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LIGNANS. 13. TOTAL SYNTHESES OF (-)-CARINOL, (-)-CARISSANOL AND (-)-HYDROXYTHUJAPLICATIN METHYL ETHER[+]

Kenza Khamlach, Robert Dhal, and Eric Brown*

Laboratoire de Synthèse Totale de Produits Naturels (URA CNRS 482),
Faculté des Sciences, Route de Laval, BP 535, 72017 Le Mans, France

Abstract - *The title compounds were obtained by α-hydroxylation of the* corresponding optically active α,β-dibenzyl-γ-butyrolactones, followed by chemical reduction of the lactonic ring and/or catalytic hydrogenolysis of the O-benzyl protecting groups.

There are numerous examples of lignans belonging to the trans-α,β-dibenzyl-γ-butyrolactone series.[1] A few representatives typically bear a hydroxyl group in the α position with respect to the carbonyl, as exemplified by (-)-trachelogenin (**1**), a potent calcium antagonist,[1b] and whose total synthesis we recently described.[2] As a continuation of our work on optically active lignans, we describe here the total syntheses of three natural compounds belonging to the trachelogenin group, namely (-)-carinol (**5**), (-)-carissanol (**7**), and (-)-hydroxythujaplicatin methyl ether (**11**).

Synthetic (-)-O-dibenzylnortrachelogenin (**2**),[2] $[\alpha]_D$ -26° ($CHCl_3$), was treated with a *twentyfold* molar excess of lithium aluminium hydride in a boiling mixture of THF and ether, and this furnished chromatographically pure (-)-O-dibenzylcarinol (**4**) as an amorphous solid, $[\alpha]_D$ -15° ($CHCl_3$) in 60% yield. When the same reduction was carried out at room temperature using a tenfold excess of lithium aluminium hydride, the diol (**4**) was obtained together with the lactol (**6**). Catalytic *hydrogenolysis of the benzyl ether groups of* **4** was carried out in EtOH/AcOEt in the presence of 10% Pd/ C at room temperature under moderate pressure, and gave after chromatography an 88% yield of (-)-carinol (**5**) as an amorphous solid, $[\alpha]_D$ -21.9° (EtOH) [Lit.[3] $[\alpha]_D$ -23° (EtOH)]. The ^{13}C and ^{1}H-nmr (acetone-d_6) data of synthetic (-)-**5** were in agreement with the data reported by Achenbach and coworkers [3] for the natural compound isolated from Carissa edulis. On account of the 8'-OH, the nmr signals of the 9'-H protons of **5** appeared at δ 3.44 and 3.50 ppm as two doublets (J = 11.1 Hz) of an AB system, whereas the 9-H protons appeared at δ 3.6 and 3.74 ppm as two doublets of doublets of an ABX system.

The carbonyl group of (-)-O-dibenzylnortrachelogenin (**2**)[2] was next reduced with diisobutylaluminium hydride in toluene at low temperatures, thus giving (-)-O-dibenzylcarissanol (**6**) as a crystalline solid, $[\alpha]_D$ -22.7° ($CHCl_3$), in 81% yield. Catalytic hydrogenolysis of the benzyl groups of **6** was *carried out as above, and after chromatography (-)-carissanol* (**7**) *was obtained as an* amorphous solid, $[\alpha]_D$ -12.9° (EtOH) in 81% yield [Lit.[3] $[\alpha]_D$ -14° (EtOH)]. The ^{13}C and ^{1}H-nmr (acetone-d_6) data of synthetic (-)-**7** were in agreement with the data reported by Achenbach[3] for the natural compound isolated from C. edulis. On account of the lactol group, the fact that the compound (**7**) is a mixture of epimers in solution was confirmed by examination of the ^{1}H and ^{13}C-nmr spectra. The signals of the epimeric 9'-H protons of **7** appeared at δ 4.92 (d, J = 3.9 Hz)

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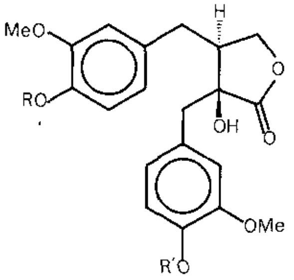
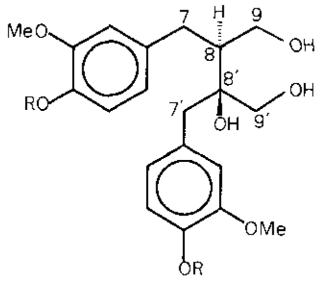
and δ 5.15 ppm, and the corresponding signals of the 9'-C carbons appeared at δ 101.4 and 104.4 ppm.

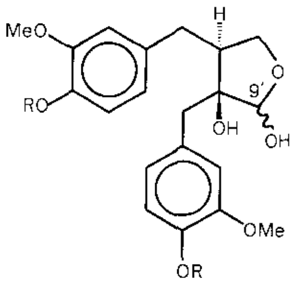
Synthetic (−)-O-dibenzylthujaplicatin methyl ether (8),[4] mp 90-92°C and $[\alpha]_D$ −20.5° ($CHCl_3$), was treated with 1.5 equivalent of lithium hexamethyldisilazide (LHDS) in the presence of 1 equivalent of 12-crown-4 and 1 equivalent of triethyl phosphite in benzene at room temperature, and dry oxygen was bubbled through the reaction mixture for 3 h. After treatment with aqueous NH_4Cl, the mixture was worked up and the reaction products were isolated by column chromatography over silica gel. This afforded approximately equimolecular amounts of the 8'α-hydroxylated epimers ((−)-**9**) (29% yield, amorphous solid), $[\alpha]_D^{34}$ −28.5° ($CHCl_3$) and ((−)-**10**) (26% yield, crystalline), $[\alpha]_D^{34}$ −15.3° ($CHCl_3$). Catalytic hydrogenolysis of the benzyl ether groups of **9** was carried out as above, and after chromatography afforded (−)-hydroxythujaplicatin methyl ether (**11**) as an amorphous solid, $[\alpha]_D^{30}$ −62.9° ($CHCl_3$) in 65% yield [Lit.[5] $[\alpha]_D^{25}$ −54,8° ($CHCl_3$)]. The ir and ^{1}H-nmr data of synthetic (**11**) were in agreement with the data reported for the natural compound isolated from *Thuja plicata* D. by Maclean and coworkers.[5] The nmr signals of the 9-H protons of **11**, on account of a second order coupling, appeared as an unresolved doublet at δ 4.05 ppm, and the isolated 7'-H protons appeared at δ 2.90 and 3.10 ppm as two doublets (J = 13.6 Hz) of an AB system. Moreover, the fact that compound (**11**) and the structurally related (−)-nortrachelogenin (**3**) have indeed the same relative configuration was confirmed by the similitude of the patterns exhibited, in ^{1}H-nmr, by the protons of the aliphatic parts of their molecules. Finally, catalytic hydrogenolysis of the O-benzyl groups of the epimer (**10**) was carried out as above, and after chromatography afforded (+)-epihydroxythujaplicatin methyl ether (**12**) as an amorphous solid, $[\alpha]_D^{27}$ +3.6° ($CHCl_3$) in 73% yield. Unlike the *trans*-α,β-dibenzyl-γ-lactone (**11**), the nmr signals of the 7'-H protons of the *cis*-epimer (**12**) appeared as a sole broad singlet at δ 2.96 ppm.



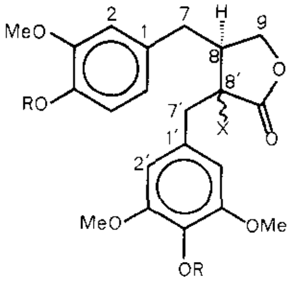
1 R = Me ; R' = H
2 R = R' = Bn
3 R = R' = H



4 R = Bn
5 R = H



6 R = Bn
7 R = H



8 X = β-H ; R = Bn
9 X = β-OH ; R = Bn
10 X = α-OH ; R = Bn
11 X = β-OH ; R = H
12 X = α-OH ; R = H

Bn = $PhCH_2$

EXPERIMENTAL

The ir spectra were recorded on a Nicolet 5DX spectrophotometer. The nmr spectra were recorded on a Varian EM 390 spectrometer for ^{1}H and a Varian FT 80 for ^{13}C. The ms were

recorded by "Centre Régional de Mesures Physiques de l'Ouest" (Rennes). Elemental analyses were carried out by "Centre de Microanalyse du CNRS" (Lyon-Vernaison and Gif-sur-Yvette). Optical rotations were determined using a Perkin-Elmer 241 micropolarimeter.
Abbreviation : LHDS, lithium hexamethyldisilazide.

(-)-O-Dibenzylcarinol (**4**)

A molar solution of $LiAlH_4$ in ether (13.5 ml) was poured into a 50-ml, 3-necked flask equipped with a reflux condenser, a magnetic stirrer and an argon inlet, followed by the addition of (-)-O-dibenzylnortrachelogenin (**2**), [2] $[\alpha]_D$ -26° (c 1, $CHCl_3$) (374 mg, 0.675 mmol) in THF (15 ml). After heating under reflux for 5 h, AcOEt (1.5 ml) was added, followed successively by H_2O (0.5 ml), 15% sodium hydroxide solution (0.5 ml) and H_2O (1.5ml). The aluminium salts were *removed by filtration and were washed with* CH_2Cl_2 *(4 x 10 ml). The organic solutions were* pooled, dried ($MgSO_4$) and evapored under reduce pressure. The oily residue was chromatographed over silica gel (10 g), using CH_2Cl_2/MeOH (99:1) for the elution, and afforded amorphous (-)-O-dibenzylcarinol (**4**) (226 mg, 60%), $[\alpha]_D$-15° (c 1.9, $CHCl_3$). Anal. Calcd for $C_{34}H_{38}O_7$: C, 73.10 ; H, 6.86 ; O, 20.05. Found : C, 73.16 ; H, 6.75 ; O, 19.79. Ir (ν_{max}, KBr) : 3400 (OH), 1606, 1512 (C=C), 1262, 1228, 1142 and 1034 cm^{-1}. ^1H-Nmr ($CDCl_3$) (δ, ppm) : 7.44 (10H, m, H arom.); 6.65-6.91 (6H, m, H arom.); 5.13 (4H, s, $PhC\underline{H}_2O$); 3.83 and 3.85 (6H, s, OCH_3); 3.63 (2H, m, 9-H); 3.46 (2H, m, 9'-H); 2.0-3.03 (8H, m, 7-H, 7'-H, 8-H and OH).

(-)-Carinol (**5**)

A solution of (-)-O-dibenzylcarinol (**4**) (285 mg, 0.51 mmol) in a 1:1 mixture (25 ml) of EtOH and AcOEt was poured into a hydrogenation flask, followed by the addition of a 10% Pd-charcoal catalyst (30 mg). After stirring for 3 h at room temperature under a hydrogen pressure of 3 bars, the catalyst was removed by triple filtration and the solvents were evaporated under reduced pressure. The oily residue was purified by chromatography over silica gel (40 g), using CH_2Cl_2/MeOH (97:3) for the elution, and gave amorphous (-)-carinol (**5**) (170 mg, 88%), $[\alpha]_D^{24}$ -21.9° (c 0.41, EtOH). Lit.[3] $[\alpha]_D$ -21° (c 0.5, EtOH) and $[\alpha]_D^{20}$ -23° (c 0.4, EtOH). Ms, Found : 378.1681. Calcd for $C_{20}H_{26}O_7$: 378.1678. ^1H-Nmr (300 MHz) (acetone-$\underline{d}_6$) (δ, ppm) : 7.00 (1H, d, $J_{2'-6'}$ = 1.8 Hz, 2'-H); 6.85 (1H, d, J_{2-6} = 1.6 Hz, 2-H); 6.81 (1H, dd, $J_{6'-2'}$ = 1.8 Hz, $J_{6'-5'}$ = 8 Hz, 6'-H); 6.74 (2H, d, J = 8 Hz, 5,5'-H ; 6.70 (1H, dd, J_{6-2} = 1.7 Hz, J_{6-5} = 8.1 Hz, 6-H) ; 3.82 (6H, s, OCH_3) ; 3.74 (1H, dd, J_{9A-B} = 2.4 Hz, J_{AB} = 11.1 Hz, 9A-H) ; 3.60 (1H, dd, J_{9B-8} = 5.4 Hz ; J_{AB} = 11.1 Hz, 9B-H) ; 3.50 (1H, d, J_{AB} = 11.1 Hz, 9'A-H) ; 3.44 (1H, d, J_{AB} = 11.1 Hz, 9'B-H) ; 3.02 (1H, dd, J_{7A-8} = 2.7 Hz ; J_{AB} = 13.6 Hz, 7A-H) ; 2.93 (2H, s, 7'-CH_2) ; 2.70-3.10 (3H, broad s, OH) ; 2.58 (1H, dd, J_{7B-8} = 11.6 Hz, J_{AB} = 13.6 Hz, 7B-H) ; 1.97 (1H, m, 8-H). ^{13}C-Nmr (acetone-$\underline{d}_6$) (δ, ppm) : 148.2 (s, 3-C) ; 147.8 (s, 3'-C) ; 145.9 (s, 4'-C) ; 145.6 (s, 4-C) ; 134.0 (s, 1-C) ; 130.0 (s, 1'-C) ; 124.3 (d, 6'-C) ; 122.5 (d, 6-C) ; 115.5 (d, 5,5'-C) ; 115.2 (d, 2'-C) ; 113.6 (d, 2-C) ; 77.4 (s, 8'-C) ; 65.4 (t, 9'-C) ; 60.5 (t, 9-C) ; 56.3 (q, OCH_3) ; 49.2 (d, 8-C) ; 41.5 (t, 7'-C) ; 32.0 (t, 7-C). These nmr spectra are in agreement with the literature.[3]

O-Dibenzylcarissanol (**6**)

A solution of (-)-O-dibenzylnortrachelogenin (**2**)[2] (221 mg, 0.4 mmol) in dry toluene (10 ml) was poured into a thoroughly dried 50-ml, 3-necked flask equipped with a magnetic stirrer. The solution was cooled to -78°C and 1.5 M diisobutylaluminium hydride in toluene (0.81 ml, 1.21 mmol) was slowly added by means of a syringe. After stirring at -78°C for 2.5 h, the excess hydride was destroyed with cold MeOH. After allowing the reaction mixture to reach room temperature, ether (2.5 ml) was added, followed successively by saturated NaCl solution (2.5 ml), distilled water (2.5 ml), 6N HCl (0.3 ml) and ether (3.5 ml). The organic phase was decanted and the aqueous phase was extracted with CH_2Cl_2 (4 x 15 ml). After drying the organic solutions over $MgSO_4$, followed by evaporation under reduced pressure, the colourless residual oil was crystallized from a CH_2Cl_2/ether mixture, thus affording the compound **(6)** (180 mg, 81%) as a white solid, mp 123-125°C and $[\alpha]_D^{24}$ -22.7° (c 0.7, $CHCl_3$). Anal. Calcd for $C_{34}H_{36}O_7$: C, 73.36 ; H, 6.52 ; O, 20.12. Found: C, 73.35 ; H, 6.53 ; O, 20.21. Ms, Found : 556.2476. Calcd for $C_{34}H_{36}O_7$: 556.2461. Ir (ν_{max}, KBr) : 3419 (OH), 1606, 1514 (C=C), 1263, 1229, 1139, 1033 and 1010 cm^{-1}. ^{1}H-Nmr ($CDCl_3$) (δ, ppm) : 7.27-7.53 (10H, m, H arom.) ; 6.62-6.90 (6H, m, H arom.) ; 5.13 (4H, s, $PhCH_2O$) ; 3.88 (6H, s, OCH_3) ; 3.67 (2H, m, 9-H) ; 3.47 (2H, m, OH) ; 2.67-2.91 (5H, m, 7-H, 7'-H and 8-H).

(-)-Carissanol **(7)**

A 10% Pd-charcoal catalyst (25 mg) was added to a solution of O-dibenzylcarissanol **(6)** (217 mg, 0.39 mmol) in a 1:1 EtOH/AcOEt mixture (20 ml), and the resulting suspension was stirred at room temperature for 3 h under a pressure of hydrogen of 3 bars. The catalyst was then removed by triple filtration and the solvents were evapored under reduced pressure. The oily residue was chromatographed over silica gel (30 g), using a CH_2Cl_2/MeOH (98:2) mixture for the elution, and afforded (-)-carissanol **(7)** (119 mg, 81%) as an amorphous solid, $[\alpha]_D^{24}$ -12.9° (c 0.12, EtOH). Lit.[3] $[\alpha]_D$ -14° (c 0.7, EtOH). Ms, Found : 376.1537. Calcd for $C_{20}H_{24}O_7$: 376.1522. ^{1}H-Nmr (300 MHz) (acetone-d_6) (δ, ppm) : 7.39 and 7.22 (2H, s, ArOH) ; 6.55-7.05 (6H, m, H arom.) ; 5.49 and 5.15 (each 1H, d, 9'-OH) ; 5.15 and 4.92 (each 1H, d, J = 3.9 Hz, 9'-H) ; 3.85, 3.84, 3.83 and 3.82 (6H, 4s, OCH_3) ; 3.55-3.90 (2H, m, 9-H) ; 2.40-3.05 (4H, m, 7,7'-H) ; 2.30 (1H, m, 8-H). ^{13}C-Nmr (acetone-d_6) (δ, ppm) : 148.3 (s, 3-C) ; 147.9 and 147.8 (2s, 3'-C) ; 146.2 and 145.9 (2s, 4'-C) ; 145.7 (s, 4-C) ; 133.5 and 133.2 (2s, 1-C) ; 130.2 and 129.4 (2s, 1'-C) ; 124.2 and 124.0 (2d, 6'-C) ; 121.8 (d, 6-C) ; 115.7 (d, 5-C) ; 115.4 and 115.1 (2d, 2'-C) ; 115.2 (d, 5'-C) ; 113.1 and 113.0 (2d, 2-C) ; 104.4 and 101.4 (2d, 9'-C) ; 82.8 and 79.6 (2s, 8'-C) ; 72.9 and 71.3 (2t, 9-C) ; 56.3 and 56.2 (q, OCH_3) ; 47.0 and 48.3 (2d, 8-C) ; 40.1 and 43.9 (2t, 7'-C) ; 33.3 and 32.8 (2t, 7-C).

(-)-O-Dibenzylhydroxythujaplicatin methyl ether **(9)** and (-)-O-dibenzyl-8'-epihydroxythujaplicatin methyl ether **(10)**

A solution of LHDS (2.8 ml, 3.17 mmol) in benzene (20 ml) was prepared in a dried 100-ml, 3-necked flask equipped with a magnetic stirrer, an argon inlet (open) and an oxygen inlet (shut). A solution of synthetic (-)-O-dibenzylthujaplicatin methyl ether **(8)**,[4] (1.2 g, 2.11 mmol), mp 90-92°C and $[\alpha]_D$ -20.5° (c 1, $CHCl_3$), in benzene (25 ml) was then slowly run in. After stirring for 2 h at room temperature, the argon inlet was shut, and 12-crown-4 (0.34 ml, 2.11 mmol) was added followed by triethyl phosphite (0.36 ml, 2.11 mmol). Dry oxygen was then bubbled through the reaction mixture for 3 h, after which the latter was treated with a saturated solution of NH_4Cl (20 ml), and was extracted with AcOEt (4 x 30 ml). The organic phases were dried ($MgSO_4$) and evapored under reduced pressure. The starting material (**8**, 265 mg) was recovered by chromatography of the final residue over silica gel (30 g, elution with CH_2Cl_2/ether (97:3)). The mixture of the two epimeric alcohols (**9+10**) (580 mg) was next separated by chromatography over silica gel (40 g), using a toluene/AcOEt mixture (95:5) for the elution, thus affording amorphous (-)-O-dibenzylhydroxythujaplicatin methyl ether **(9)** (277 mg, 29% yield, based upon the consumed starting material), $[\alpha]_D^{34}$ -28.5° (c 0.91, $CHCl_3$), and (-)-O-dibenzyl-8'-epihydroxythujaplicatin methyl ether **(10)** (255 mg, 26.5%), mp 138-139.5°C (EtOH) and $[\alpha]_D^{34}$ -15.3° (c 0.82, $CHCl_3$). O-Dibenzylhydroxythujaplicatin methyl ether **(9)** : Anal. Calcd for $C_{35}H_{36}O_8$: C, 71.90 ; H, 6.20 ; O, 21.89. Found : C, 71.60 ; H, 6.42 ; O, 22.06. Ms, Found : 584.2405. Calcd for $C_{35}H_{36}O_8$: 584.2410. Ir (ν_{max}, KBr) : 3450 (OH), 1773 (C=O), 1591 and 1509 (C=C), 1263, 1235, 1126 and 1022 cm^{-1}. ^{1}H-Nmr ($CDCl_3$) (δ, ppm) : 7.33-7.63 (10H, m, H arom.) ; 7.57-6.93 (4H, m, H arom.) ;

6.50 (2H, s, H arom.) ; 5.25 and 5.07 (4H, 2s, PhC$\underline{H}_2$O) ; 4.19 (1H, m, 9A-H) ; 3.90 (4H, s, 9B-H and OCH_3) ; 3.82 (6H, s, OCH_3) ; 2.62-3.23 (6H, m, OH, 7-H, 7′-H and 8-H). O-Dibenzyl-8′-epihydroxythujaplicatin methyl ether (**10**) : Anal. Calcd for $C_{35}H_{36}O_8$: C, 71.90 ; H, 6.20 ; O, 21.89. Found : C, 71.92 ; H, 6.27 ; O, 22.10. Ms, Found : 584.2399. Calcd for $C_{35}H_{36}H_8$: 584.2410. Ir (ν_{max}, KBr) : 3538 (OH), 1796 (C=O), 1589 and 1514 (C=C), 1265, 1238, 1130 and 1085 cm^{-1}. ^{1}H-Nmr ($CDCl_3$) (δ, ppm) : 7.35-7.62 (10H, m, H arom.) ; 6.63-6.93 (3H, m, H arom.) ; 6.43 (2H, s, H arom.) ; 5.20 and 5.07 (4H, 2s, PhC$\underline{H}_2$O) ; 4.07 (2H, d, J = 6 Hz, 9-H) ; 3.88 (3H, s, OCH_3) ; 3.78 (6H, s, OCH_3) ; 2.47-3.07 (6H, m, OH, 7-H, 7′-H and 8-H).

(–)-Hydroxythujaplicatin methyl ether (**11**)

A 10% Pd-charcoal catalyst (30 mg) was added to a solution of (–)-O-dibenzylhydroxythujaplicatin methyl ether (**9**) (246 mg, 0.42 mmol) in a 1:1 EtOH/AcOEt mixture (20 ml), and the *resulting suspension was stirred at room temperature* for 3 h under a pressure of hydrogen of 3 bars. After removal of the catalyst and the solvents, the residual oil was chromatographed over silica gel using CH_2Cl_2/ether (95:5), and afforded (–)-hydroxythujaplicatin methyl ether (**11**) (110 mg, 64.8%) as an amorphous solid, $[\alpha]_D^{30}$-62.9° (c 2.2, $CHCl_3$). Lit.[5] $[\alpha]_D^{25}$-54.8° (c 0.88, $CHCl_3$). Anal. Calcd for $C_{21}H_{24}O_8$; C, 62.37 ; H, 5.98 ; O, 31.65. Found : C, 62.40 ; H, 5.90 ; O, 31.69. Ms, Found : 404.1475. Calcd for $C_{21}H_{24}O_8$: 404. 1471. Ir (ν_{max}, KBr) : 3432 (OH), 1762 (C=O), 1617, 1518 (C=C), 1273, 1238, 1217, 1114 and 1029 cm^{-1}. ^{1}H-Nmr (300 MHz) ($CDCl_3$) (δ, ppm) : 6.85 (1H, d, J = 7.9 Hz, 5-H) ; 6.66 (1H, dd, J = 1.9 Hz and 7.9 Hz, 6-H) ; 6.63 (1H, d, J = 1.9 Hz, 2-H) ; 6.36 (2H, s, 2′,6′-H) ; 5.52 and 5.46 (2H, 2s, 4,4′-OH) ; 4.05 (2H, m, 9-H) ; 3.86 (3H, s, OCH_3) ; 3.85 (6H, s, OCH_3) ; 3.10 (1H, d, J = 13.6 Hz, 7′A-H) ; 2.95 (1H, dd, J_{7A-8} = 9.6 Hz, J_{AB} = 18.2 Hz, 7A-H) ; 2.90 (1H, d, J = 13.6 Hz, 7′B-H) ; 2.53 (2H, m, 7B-H and 8-H) ; 2.41 (1H, s, 8′-OH).

(+)-8′-Epihydroxythujaplicatin methyl ether (**12**)

A 10% Pd-Pt-charcoal catalyst (20 mg) was added to a solution of O-dibenzyl-8′-epihydroxythujaplicatin methyl ether (**10**) (188 mg, 0.3 mmol) in an EtOH/AcOEt mixture (1:1) (20 ml), and the resulting suspension was hydrogenated for 16 h at room temperature under a pressure of 3 bars. After removal of the catalyst and the solvents, the crude reaction product was purified by chromatography over silica gel (CH_2Cl_2/ether 95:5), and afforded (+)-8′-epihydroxythujaplicatin methyl ether (**12**) (95 mg, 73 %) as an amorphous solid, $[\alpha]_D^{27}$ +3.6° (c 0.69, $CHCl_3$). Anal. Calcd for $C_{21}H_{24}O_8$: C, 62.37 ; H, 5.98 ; O, 31.65. Found : C, 62.21 ; H, 5.87 ; O, 31.61. Ms, Found : 404.1475. Calcd for $C_{21}H_{24}O_8$: 404.1471. Ir (ν_{max}, KBr) : 3485 and 3407 (OH), 1786 (C=O), 1615 and 1514 (C=C), 1259, 1240, 1219, 1114, 1093, 1033 and 1022 cm^{-1}. ^{1}H-Nmr (300 MHz) ($CDCl_3$) (δ, ppm) : 6.86 (1H, d, J = 7.9 Hz, 5-H) ; 6.69 (1H, d, J = 1.8 Hz, 2-H) ; 6.66 (1H, dd, J = 2Hz and 7.9 Hz, 6-H) ; 6.45 (2H, s, 2′,6′-H) ; 5.54 and 5.50 (2H, 2s, 4,4′-OH) ; 4.20 (1H, dd, J_{9A-8} = 7.8 Hz, J_{AB} = 9.1 Hz, 9A-H) ; 3.98 (9H, s, OCH_3) ; 3.98 (1H, m, 9B-H) ; 3.14 (1H, dd, J_{7A-8} = 4 Hz, J_{AB} = 13.5 Hz, 7A-H) ; 2.96 (2H, s, 7′-H) ; 2.95 (1H, m, 8-H) ; 2.74 (1H, s, 8′-H) ; 2.66 (1H, dd, J_{7B-8} = 11.5Hz, J_{AB} = 13.5Hz, 7B-H).

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