Stereoselective Total Synthesis of Botryolide E[1])

by **Boyapati Veeranjaneyulu**, **Malampati Srilatha**, **Gandolla Chinna Reddy**, and **Biswanath Das***

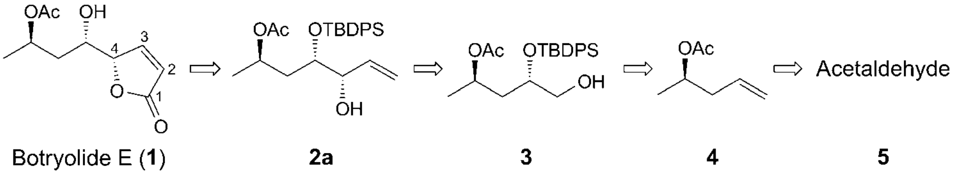
Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad-500007, India
(phone: +91-40-7193434; fax: +91-40-7160512; e-mail: biswanathdas@yahoo.com)

The stereoselective total synthesis of the naturally occurring γ-lactone derivative botryolide E (**1**) was accomplished with acetaldehyde as the starting material (*Scheme 2*). The asymmetric allyl boration, asymmetric dihydroxylation, chelation-mediated diastereoselective vinylation, and ring-closing metathesis reaction are the key steps. The method can conveniently be utilized for the preparation of other related γ-lactone derivatives.

Introduction. – The γ-lactone (butenolide) moiety is an integral structural component of an ever increasing number of biologically active natural products [1]. These compounds exhibit a wide range of biological activities including cytotoxic [2], antibacterial [3], antifungal [3], cyclooxygenase [4], and antiproliferative properties [5]. Botryolide E (=(5*S*)-5-[(1*S*,3*R*)-3-(acetyloxy)-1-hydroxybutyl]furan-2(5*H*)-one; **1**), a member of this group, was isolated from cultures of a fungicolous isolate of *Botryotrichum* sp. (NRRL 38180) along with other botryolides [6]. The biological activities of this compound have not been completely studied but recently it was found to possess antibacterial and antifungal activities [3]. The structure of **1** was confirmed by its NMR and MS data [6]. The absolute configuration of **1** was confirmed by its first stereoselective synthesis [3]. Later, so far, no other asymmetric synthesis of botryolide E (**1**) has been reported. In continuation of our work [7] on the synthesis of bioactive natural products, we have taken up the asymmetric synthesis of **1** which we describe here.

Results and Discussion. – The retrosynthetic analysis of botryolide E (**1**) is summarized in *Scheme 1*. The disconnection process began with the C(2)=C(3) bond, which could be realized by ring-closing metathesis. This led to the key intermediate **2a**

Scheme 1. *Retrosynthetic Pathway to Botryolide E* (**1**)



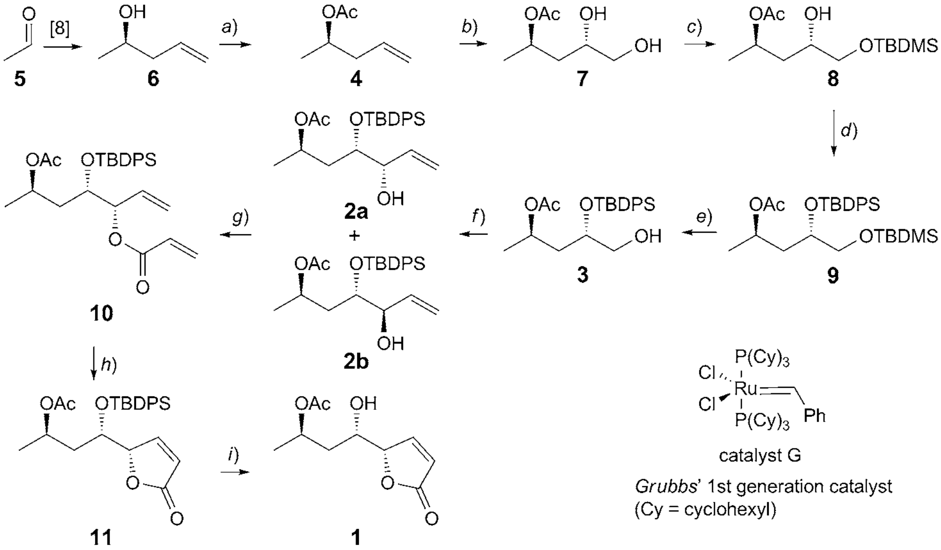
---

[1]) Part 55 in the series, 'Synthetic Studies on Natural Products'.

which could be prepared by chelation-mediated *syn*-selective vinylation of the aldehyde obtained by oxidation of the primary alcohol **3**. Compound **3** could be obtained by a *Sharpless* asymmetric dihydroxylation reaction of **4**, generated by asymmetric allylation of acetaldehyde (**5**).

The synthesis of **1** started from freshly distilled acetaldehyde (**5**; *Scheme 2*) to produce (2*R*)-pent-4-en-2-ol (**6**) with high enantioselectivity by following the literature procedure [8]. The OH group of **6** was acetylated with Ac_2O and Et_3N to give ester **4**. Asymmetric dihydroxylation of compound **4** by the *Sharpless* protocol [9] yielded diol **7** with high diastereoselectivity. The primary OH function of the latter was protected as its corresponding (*tert*-butyl)dimethylsilyl (^{t}BuMe$_2$Si) ether **8** with ^{t}BuMe$_2$SiCl and 1*H*-imidazole. Next, the protection of the secondary OH function in **8** with ^{t}BuMe$_2$SiCl, 1*H*-imidazole, and catalytic amounts of *N*,*N*-dimethylpyridin-4-amine (DMAP) produced compound **9**. Selective deprotection of the ^{t}BuMe$_2$Si ether in **9** with pyridinium *p*-toluenesulfonate (= pyridinium 4-methylbenzenesulfonate; PPTS) in MeOH afforded the primary alcohol **3** [10]. Initially this deprotection failed by carrying out the reaction in MeOH with *p*-toluenesulfonic acid (TsOH) which led to a mixture of products with complete consumption of the starting material. Attempts to oxidize alcohol **3** to the corresponding aldehyde with 2-iodoxybenzoic acid (IBX) or pyridinium dichromate (PDC) were not successful and led to a mixture of compounds along with the starting material. Later the oxidation was successful with pyridinium

Scheme 2. *Synthesis of Botryolide E* (**1**). TBDMS = ^{t}BuMe$_2$Si, TBDPS = ^{t}BuPh$_2$Si.



a) Ac_2O, Et_3N, CH_2Cl_2, 0° – r.t., 4 h; 91%. *b*) $K_3[Fe(CN)_6]$, K_2CO_3, $K_2OsO_4 \cdot 2\,H_2O$, $(DHQD)_2$PHAL (*Aldrich*), ^{t}BuOH/H_2O (1:1), 0°, 8 h; 83%. *c*) ^{t}BuMe$_2$SiCl, 1*H*-imidazole, CH_2Cl_2, 0° – r.t., 3 h; 81%. *d*) ^{t}BuPh$_2$SiCl, 1*H*-imidazole, cat. DMAP, CH_2Cl_2, 0° – r.t., 8 h; 87%. *e*) PPTS, MeOH, r.t, 12 h; 79%. *f*) 1. PCC, CH_2Cl_2, r.t., 5 h; 84%; 2. $CH_2{=}CHMgBr$, $MgBr_2 \cdot Et_2O$, CH_2Cl_2, –78°, 12 h; 61%. *g*) $CH_2{=}CHCOCl$, ^{i}Pr$_2$NEt, CH_2Cl_2, 0°, 5 h; 84%. *h*) Catalyst G (5 mol-%), CH_2Cl_2, reflux, 6 h; 69%. *i*) $Bu_4N^+F^-$, THF, 0°, 1 h; 64%.

chlorochromate (PCC) to afford aldehyde **3a** (*Table*). The latter was subjected to chelation-mediated selective vinylation under different conditions; the best result was achieved with vinyl magnesium bromide ($H_2C{=}CHMgBr$) and $MgBr_2 \cdot Et_2O$ in CH_2Cl_2 at −78° which yielded a mixture of *syn*- and *anti*-diastereoisomers **2a** and **2b** in the ratio of 95:5 (*Table*) [11]. The compounds **2a** and **2b** were separated by column chromatography. Acrylation of **2a** with acryloyl chloride (= prop-2-enoyl chloride) and diisopropylethylamine (Pr_2NEt) afforded **10**, which underwent a ring-closing metathesis reaction induced by *Grubbs*' 1st-generation catalyst G [12] to yield the unsaturated γ-lactone **11**. Selective deprotection of the $^t BuMe_2Si$ group of **11** with Bu_4NF in THF led to botryolide E (**1**), the spectroscopic data of which were identical to those of natural **1** [3][6].

Table. *Metal-Catalyzed Diastereoselective Vinylation*

Conditions[a])	Yield [%][b])	*syn*/*anti* (**2a**/**2b**)[c])
$CH_2{=}CHMgBr$, $MgBr_2 \cdot Et_2O$, dry THF, −78°, 5 h	81	60:40
$CH_2{=}CHMgBr$, $MgBr_2 \cdot Et_2O$, dry Et_2O, −78°, 5 h	77	67:33
$CH_2{=}CHMgBr$, $MgBr_2 \cdot Et_2O$, dry CH_2Cl_2, −78°, 12 h	61	95:5
$CH_2{=}CHMgBr$, $MgBr_2 \cdot Et_2O$, dry CH_2Cl_2, −20°, 12 h	67	80:20
$CH_2{=}CHMgBr$, dry Et_2O, 0°, 4 h	89	55:45[d])

[a]) Reaction conditions: aldehyde **3a** (1.0 equiv.), $CH_2{=}CHMgBr$ (2.5 equiv.), and $MgBr_2 \cdot Et_2O$ (1.2 equiv). [b]) Yield of isolated products after column chromotography. [c]) The ratio *syn*/*anti* was determined from the mixture. [d]) The reaction was carried out without catalyst.

In conclusion, the stereoselective synthesis of botryolide E was successfully accomplished by means of an asymmetric allyl boration [8], an asymmetric dihydroxylation, a chelation-mediated diastereoselective vinylation, and a ring-closing metathesis reaction as the key steps. This method can conveniently be utilized for the preparation of other related γ-lactone derivatives.

The authors thank *UGC* and *CSIR*, New Delhi, for financial assistance.

Experimental Part

General. All commercially available reagents were used directly without further purification unless otherwise stated. The solvents used were all of AR grade and were distilled under a positive pressure of dry N_2 where necessary. All reactions were performed in a pre-dried apparatus unless otherwise stated. Yields were those of purified compounds unless otherwise stated. Column chromatography (CC): silica gel (SiO_2; 60–120 mesh; *Qingdao Marine Chemical*, P. R. China); FC = flash chromatography. TLC: SiO_2 *60 F_{254}* plates (*Merck*). Optical rotations: *Jasco-DIP-300* digital polarimeter. IR Spectra: *Perkin–Elmer-RX1* FT-IR spectrophotometer; ν in cm^{-1}. NMR Spectra: *Gemini* 200 MHz spectrometer;

in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, J in Hz. ESI-MS: *VG-Autospec* micromass; in *m/z*. HR-MS: *QSTAR XL*, hybrid MS system (*Applied Biosystems*); in *m/z*.

*(*2R*)-Pent-4-en-2-yl Acetate* (=*(*2R*)-Pent-4-en-2-ol Acetate*; **4**). To a soln. of (2*R*)-pent-4-en-2-ol (**6**; 4.0 g, 46.51 mmol) in dry CH_2Cl_2 (50 ml) at 0°, Et_3N (12.96 ml, 93.02 mmol) and a cat. amounts of DMAP were added. The mixture was stirred for 15 min, then Ac_2O (14.23 g, 13.15 ml) was slowly added, and the mixture warmed to r.t. After stirring for 4 h, the mixture was diluted with CH_2Cl_2 (10 ml) and the reaction quenched by slow addition of H_2O (20 ml). The org. layer was washed with brine (2 × 30 ml), dried (anh. Na_2SO_4), and concentrated, and the residue purified by CC (AcOEt/hexane 2 : 8): pure **4** (5.41 g, 91%). IR: 1733, 1637, 1239, 1108. ^{1}H-NMR (200 MHz): 5.76–5.63 (*m*, 1 H); 5.06–5.04 (*m*, 2 H); 4.92–4.85 (*m*, 1 H); 1.98 (*s*, 3 H); 1.85–1.77 (*m*, 2 H); 1.28 (*d*, $J = 6.0$, 3 H). ^{13}C-NMR (50 MHz): 176.2; 133.6; 117.6; 69.7; 40.3; 20.8; 19.5. Anal. calc. for $C_7H_{12}O_2$ (128.17): C 65.60, H 9.44; found: C 65.56, H 9.49.

*(*2R*,*4S*)-4,5-Dihydroxypentan-2-yl Acetate* (=*(*2S*,*4R*)-Pentane-1,2,4-triol 4-Acetate;* **7**). To a stirred suspension of $K_3[Fe(CN)]_6$ (40.1g, 121.8 mmol), K_2CO_3 (16.8 g, 121.8 mmol), $K_2OsO_4 \cdot 2\ H_2O$ (0.019 g, 0.052 mmol) and 1,4-bis(9-*O*-dihydroquinidinyl)phthalazine (=(9*S*,9''*S*)-9,9''-[phthalazine-1,4-diylbis(oxy)]bis[10,11-dihydro-6'-methoxycinchonane]; $(DHQD)_2PHAL$; 0.079 g, 0.101 mmol) in ^{t}BuOH/H_2O 1 : 1 (500 ml) at 0°, a soln. of **6** (5.2 g, 40.62 mmol) in ^{t}BuOH (5 ml) was added slowly within 30 min. The mixture was stirred for 8 h at 0°. After completion of the reaction, the mixture was quenched with Na_2SO_3 and stirred for another 20 min. The mixture was filtered over a *Celite* pad. The residue thus obtained was washed with hot AcOEt. The org. layer from the filtrate was separated, and the aq. layer thus obtained was extracted with AcOEt (2 × 400 ml). The combined org. layers were washed with brine (300 ml), dried (anh. Na_2SO_4), and concentrated. The residue was purified by CC (AcOEt/hexane 5 : 5): pure **7** (5.46 g, 83%). $[\alpha]_D^{25} = -2.3$ ($c = 1.0$, $CHCl_3$). IR: 3430, 2928, 1713, 1634, 1253, 1165. ^{1}H-NMR (200 MHz): 5.11–5.05 (*m*, 1 H); 3.58–3.48 (*m*, 2 H); 3.37–3.32 (*m*, 1 H); 2.02 (*s*, 3 H); 1.56–1.51 (*m*, 2 H); 1.24 (*d*, $J = 6.0$, 3 H). ^{13}C-NMR (50 MHz): 171.4; 68.3; 68.0; 66.4; 39.9; 21.2; 20.8. Anal. calc. for $C_7H_{14}O_4$: C 51.84, H 8.70; found: C 51.73, H 8.77.

*(*2R*,*4S*)-5-{[(*tert*-Butyl)dimethylsilyl]oxy}-4-hydroxypentan-2-yl Acetate* (=*(*2R*,*4S*)-5-{[(*tert*-Butyl)dimethylsilyl]oxy}pentane-2,4-diol 2-Acetate*; **8**). To a stirred soln. of **7** (5.2 g, 32.09 mmol) in dry CH_2Cl_2 (70 ml) were added 1*H*-imidazole (2.4 g, 35.3 mmol) and ^{t}BuMe$_2$SiCl (5.31 g, 35.3 mmol) at 0°. The mixture was allowed to reach r.t. and then stirred for 3 h. After diluation with CH_2Cl_2 (15 ml), the org. layer was washed with brine (50 ml), dried (Na_2SO_4), and concentrated, and the residue subjected to CC (AcOEt/hexane 2 : 8): **8** (7.16 g, 81%). $[\alpha]_D^{25} = -10.2$ ($c = 0.95$, $CHCl_3$). IR: 3458, 2955, 2857, 1738, 1465, 1373, 1254, 1097. ^{1}H-NMR (200 MHz): 5.14–5.02 (*m*, 1 H); 3.60–3.51 (*m*, 2 H); 3.45–3.38 (*m*, 1 H); 2.58 (br. *s*, 1 H); 2.02 (*s*, 3 H); 1.65–1.45 (*m*, 2 H); 1.26 (*d*, $J = 6.4$, 3 H); 0.89 (*s*, 9 H); 0.05 (*s*, 6 H). ^{13}C-NMR (50 MHz): 170.3; 68.3; 68.1; 67.4; 39.9; 26.0; 21.2; 20.9; 18.4; −5.1. ESI-MS: 294 ($[M + 18]^+$).

*(*2R*,*4S*)-5-{[(*tert*-Butyl)dimethylsilyl]oxy}-4-{[(*tert*-butyl)diphenylsilyl]oxy}pentan-2-yl Acetate* (=*(*2R*,*4S*)-5-{[(*tert*-Butyl)dimethylsilyl]oxy}-4-{[(*tert*-butyl)diphenylsilyl]oxy}pentan-2-ol Acetate*; **9**). To a stirred soln. of **8** (7.0 g, 25.36 mmol) in dry CH_2Cl_2 (90 ml) were added 1*H*-imidazole (2.58 g, 38.04 mmol) and a cat. amount of DMAP at 0° and stirred for 20 min. ^{t}BuPh$_2$SiCl (9.73 ml, 38.04 mmol) was added to this at 0°. The mixture was warmed to r.t., stirred for 8 h, and then diluted with CH_2Cl_2 (25 ml). The org. layer was washed with brine (70 ml), dried (Na_2SO_4), and concentrated, and the residue subjected to CC (AcOEt/hexane 1 : 9): **9** (11.31 g, 87%). $[\alpha]_D^{34} = -13.9$ ($c = 1.9$, $CHCl_3$); IR: 2955, 2857, 1738, 1466, 1369, 1245, 1108. ^{1}H-NMR (200 MHz): 7.66–7.64 (*m*, 4 H); 7.40–7.32 (*m*, 6 H); 5.04–5.01 (*m*, 1 H); 3.71–3.66 (*m*, 1 H); 3.43–3.37 (*m*, 2 H); 1.90–1.86 (*m*, 1 H); 1.84 (*s*, 3 H); 1.64–1.59 (*m*, 1 H); 1.16 (*d*, $J = 5.9$, 3 H); 1.04 (*s*, 9 H); 0.81 (*s*, 9 H); −0.09 (*s*, 3 H); −0.15 (*s*, 3 H). ^{13}C-NMR (50 MHz): 170.1; 136.0; 135.8; 134.6; 133.6; 129.7; 129.5; 127.7; 127.4; 70.9; 68.1; 66.8; 41.1; 27.1; 25.9; 21.2; 20.8; 19.4; 18.3; −5.4. ESI-MS: 537 ($[M + Na]^+$).

*(*2R*,*4S*)-4-{[(*tert*-Butyl)diphenylsilyl]oxy}-5-hydroxypentan-2-yl Acetate* (=*(*2S*,*4R*)-2-{[(*tert*-Butyl)diphenylsilyl]oxy}pentane-1,4-diol 4-Acetate*; **3**). To a stirred soln. of **9** (7.2 g, 13.98 mmol) in anh. MeOH at 0° was added PPTS (0.702 g, 2.79 mmol). Then the mixture was warmed to r.t. and stirred for 12 h. After completion of the reaction, the mixture was concentrated and the residue purified by CC (AcOEt/hexane 3 : 7): pure **3** (4.41 g, 79%). $[\alpha]_D^{34} = -2.9$ ($c = 1.9$, $CHCl_3$). IR: 3489, 3071, 2931, 2858, 1735, 1247, 1110. ^{1}H-NMR (200 MHz): 7.66–7.60 (*m*, 4 H); 7.38–7.34 (*m*, 6 H); 4.88–4.78 (*m*, 1 H); 3.77–3.71 (*m*, 1 H); 3.49–3.44 (*m*, 2 H); 1.81 (*s*, 3 H); 1.76–1.59 (*m*, 2 H); 1.07 (*d*, $J = 6.0$, 3 H); 1.06 (*s*,

9 H). ^{13}C-NMR (50 MHz): 170.3; 135.9; 135.5; 134.0; 133.0; 129.8; 127.7; 71.3; 68.2; 66.6; 40.3; 26.9; 21.2; 20.3; 19.2. ESI-MS: 423 ([M + Na]$^+$).

*(*2R*,*4S*,*5S*)-4-{[(*tert*-Butyl)diphenylsilyl]oxy}-5-hydroxyhept-6-en-2-yl Acetate* (= *(*2R*,*4S*,*5S*)-4-{[(*tert*-Butyl)diphenylsilyl}oxy}hept-6-ene-2,5-diol 2-Acetate*; **2a**). To a soln. of **3** (2.1 g, 5.25 mmol) in dry CH_2Cl_2 (30 ml) at r.t., *Celite* (1.0 g) and PCC (1.69 g, 7.87 mmol) were added while stirring. After 5 h stirring, the mixture was diluted with CH_2Cl_2 (10 ml) and filtered over a *Celite* pad. The residue thus obtained was washed with CH_2Cl_2. The combined org. layers were washed with brine, dried (Na_2SO_4), and concentrated, and the residue was purified by FC: aldehyde **3a** (1.74 g, 84%) which was used immediately for the next step.

To a soln. of **3a** (1.74 g, 4.37 mmol) in dry CH_2Cl_2 (50 ml), $MgBr_2 \cdot E_2O$ (1.35 g, 5.24 mmol) was added while stirring. The soln. was stirred well for 1 h and cooled to – 78°. A soln. of 1M $CH_2{=}CHMgBr$ in THF (10.9 ml, 10.9 mmol) was added slowly within 15 min. The mixture was stirred for 12 h and then allowed to reach r.t. The reaction was quenched with sat. NH_4Cl soln. (10 ml) and H_2O (20 ml), the aq. layer washed with CH_2Cl_2 (2 × 50 ml), the combined org. layer dried (Na_2SO_4) and concentrated, and the residue purified by CC (AcOEt/hexane 2 : 8): **2a**/**2b** 95 : 5; 0.55 g of **2a** was isolated in 93% yield. $[\alpha]^{34}_{D} = -1.6$ ($c = 2.3$, $CHCl_3$). IR: 3452, 3071, 2931, 2857, 1735, 1634, 1241, 1104. ^{1}H-NMR (200 MHz): 7.66 – 7.60 (*m*, 4 H); 7.41 – 7.32 (*m*, 6 H); 5.94 – 5.83 (*m*, 1 H); 5.31 – 5.16 (*m*, 2 H); 4.71 – 4.62 (*m*, 1 H); 4.03 – 3.99 (*m*, 1 H); 3.67 (*m*, 1 H); 2.03 (br. *s*, 1 H); 1.78 (*s*, 3 H); 1.49 – 1.41 (*m*, 2 H); 1.04 (*s*, 9 H); 0.94 (*d*, $J = 6.0$, 3 H). ^{13}C-NMR (50 MHz): 170.2; 135.9; 135.7; 133.9; 133.0; 129.8; 127.7; 116.5; 75.6; 73.5; 68.3; 38.0; 27.0; 21.1; 20.4; 19.3. ESI-MS: 449 ([M + Na]$^+$).

*(*3S*,*4S*,*6R*)-6-(Acetyloxy)-4-{[(*tert*-butyl)diphenylsilyl]oxy}hept-1-en-3-yl Acrylate* (= *(*1S*,*2S*,*4R*)-4-(Acetyloxy)-4-(*tert*-butyldiphenylsilyl]oxy}-1-ethenylpentyl Prob-2-enoate*; **10**). To a stirred soln. of **2a** (0.8 g, 1.87 mmol) in dry CH_2Cl_2 (8 ml) under N_2 atmosphere at 0° were added $^iPr_2NEt$ (1.62 ml, 9.35 mmol) and acryloyl chloride (0.45 ml, 5.61 mmol), and the mixture was stirred for 5 h and then diluted with CH_2Cl_2 (10 ml). The org. layer was washed with $NaHCO_3$ (10 ml), dried (anh. Na_2SO_4), and concentrated and the residue subjected to CC (AcOEt/hexane 2 : 8): **10** (0.75 g, 84%). $[\alpha]^{29}_{D} = +7.5$ ($c = 1.5$, $CHCl_3$). IR: 3065, 2928, 2854, 1735, 1724, 1637, 1239, 1104. ^{1}H-NMR (200 MHz): 7.70 – 7.66 (*m*, 4 H); 7.42 – 7.34 (*m*, 6 H); 6.31 (*dd*, $J = 1.5$, 17.2, 1 H); 5.98 – 5.82 (*m*, 2 H); 5.71 (*dd*, $J = 1.5$, 10.5, 1 H); 5.32 – 5.18 (*m*, 3 H); 4.83 – 4.72 (*m*, 1 H); 3.89 – 3.75 (*m*, 1 H); 1.78 (*s*, 3 H); 1.59 – 1.48 (*m*, 2 H); 1.07 – 1.04 (*m*, 2 H). ^{13}C-NMR (50 MHz): 170.1; 164.5; 136.0; 135.8; 133.6; 133.2; 132.4; 130.4; 128.3; 127.7; 127.6; 118.4; 76.3; 70.8; 68.0; 39.7; 27.1; 21.1; 20.4; 19.5. ESI-MS: 503 ([M + Na]$^+$).

*(*2R*,*4S*)-4-{[(*tert*-Butyl)diphenylsilyl]oxy}-4-[(*2S*)-2,5-dihydro-5-oxo-furan-2-yl)butan-2-yl Acetate* (= *(*5S*)-5-{(*1S*,*3R*)-3-(Acetyloxy)-1-{[(tert-butyl)diphenylsilyl]oxy}butyl}furan-2(*5H*)-one;* **11**). A soln. of **10** (0.25 g, 0.52 mmol) in dry CH_2Cl_2 (180 ml) was first flushed by bubbling with an N_2 flow, after which *Grubbs'* 1st-generation catalyst G (0.021 g, 0.026 mmol) was added at once, and the resulting mixture was heated under N_2 at 50° for 6 h. After cooling, the solvent was evaporated and the residue purified by CC (AcOEt/hexane 2 : 8): pure **11** (0.16 g, 69%). $[\alpha]^{25}_{D} = -24.3$ ($c = 0.2$, $CHCl_3$). ^{1}H-NMR (200 MHz): 7.70 – 7.66 (*m*, 4 H); 7.44 (*dd*, $J = 5.9$, 1.6, 1 H); 7.42 – 7.34 (*m*, 6 H); 6.21 (*dd*, $J = 5.9$, 1.6, 1 H); 5.16 – 5.03 (*m*, 2 H); 3.91 – 3.86 (*m*, 1 H); 1.98 (*s*, 1 H); 1.84 – 1.73 (*m*, 2 H); 1.15 (*d*, $J = 6.0$, 2 H); 1.05 (*s*, 9 H). ^{13}C-NMR (50 MHz): 172.3; 171.9; 152.8; 136.0; 135.7; 132.6; 132.2; 127.6; 127.5; 120.4; 84.5; 68.0; 67.9; 38.7; 27.0; 21.0; 20.4; 19.4. ESI-MS: 475 ([M + Na]$^+$).

*(*2R*,*4S*)-4-Hydroxy-4-[(*2S*)-2,5-dihydro-5-oxo-furan-2-yl]butan-2-yl Acetate* (= *Botryolide E* = *(*5S*)-5-[(*1S*,*3R*)-3-(Acetyloxy)-1-hydroxybutyl]furan-2(*5H*)-one*; **1**). To a soln. of **10** (0.12 g, 0.265 mmol) in dry THF (4 ml), 1M Bu_4N in THF (0.52 ml, 0.52 mmol) at 0° was added dropwise. The mixture was stirred at 0° for 1 h. After completion of the reaction, the mixture was diluted with AcOEt (10 ml), the org. layer washed with brine (2 × 8 ml), dried (Na_2SO_4), and concentrated, and the residue subjected to CC (AcOEt/hexane 3 : 7): pure **1** (0.036 g, 64%). $[\alpha]^{25}_{D} = -36.4$ ($c = 0.05$, $CHCl_3$). ^{1}H-NMR (200 MHz): 7.46 (*dd*, $J = 6.0$, 1.8, 1 H); 6.17 (*dd*, $J = 6.0$, 1.8, 1 H); 5.14 – 5.08 (*m*, 1 H); 5.04 – 5.01 (*m*, 1 H); 3.89 – 3.85 (*m*, 1 H); 2.01 (*s*, 1 H); 1.81 – 1.70 (*m*, 2 H); 1.26 (*d*, $J = 6.0$, 3 H). ^{13}C-NMR (50 MHz): 172.8; 171.9; 153.2; 123.0; 85.1; 67.6; 67.4; 39.1; 21.1; 20.6. ESI-MS: 237 ([M + Na]$^+$).

REFERENCES

[1] A. D. Rodríguez, *Tetrahedron* **1995**, *51*, 4571; F. W. Alali, X.-X. Liu, J. L. McLaughlin, *J. Nat. Prod.* **1999**, *62*, 504; J. R. Hanson, *Nat. Prod. Rep.* **2002**, *19*, 381; A. Bermejo, B. Figadère, M.-C. Zafra-Polo, I. Barrachina, E. Estornell, D. Cortes, *Nat. Prod. Rep.* **2005**, *22*, 269; R. Bandichhor, B. Nosse, O. Reiser, *Top. Curr. Chem.* **2005**, *243*, 43; P. A. Roethle, D. Trauner, *Nat. Prod. Rep.* **2008**, *25*, 298; I. Prassas, E. P. Diamandis, *Nat. Rev. Drug Discovery* **2008**, *7*, 926; R. R. A. Kitson, A. Millemaggi, R. J. K. Taylor, *Angew. Chem., Int. Ed.* **2009**, *48*, 9426.

[2] D.-H. Li, T.-J. Zhu, H.-B. Liu, Y.-C. Fang, Q.-Q. Gu, W.-M. Zhu, *Arch. Pharmacal Res.* **2006**, *29*, 624; R. R. Parvatkar, C. D'Souza, A. Tripathi, C. G. Naik, *Phytochemistry* **2009**, *70*, 128.

[3] D. K. Reddy, V. Shekhar, P. Prabhakar, D. Chanti Babu, D. Ramesh, B. Siddhardha, U. S. N. Murthy, Y. Venkateswarlu, *Bioorg. Med. Chem. Lett.* **2011**, *21*, 997.

[4] S. Ma, Z. Shi, Z. Yu, *Tetrahedron* **1999**, *55*, 12137.

[5] P. P. Yadav, A. Arora, H. K. Bid, R. R. Konwar, S. Kanojiya, *Tetrahedron Lett.* **2007**, *48*, 7194.

[6] A. A. Sy, D. C. Swenson, J. D. Gloer, D. T. Wicklow, *J. Nat. Prod.* **2008**, *71*, 415.

[7] B. Das, M. Krishnaiah, C. Sudhakar, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 2303; B. Das, B. Veeranjaneyulu, P. Balasubramanyam, M. Srilatha, *Tetrahedron: Asymmetry* **2010**, *21*, 2762; B. Das, P. Balsubramanyam, B. Veeranjaneyulu, G. C. Reddy, *Helv. Chim. Acta* **2011**, *94*, 881.

[8] H. C. Brown, P. K. Jadhav, *J. Am. Chem. Soc.* **1983**, *105*, 2092; M. V. R. Reddy, A. J. Yucel, P. V. Ramachandran, *J. Org. Chem.* **2001**, *66*, 2512.

[9] K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K. S. Jeong, H. L. Kwong, K. M. Morikawa, Z. M. Wan, *J. Org. Chem.* **1992**, *57*, 2768.

[10] P. Balasubramanyam, G. C. Reddy, N. Salvanna, B. Das, *Synthesis* **2011**, 3706.

[11] G. E. Keck, M. B. Andrus, D. R. Romer, *J. Org. Chem.* **1991**, *56*, 417; K. Venkatesan, K. V. Srinivasan, *Tetrahedron: Asymmetry* **2008**, *19*, 209; G. Sabitha, C. N. Reddy, P. Gopal, J. S. Yadav, *Tetrahedron Lett.* **2010**, *51*, 5736.

[12] R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413.

Received December 20, 2011