Concise Stereoselective Total Synthesis of Leiocarpin C

by **Dasireddi Chandra Rao**, **Vanam Shekhar**, **Dorigondla Kumar Reddy**, **Baggu Chinnababu**, and **Yenamandra Venkateswarlu***[†1])

Division of Natural Products Chemistry, Natural Products Laboratory, Indian Institute of Chemical Technology, Hyderabad – 500007, India
(phone: +91-40-27191881; fax: +91-40-27160512; e-mail: suresh@iict.res.in)

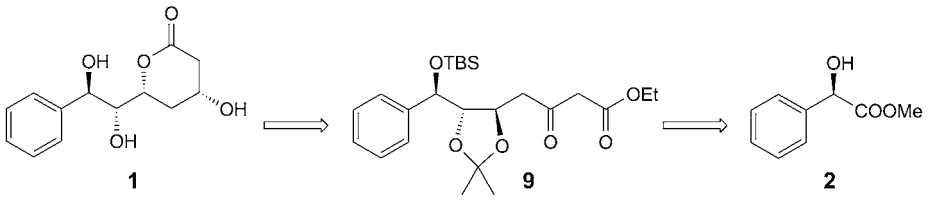
A simple and highly concise strategy has been developed for the stereoselective total synthesis of leiocarpin C starting from commercially available mandelic ester. The strategy utilizes the OsO_4-catalyzed *cis*-hydroxylation and selective reduction with *K-Selectride* as key steps.

Introduction. – The styryl lactones have become a hot topic of phytochemistry and oncopharmacology after taxol. The genus *Goniothalamus* (Annonaceae) comprises a broad spectrum of styryl lactones, and its species were widely used as traditional medicines in China as antalgic and pesticide agents [1]. The extract of the seeds of *Goniothalamus amuyon* has been employed for the treatment of edema and rheumatism [2]. Other general applications include their use as painkillers and mosquito repellents. Taking into account their medicinal properties [3], these plants are considered a potential source of antitumor, antifungal, and antibiotic agents [4]. Leiocarpin C (**1**) is a natural styryl lactone, which was isolated from the stem bark of the tropical plant *Goniothalamus leiocarpus* [5]; it possesses significant cytotoxic activity against several human tumor cell lines [6]. The synthesis of styryl lactones is of considerable interest due to the prevalence of these structures in natural products as biologically active compounds. Our continued interest in the total synthesis of lactones [7] prompted us to undertake the synthesis of leiocarpin C (**1**). Three cumbersome syntheses were reported in the literature for the synthesis of **1** [8]. Herein, we report a simple synthesis of **1** using *cis*-dihydroxylation with OsO_4 [7a][9] and selective 1,3-*anti*-reduction with *K-Selectride* [10], starting from commercially available methyl (*R*)-mandelate (= methyl (*R*)-2-hydroxy-2-phenylylacetate; **2**).

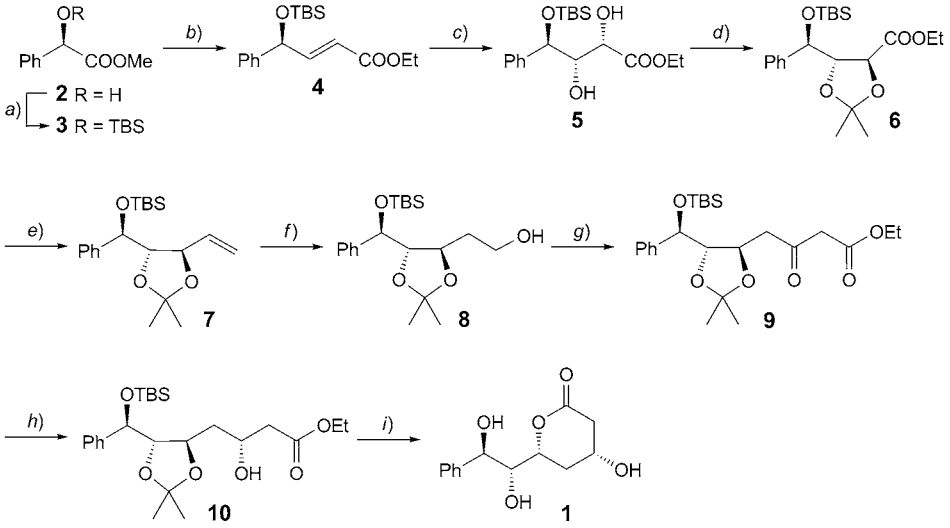
Results and Discussion. – The retrosynthetic analysis for leiocarpin C (**1**) is depicted in *Scheme 1*. As shown in *Scheme 2*, the secondary OH group of **2** was protected with the (*tert*-butyl)(dimethyl)silyl (TBS) group using TBSCl and 1*H*-imidazole in anhydrous CH_2Cl_2 to afford silyloxy derivative **3**, which was reduced with DIBAL-H at $-78°$ to give the corresponding aldehyde 90% yield. The aldehyde was subjected to C_2 homologation with ethyl (triphenylphosphoranylidene)acetate in anhydrous toluene to furnish the *Wittig* product, *i.e.*, α,β-unsaturated ester **4** with (*E*)-configuration in

[1]) Deceased July 17, 2013; correspondence should be addressed to Dr. *K. Suresh Babu* (phone: +91-40-27181881; e-mail: suresh@iict.res.in)

Scheme 1. *Retrosynthetic Analysis*



Scheme 2



a) (^{t}Bu)Me$_2$SiCl (TBSCl), 1*H*-Imidazole, dry CH_2Cl_2, 3 h, r.t.; 95%. *b*) 1. DIBAL-H (= Diisobutylaluminium hydride), dry CH_2Cl_2, $-78°$, 30 min; 2. Ph_3PCHCO_2Et, dry toluene, 6 h, r.t.; 93.5% (over two steps). *c*) OsO_4, *N*-methylmorpholine *N*-oxide (NMO), acetone/H_2O 5:1, r.t., 8 h; 90%. *d*) Pyridinium *p*-toluenesulfonate (PPTS), acetone, 2,2-dimethoxypropane, 12 h; 93%. *e*) 1. DIBAL-H, dry CH_2Cl_2, $-78°$, 30 min; 90%; 2. PPh_3CH_3I, ^{t}BuOK THF, 0° to r.t., 15 min; 90%. *f*) BH_3·DMS, THF, 0° to r.t., 4 h, then 20% NaOH, 30% H_2O_2, 3 h; 89%. *g*) 1. 2-Iodoxybenzoic acid (IBX), DMSO, r.t., 3 h; 90%; 2. N_2CHCO_2Et, $SnCl_2$, dry CH_2Cl_2, 2 h; 89%. *h*) 1. *K-Selectride*, THF, $-78°$, 2 h; 2. $LiEt_3BH$, $-78°$, 1 h; 90%. *i*) TsOH, MeOH, r.t., 3 h; 75%.

92% yield. Compound **4** was reacted with a catalytic amount of OsO_4 in the presence of excess *N*-methylmorpholine *N*-oxide in acetone/H_2O 5:1 to afford α,β-dihydroxy ester **5**. The reaction afforded high *anti*-selectivity (*anti*/*syn* 90:10) [7a][9] with respect to the existing stereogenic center, and the *anti*-isomer **5** was separated chromatographically in 90% yield. The dihydroxy ester **5** was masked as acetonide using 2,2-dimethoxypropane in the presence of a catalytic amount of TsOH to give compound **6** in 93% yield, which was reduced with DIBAL-H, at $-78°$ to furnish the corresponding aldehyde in good yield. The latter was further subjected to a C_1 *Wittig* reaction to give the olefin **7**, which was selectively hydroborated to yield the primary alcohol **8** using

$BH_3 \cdot DMS$ in THF. Oxidation of **8** resulted in the corresponding aldehyde in 90% yield, which was converted into β-keto ester **9** (89% yield) by the reaction with ethyl diazoacetate in the presence of a catalytic amount of $SnCl_2$. The stereoselective reduction of the ketone formation in compound **9** by using *K-Selectride* gave compound **10** with *anti*-configuration [10]. Finally, reaction of **10** with TsOH in MeOH at room temperature afforded leiocarpin C (**1**) by concomitant deprotecting of the acetonide, and the TBS groups, followed by cyclization in one pot. The physical and spectroscopic data of compound **1** were found to be identical with those reported for the natural product leiocarpin C ($[\alpha]_D^{25} = -62.5$ ($c = 0.5$, $CHCl_3$)) [5][8].

Conclusions. – In conclusion, we have accomplished the total synthesis of leiocarpin C (**1**) starting from methyl (*R*)-mandelate (**2**) employing the OsO_4-catalyzed *cis*-hydroxylation and selective reduction with *K-Selectride* as key steps. This synthetic sequence provides an easy preparation of **1** in nine steps with 28% overall yield, compared with earlier reported overall yields of 4.6 and 24.5%, respectively [8].

The authors are grateful to *MoES* and *CSIR*, New Delhi, India, for the financial support, and to the Director, Indian Institute of Chemical Technology (IICT), for his constant encouragement.

Experimental Part

General. Solvents were dried over standard drying agents and freshly distilled prior to use. The reagents were purchased from *Aldrich* and *Across*, and were used without further purification unless otherwise stated. All moisture-sensitive reactions were carried out under N_2. Org. solns. were dried (Na_2SO_4) and concentrated *in vacuo* below 40°. Column chromatography (CC): silica gel (*Acme*'s 60–120 mesh and 100–200 mesh). Optical rotations: *Horiba* high sensitive polarimeter *SEPA-300* at 25°. IR Spectra: *Perkin-Elmer IR-683* spectrophotometer with NaCl optics; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR (300 and 75 MHz, resp.) spectra: *Bruker Avance 300* instrument; δ [ppm] rel. to Me_4Si as internal standard in $CDCl_3$; *J* in Hz. MS: *Agilent Technologies 1100 Series* (*Agilent* Chemstation Software); *m*/*z*.

*Methyl (*R*)-2-{[(*tert*-butyl)(dimethyl)silyl]oxy}-2-phenylacetate* (**3**). To a cooled (0°) soln. of *methyl (*R*)-mandelate* (**2**; 2.5 g, 15.06 mmol) and 1*H*-imidazole (2.56 g, 37.65 mmol) in dry CH_2Cl_2 (30 ml) was added (*tert*-butyl)dimethylsilyl chloride (TBSCl; 4.06 g, 27.10 mmol) portionwise, and the mixture was stirred for 4 h. After the completion of reaction, the mixture was diluted with H_2O (20 ml) and extracted into CH_2Cl_2 (3×30 ml). The combined org. layer was washed with brine (10 ml), dried (Na_2SO_4), and concentrated *in vacuo* to furnish the crude residue, which was purified by CC (AcOEt/hexane 0.5: 9.5) to give **3** (4.02 g, 95%). Pale yellow liquid. $[\alpha]_D^{25} = -44.4$ ($c = 0.25$, $CHCl_3$). IR (neat): 2954, 2932, 1759, 1256, 1129. ^1H-NMR: 7.47 (*d*, $J = 7.0$, 2 H); 7.36–7.26 (*m*, 3 H); 5.24 (*s*, 1 H); 3.68 (*s*, 3 H); 0.92 (*s*, 9 H); 0.11 (*s*, 3 H); 0.03 (*s*, 3 H). ^{13}C-NMR: 172.2; 138.8; 128.1; 127.8; 126.1; 74.1; 51.7; 25.4; 18.0; −5.3; −5.4. EI-MS: 281 ($[M+H]^+$).

*Ethyl (2*E*,4*S*)-4-{[(*tert*-Butyl)(dimethyl)silyl]oxy}-4-phenylbut-2-enoate* (**4**). To a cooled (−78°) soln. of **3** (2 g, 7.11 mmol) in dry CH_2Cl_2 (22 ml) was added dropwise DIBAL-H (1M in hexane, 7.1 ml, 7.1 mmol). After completion of the reaction, sat. Na K tartarate soln. (5 ml) was added, the mixture was extracted with CH_2Cl_2 (3×30 ml) and concentrated under reduced pressure. Thus obtained aldehyde (1.69 g, 6.7 mmol) was dissolved in dry toluene (50 ml), ethyl (triphenylphosphoranylidene) acetate (2.81 g, 8.07 mmol) was added, and the mixture was refluxed for 6 h, cooled to r.t. subsequently, filtered through *Celite*, and concentrated *in vacuo*. The residue was purified by FC (AcOEt/hexane 1:9) to give first the (*Z*)-isomer **4a** as an oil (0.18 g, 8%), followed by the (*E*)-isomer **4** as liquid (1.98 g, 92%). $[\alpha]_D^{25} = -69$ ($c = 1$, $CHCl_3$). IR (neat): 2954, 2932, 1730, 1660, 1440. ^1H-NMR: 7.31–7.19 (*m*, 5 H); 6.89 (*dd*, $J =$ 15.4, 5.1, 1 H); 6.02 (*dd*, $J = 15.4$, 1.5, 1 H); 5.26 (*dd*, $J = 4.4$, 1.5, 1 H); 4.18–4.09 (*m*, 2 H); 1.27 (*t*, $J = 7.3$,

3 H); 0.90 (*s*, 9 H); 0.05 (*s*, 3 H); −0.08 (*s*, 3 H). ^{13}C-NMR: 166.7; 150.2; 141.6; 128.5; 127.6; 126.2; 118.8; 74.1; 60.4; 25.8; 18.3; 14.2; −4.9; −5.2. LC/MS: 343 ($[M + Na]^+$).

*Ethyl (2*S*,3*S*,4*R*)-4-{[(*tert*-Butyl)(dimethyl)silyl]oxy}-2,3-dihydroxy-4-phenylbutanoate* (**5**). To a soln. of **4** (1.8 g, 5.6 mmol) in acetone/H_2O 5:1 (15 ml) was added *N*-methylmorpholine *N*-oxide hydrate (NMO; 1.31 g, 11.21 mmol), followed by OsO_4 soln. (2.5 wt.-% in ^{t}BuOH, 0.57 ml, 0.056 mmol, 0.01 equiv.), and the mixture was stirred for 14 h. After completion of the reaction, the mixture was concentrated *in vacuo*, and the crude residue was purified by FC (AcOEt/hexane, 4:6) to give **5** (1.79 g, 90%). Liquid. $[\alpha]_D^{25} = -32.9$ ($c = 2.5$, $CHCl_3$). IR (neat): 3488, 2995, 2942, 2860, 1735. ^{1}H-NMR: 7.28–7.42 (*m*, 5 H); 4.68 (*d*, *J* = 8.3, 1 H); 4.52 (*dd*, *J* = 5.6, 0.94, 1 H); 4.22–4.31 (*m*, 2 H); 3.83 (*td*, *J* = 8.3, 1.1, 1 H); 3.05 (*d*, *J* = 5.4, 1 H); 1.62 (*d*, *J* = 7.6, 1 H); 1.32 (*t*, *J* = 7.1, 3 H); 0.9 (*s*, 9 H); 0.1 (*s*, 3 H); −0.2 (*s*, 3 H). ^{13}C-NMR: 173.5; 141.5; 128.3; 127.9; 127.1; 77.3; 76.4; 75.1; 70.0; 61.8; 25.7; 18.0; 14.1; −4.7; −5.3. HR-ESI-MS: 377.1754 ($[M + Na]^+$, $C_{18}H_{30}NaO_5Si^+$; calc. 377.1755).

*Ethyl (4*S*,5*S*)-5-[(*R*)-{[(*tert*-Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolane-4-carboxylate* (**6**). To a cooled (0°) soln. of **5** (1.2 g, 3.38 mmol) in anh. CH_2Cl_2 (10 ml) was added 2,2-dimethoxypropane (0.53 ml, 4.39 mmol) and pyridinium *p*-toluenesulfonate (PPTS; 0.084 g, 0.33 mmol), and mixture was stirred at r.t. for 3 h. After completion of the reaction, solid $NaHCO_3$ (500 mg) was added to neutralize the PPTS, and the mixture was filtered. The filtrate was concentrated to give a crude product which was purified by CC (AcOEt/hexane 0.5:9.5) to afford **6** (1.23 g, 93%). Colorless liquid. $[\alpha]_D^{25} = -28.2$ ($c = 1.02$, $CHCl_3$). IR (neat): 2932, 2857, 1752, 1068, 839. ^{1}H-NMR: 7.30–7.17 (*m*, 5 H); 4.83 (*d*, *J* = 3.9, 1 H); 4.51 (*d*, *J* = 5.9, 1 H); 4.37 (*t*, *J* = 4.9, 1 H); 3.82–3.98 (*m*, 2 H); 1.40 (*s*, 3 H); 1.34 (*s*, 3 H); 1.03 (*t*, *J* = 6.9, 3 H); 0.85 (*s*, 9 H); 0.03 (*s*, 3 H); −0.18 (*s*, 3 H). ^{13}C-NMR: 171.4; 140.4; 127.9; 127.6; 126.5; 111.5; 83.8; 75.2; 74.1; 61.0; 29.6; 25.7; 18.1; 14.1; −4.9; −4.7. LC/MS: 417 ($[M + Na]^+$).

*(*tert*-Butyl)[(*R*)-[(4*S*,5*R*)-5-ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl](phenyl)methoxy]dimethylsilane* (**7**). To a cooled (−78°) soln. of **6** (1.2 g, 3.038 mmol) in dry CH_2Cl_2 (15 ml) was added dropwise DIBAL-H (1M in hexane, 3.01 ml, 3.038 mmol), and the mixure was stirred for 20 min at −78°. After completion of the reaction, H_2O (2 ml) was added, and the mixture was filtered over a pad of *Celite* and concentrated *in vacuo* to give the aldehyde. Thus obtained crude aldehyde (0.9 g) was dissolved in dry THF (10 ml) and reacted with PPh_3CH_3I salt (1.55 g, 3.84 mmol) in the presence of ^{t}BuOK (0.384 g, 0.384 mmol). After completion of the reaction, the mixture was diluted with H_2O, extracted with AcOEt (3 × 10 ml), dried ($NaSO_4$), and the combined extract was concentrated *in vacuo* to give a crude product which was purified by CC (AcOEt/hexane 1:9) to yield **7** (0.80 g, 90%). Colorless liquid. $[\alpha]_D^{25} = -24.3$ ($c = 0.5$, $CHCl_3$). IR (neat): 2930, 2889, 2870, 1365, 1072. ^{1}H-NMR: 7.34–7.27 (*m*, 5 H); 5.84–5.89 (*m*, 1 H); 5.20–5.15 (*m*, 2 H); 4.81 (*d*, *J* = 6.0, 1 H); 4.50 (*d*, *J* = 6.5, 1 H); 4.35–4.44 (m, 1 H); 1.41 (*s*, 3 H); 1.33(*s*, 3 H) 0.89 (*s*, 9 H); 0.06 (*s*, 3 H); −0.12 (*s*, 3 H). ^{13}C-NMR: 141.3; 132; 128.3; 128.1; 127.7; 119.7; 109.7; 87.2; 78.4; 75.3; 29.8; 26.4; 25.4; 18.1; −4.2; −4.4. LC/MS: 371 ($[M + Na]^+$).

*2-{(4*R*,5*S*)-5-[(*R*)-{[(*tert*-Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}ethanol* (**8**). To a cooled (−78°) soln. of **7** (0.7 g, 2.04 mmol) in dry THF (10 ml) was added dropwise $BH_3 \cdot DMS$ (2M in THF, 1.125 ml, 2.25 mmol, 1.1 equiv.). After stirring for 20 min at −78°, the reaction was quenched with 30% H_2O_2 (0.347 ml, 3.07 mmol) and 2M NaOH (1.53 ml, 3.07 mmol), and the mixture was filtered over a pad of *Celite*, and concentrated under reduced pressure. The residue was purified by FC (AcOEt/hexane 2:8) to afford **8** (0.763 g, 89%). $[\alpha]_D^{25} = -28.3$ ($c = 1.0$, $CHCl_3$). IR (neat): 3388, 2930, 2858, 1253, 1067, 837. ^{1}H-NMR: 7.34–7.27 (*m*, 5 H); 4.81 (*d*, *J* = 6.0, 1 H); 4.25–4.21(*m*, 1 H); 3.94(*t*, *J* = 7.0, 1 H); 3.51–3.46 (*m*, 1 H); 3.26–3.20 (*m*, 1 H); 1.91 (br. *s*, 1 H). ^{13}C-NMR: 170.3; 141.2; 128.0; 127.8; 127.2; 110.5; 82.5; 75.8; 73.5; 51.8; 29.6; 26.6; 25.7; 18.1; −4.5; −5.1. ESI-MS: 389 ($[M + Na]^+$).

*Ethyl 4-{(4*R*,5*S*)-5-[(*R*)-{[(*tert*-Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-3-oxobutanoate* (**9**). To a cooled (0°) soln. of 2-iodoxybenzoic acid (IBX; 0.687g, 2.45 mmol) in dry DMSO (10 ml) was added **8** (0.6 g 1.63 mmol) in dry CH_2Cl_2 (5 ml), and the mixture was stirred for 3 h. After completion of the reaction, the mixture was poured on to chilled ice and extracted with AcOEt. The crude extract was concentrated *in vacuo*, the crude was purified by CC to give pure aldehyde (0.635 g 90% yield), which was used in the next step. To a soln. of the aldehyde (0.5 g, 1.36 mmol) and ethyl diazoacetate (0.17 g, 1.5 mmol) in dry CH_2Cl_2 (10 ml) was added portionswise $SnCl_2$ (0.025 g, 0.1369 mmol) within 10 min, and the mixture was stirred for 30 min. After completion of the reaction,

the mixture was diluted with H_2O and extracted with CH_2Cl_2 (3×10 ml). The combined org. layer was dried (Na_2SO_4), and concentrated *in vacuo* to give a crude residue which was purified by CC (AcOEt/hexane 2.5:7.5) to afford **9** (0.549, 89%). $[\alpha]_D^{25} = -27.5$ ($c = 0.5$, $CHCl_3$). IR (neat): 2931, 2857, 1745, 1722, 1254, 1067, 839. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.36–7.25 (*m*, 5 H); 4.82 (*d*, *J* = 5.0, 1 H); 4.52 (*td*, *J* = 2.0, 9.9, 1 H); 4.16 (*q*, *J* = 6.9, 2 H); 3.76 (*dd*, *J* = 7.9, 5.9, 1 H); 3.41(*s*, 2 H); 2.54 (*dd*, *J* = 15.8, 8.9, 2 H); 2.30 (*d*, *J* = 15.8, 1 H); 1.40 (*s*, 3 H); 1.33 (*s*, 3 H); 1.26 (*t*, *J* = 6.9, 3 H); 0.88 (*s*, 9 H); 0.07 (*s*, 3 H); −0.14 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 200.3; 166.9; 141.2; 128.2; 127.7; 126.4; 109.2; 84.4; 74.9; 73.2; 61.2; 50.0; 47.5; 29.7; 27.0; 25.8; 18.2; 14.1; −4.79. ESI-MS: 475 ($[M + Na]^+$).

*Ethyl (3*R*)-4-{(4*R*,5*S*)-5-[(*R*)-{[(*tert*-Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-3-hydroxybutanoate* (**10**). To a cooled (−78°) soln. of **9** (0.41 g, 0.90 mmol) in dry THF (10 ml) was added a 1M soln. of *K-Selectride* (1.07 ml, 1.07 mmol), and the mixture was stirred for 2 h. Then, $LiEt_3BH$ (1.076 ml, 1.077 mmol) was added, and the mixture was stirred for 1 h at −78°. After completion of the reaction (TLC), H_2O was added, and contents were extracted with Et_2O and dried (Na_2SO_4), and the solvent was removed *in vacuo*. The crude product was purified by CC (AcOEt/hexane 3:7) to yield pure *anti*-isomer **10** (0.369 g, 90%). Colorless liquid. $[\alpha]_D^{25} = -30.1$ ($c = 1.0$, $CHCl_3$). IR (neat): 3444, 2930, 2857, 1729, 1254, 1068, 838. ^{1}H-NMR: 7.34–7.24 (*m*, 5 H); 4.81 (*d*, *J* = 5.1, 1 H); 4.51–4.48 (*m*, 1 H); 4.14 (*q*, *J* = 6.8, 2 H); 3.83 (*dd*, *J* = 5.1, 0.96, 1 H); 3.70–3.67 (*m*, 2 H); 2.53–2.49 (*m*, 1 H); 2.29–2.25 (*m*, 1 H); 1.59–1.55 (*m*, 2 H); 1.41 (*s*, 3 H); 1.33 (*s*, 3 H); 1.25 (*t*, *J* = 6.8 , 3 H); 0.89 (*s*, 9 H); 0.06 (*s*, 3 H); −0.014 (*s*, 3 H). ^{13}C-NMR: 172.5; 140.3; 128.3; 127.9; 127.0; 110.0; 84.5; 74.0; 73.0; 63.0; 61.3; 42.7; 34.9; 29.6; 27.1; 25.8; 18.1; 14.1; −4.8. ESI-MS: 461 ($[M + Na]^+$).

Leiocarpin C (= *(4*R*,6*R*)-6-[(1*R*,2*R*)-1,2-Dihydroxy-2-phenylethyl]-4-hydroxytetrahydro-2*H*-pyran-2-one*; **1**). To a stirred soln. of **10** (0.12 g, 0.26 mmol) in dry CH_2Cl_2 (5 ml) was added a cat. amount of TsOH under N_2, and the mixture was stirred at r.t. for 3 h. After completion of the reaction, solid $NaHCO_3$ (0.005 g) was added. The mixture was filtered, and the solvent was removed *in vacuo*. The crude residue was purified by CC (AcOEt/hexane 4:6) to afford **1** (0.049 g, 75%). Colorless needles. $[\alpha]_D^{25} = -62.5$ ($c = 0.5$, $CHCl_3$). IR: 3423, 2920, 2850, 1720, 1656, 1460, 1219 and 606. ^{1}H-NMR: 7.51–7.27 (*m*, 5 H); 4.92 (*d*, *J* = 7.8, 1 H); 4.72 (*dd*, *J* = 4.4, 9.8, 1 H); 4.29 (*quint.*, *J* = 6.8, 1 H); 3.71 (*d*, *J* = 8.8, 1 H); 2.87 (*dd*, *J* = 5.4, 17.2, 1 H); 2.56 (*dd*, *J* = 7.3, 17.2, 1 H); 2.21–2.14 (*m*, 1 H); 2.11–2.0 (*m*, 1 H). ^{13}C-NMR: 172.0; 141.2; 128.6; 127.7; 127.3; 78.1; 68.8; 67.1; 66.7; 41.2; 40.3. ESI-MS: 275 ($[M + Na]^+$). HR-MS: 275.0907 ($[M + Na]^+$, $C_{13}H_{16}NaO_5^+$; calc. 275.0895).

REFERENCES

[1] Z. Tian, S. Chen, Y. Zhang, M. Huang, L. Shi, F. Huang, C. Fong, M. Yang, P. Xiao, *Phytomedicine* **2006**, *13*, 181.

[2] Y. C .Wu, C. Y. Duh, F. R. Chang, G. Y. Chang, S. K. Wang, J. J. Chang, D. R. McPhail, A. T. McPhail, K. H. Lee, *J. Nat. Prod.* **1991**, *54*, 1077.

[3] T. W. Sam, C. S. Yeu, S. Matsjeh, E. K. Gan, D. Razak, A. L. Mohamed, *Tetrahedron Lett*. **1987**, *28*, 2541; S. K. Talapatra, D. Goswami, B. Talapatra, *Indian J. Chem., Sect B* **1985**, *24*, 29; A. De Fatima, L. V. Modolo, L. S. Conegero, R. A. Pilli, C. V. Ferreia, L. K. Kohn, J. E. de Carvalho, *Curr. Med. Chem*. **2006**, *13*, 3371; H. B. Mereyala, M. Joe, *Curr. Med. Chem Anticancer Agents* **2001**, *1*, 293; M. A. Blazquez, A Bermejo, M. C. Zafra-Polo, D. Cortes, *Phytochem. Anal*. **1999**, *10*, 161.

[4] Q. Mu, W. D. Tang, R. Y. Liu, C. M. Li, L. G. Lou, H. D. Sun, C. Q. Hu, *Planta Med*. **2003**, *69*, 826; A. H. Pihie, J. Stanslas, L. B. Din, *Anticancer Res.* **1998**, *18*, 1739.

[5] Q. Mu, W. Tang, C. Li, Y. Lu, H. Sun, H. Zheng, X. Hao, Q. Zheng, N. Wu, L. Lou, B. Xu, *Heterocycles* **1999**, *51*, 2969.

[6] Q. Mu, C. M. Li, Y. N. He, H. D. Sun, H. L. Zheng, Y. Lu, Q. T. Zheng, R. W. Jiang, *Chin. Chem. Lett.* **1999**, *10*, 135.

[7] a) V. Shekhar, D. K. Reddy, V. Suresh, D. C. Babu, Y. Venkateswarlu, *Tetrahedron Lett.* **2010**, *51*, 946; b) D. K. Reddy, V. Shekhar, T. S. Reddy, S. P. Reddy, Y. Venkateswarlu, *Tetrahedron: Asymmetry* **2009**, *20*, 2315; c) D. K. Reddy, V Shekhar, P. Prabhakar, B. C. Babu, B. Siddhardha, U. S. N. Murthy, Y. Venkateswarlu, *Eur. J. Med. Chem.* **2010**, *45*, 4657; d) M. Narasimhulu, A. Sai

Krishna, J. Venkateswara Rao, Y. Venkateswarlu, *Tetrahedron* **2009**, *65*, 2989; e) D. Chandra Rao, D. Kumar Reddy, V. Shekhar, Y. Venkateswarlu, *Tetrahedron Lett.* **2013**, *54*, 828.

[8] J. S. Yadav, K. Premalatha, S. J. Harshavardhan, B. V. Subba Reddy, *Tetrahedron Lett*. **2008**, *49*, 6765; P. Radha Krishna, M. Alivelu, *Helv. Chim. Acta* **2011**, *94*, 1102; J. S. Yadav, V. H. Krishna, A. Srilatha, R. Somaiah, B. V. S. Reddy, *Synthesis* **2010**, 3004.

[9] J. K. Cha, W. J. Christ, Y. Kishi, *Tetrahedron* **1984**, *40*, 2247; T. Oishi, K. Y. Iida, M. Hirama, *Tetrahedron Lett*. **1993**, *34*, 3573;

[10] S. Kobayashi, R. Matsubara, Y. Nakamura, H. Kitagawa, M. Sugiura, *J. Am. Chem. Soc.* **2003**, *125*, 2507; M. Sridhar, G. K. Reddy, B. C. Ramanaiah, C. Narasaiah, *Tetrahedron Lett.* **2012**, *53*, 5539.

Received December 21, 2012