 mg, 0.55 mmol, 82%) as a colorless oil. $[\alpha]_D^{20}$ −3.19 (c 1.2, $CHCl_3$); IR (film): ν_{max}=3072, 2951, 2856, 1718, 1636, 1598, 1511, 1464, 1255, 1164, 983, 838 cm^{-1}; EIMS (*m/z*): 417 (M−57, 1%), 345 (2), 323 (3), 307 (4), 267 (52), 265 (54), 250 (43), 219 (12), 208 (100), 185 (18), 135 (10), 107 (12),

93 (20), 75 (8), 73 (9). ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.64 (1H, d, J=16.0 Hz, CH=), 7.08 (1H, dd, J=8.2, 1.7 Hz, ArH), 7.05 (1H, d, J=1.7 Hz, ArH), 6.86 (1H, d, J=8.2 Hz, ArH), 6.32 (1H, d, J=16.0 Hz, CH=), 5.51 (1H, t, J=6.4 Hz, CH=), 4.76, 4.84 (2H, brs, CH_2=), 4.65 (2H, d, J=6.4 Hz, OCH_2), 4.01 (1H, t, J=6.2 Hz, OCH), 3.90 (3H, s, OCH_3), 3.60 (3H, s, OCH_3), 1.97–2.09 (2H, m, CH_2), 1.55–1.65 (2H, m, CH_2), 1.74 (3H, s, CH_3), 1.67 (3H, s, CH_3), 0.88 (9H, s, $C(CH_3)_3$), 0.029, 0.021 (6H, s, $2SiCH_3$). Anal. calcd for $C_{27}H_{42}O_5Si$: C, 68.31; H, 8.92. Found: C, 68.20; H, 8.95.

3.12. (6′S)-4-O-(6′-Hydroxy-7′(9′)-dehydro-6′,7′-dihydrogeranyl)-coniferol **7**

To a solution of $LiAlH_4$ (5 mg, 0.13 mmol) in dry Et_2O (5 ml) was added, dropwise, 1 ml of dry Et_2O solution of ester **12** (82 mg, 0.173 mmol) at 0°C, and the mixture was stirred at 0°C for 12 h. MeOH (0.2 ml) was added to decompose the excess reagent and the reaction mixture was extracted with Et_2O (50 ml). The organic phase was washed with water, followed by brine and then dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel (pet. ether:ethyl acetate 6:1) to give the alcohol (72 mg, 0.161 mmol, 93%) as a colorless oil. To a solution of alcohol (32 mg, 71.7 μmol) was added a 1 M THF solution (0.2 ml) of tetrabutylammonium fluoride (TBAF), and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was then extracted with Et_2O, and the organic phase was washed with water, followed by brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel (pet. ether:ethyl acetate 3:1) to give the title compound (**7**) (23 mg, 69.2 μmol, 97%) as a white solid, mp 83–84°C. $[\alpha]_D^{20}$ −3.93 (c 0.89, $CHCl_3$); IR (film): ν_{max}=3312, 3079, 2940, 2868, 1669, 1651, 1586, 1512, 1452, 1418, 1260, 1198, 1091, 991, 901, 862 cm^{-1}; MS (FAB): 332; EIMS (*m/z*): 180 (100%), 152 (7), 137 (33), 124 (25), 107 (6), 91 (8), 77 (5), 55 (8). ^{1}H NMR (400 MHz; $CDCl_3$): δ 6.94 (1H, d, J=1.3 Hz, ArH), 6.90 (1H, dd, J=8.2 Hz, 1.3 Hz, ArH), 6.83 (1H, d, J=8.2 Hz, ArH), 6.54 (1H, d, J=15.8 Hz, CH=), 6.24 (1H, dt, J=15.8, 5.8 Hz, CH=), 5.54 (1H, t, J=6.2 Hz, CH=), 4.92, 4.84 (2H, brs, CH_2=), 4.62 (2H, d, J=6.2 Hz, CH_2O), 4.30 (2H, d, J=5.8 Hz, CH_2O), 4.03 (1H, t, J=5.8 Hz, CHO), 3.88 (3H, s, OCH_3), 2.01–2.07 (2H, m, CH_2), 1.62–1.69 (2H, m, CH_2), 1.74 (3H, s, CH_3), 1.72 (3H, s, CH_3). ^{13}C NMR (100 MHz; $CDCl_3$): δ 149.50, 148.07, 147.29, 140.38, 131.15, 129.81, 126.48, 119.95, 119.52, 113.14, 111.13, 109.14, 75.39, 65.81, 63.77, 55.60, 35.40, 32.68, 17.51, 16.69. Anal. calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.11; H, 8.46.

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