Total Synthesis of Umuravumbolide

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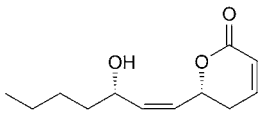
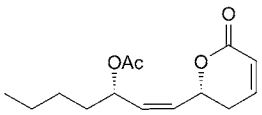
A simple and efficient stereoselective total synthesis of (+)-umuravumbolide (**1b**) and (−)-deacetylumuravumbolide (**1a**) starting from commercially available pentanal is described. The synthesis involves *Sharpless* asymmetric epoxidation, *Jacobsen*'s hydrolytic kinetic resolution (HKR), and the *Yamaguchi* oxirane opening as key steps (*Scheme 2*).

Introduction. – α,β-Unsaturated δ-lactones are structural elements generally found with diverse array of biological activity in natural products [1]. The α,β-unsaturated δ-lactone structural units are excellent potential *Michael* acceptors for nucleophilic amino acid residues of the natural receptors [2]. They inhibit HIV protease [3], induce apoptosis [4], and have even been shown to be antileukemic [5] and anticancer agents [6]. Further, they have shown a variety of biological activities, such as plant-growth inhibitors, pheromones, and antifeedant, antifungal, and antibacterial reagents [7]. In recent times, we have been interested in the synthesis of natural products containing pyranone units [8]. The two 2*H*-pyran-2-ones deacetylumuravumbolide and umuravumbolide were isolated from *Tetradenia riparia* (Lamiaceae) from central and southern Africa [9]. The structures of (−)-deacetylumuravumbolide (**1a**) and (+)-umuravumbolide (**1b**) were revised by *Davies-Coleman* and *Rivett*, and they determined the absolute configuration on the basis of NMR and CD spectral studies and also reported the optical rotations of these compounds [10]. Recently, we reported the synthesis of (−)-deacetylumuravumbolide (**1a**) and (+)-umuravumbolide (**1b**) [11]. Herein, we report another simple and practical route for the synthesis of compounds **1a** and **1b** using *Sharpless* asymmetric epoxidation and *Jacobsen*'s hydrolytic kinetic resolution (HKR) as chirality-introducing steps, and the *Yamaguchi* method for the oxirane-opening step.



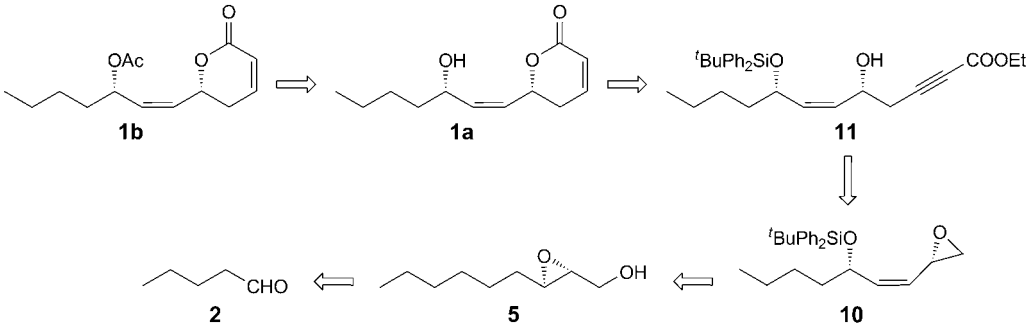
(−)-Deacetylumuravumbolide (**1a**)



(+)-Umuravumbolide (**1b**)

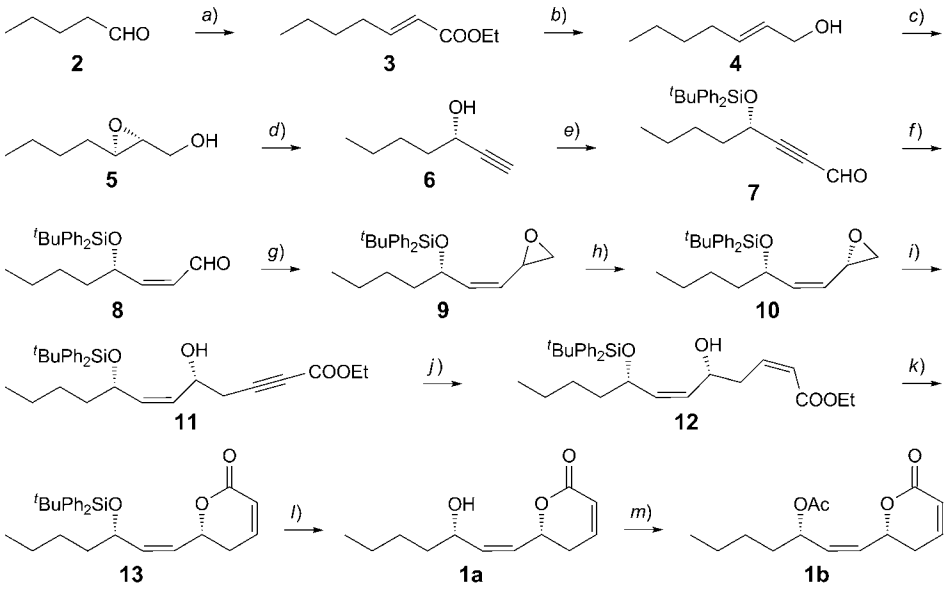
Our retrosynthesis of (+)-umuravumbolide (**1b**) and (−)-deacetylumuravumbolide (**1a**), is depicted in *Scheme 1* starting from pentanal (**2**).

Scheme 1. *Retrosynthetic Analysis*



Results and Discussion. – As outlined in *Scheme 2*, pentanal (**2**) was subjected to a *Wittig* reaction with (ethoxycarbonylmethylene)triphenylphosphorane in dry CH_2Cl_2 to furnish α,β-unsaturated ester **3** with *trans*-configuration in 87% yield. Reduction of

Scheme 2



a) PPh_3CHCO_2Et, CH_2Cl_2, 6 h, r.t.; 87%. *b*) DIBAL-H, dry CH_2Cl_2, 0°, 2 h; 90%. *c*) (+)-Diethyl L-tartrate, cumene hydroperoxide, $Ti(O^iPr)_4$, dry CH_2Cl_2, −20°, 12 h; 80%. *d*) 1. PPh_3, CCl_4, $NaHCO_3$, reflux, 6 h; 78%; 2. BuLi, dry THF, 10 min; 70%. *e*) 1. ^{t}BuPh$_2$SiCl, 1*H*-imidazole, dry CH_2Cl_2, 3 h, 0° to r.t.; 93%; 2. BuLi, DMF, dry THF, −78°, 1 h; 65%. *f*) *Lindlar*'s catalyst, CH_2Cl_2, H_2, 8 h; 85%. *g*) $(Me_3S)I$, 50% aq. NaOH soln., $(Bu_4N)I$, CH_2Cl_2, 40°, 24 h; 84%. *h*) (*S*,*S*)-*Jacobsen* catalyst, H_2O, r.t., 72 h; 40%. *i*) $HC{\equiv}CCO_2Et$, BuLi, $BF_3 \cdot Et_2O$, dry THF, −78°, 2 h; 79%. *j*) *Lindlar*'s catalyst, benzene, H_2; 88%. *k*) PPTS, $CHCl_3$, reflux, 4 h, 95%. *l*) $Et_3N \cdot 3$ HF, MeCN, 12 h, 94%. *m*) Ac_2O, pyridine, CH_2Cl_2, 18 h; 97%.

the ethyl ester with diisobutylaluminum hydride (DIBAL-H) at 0° afforded the corresponding alcohol **4** in 90%, which was subjected to *Sharpless* asymmetric epoxidation [12] with (+)-diethyl L-tartrate, cumene hydroperoxide (=1-methyl-1-phenylethyl hydroperoxide), and $Ti(O^iPr)_4$ in CH_2Cl_2 to give the desired oxiranemethanol **5** in 80% yield with an enantiomer excess (e.e.) of 99.2%. Oxiranemethanol **5** was converted into the corresponding (chloromethyl)oxirane [13] with Ph_3P and a catalytic amount of $NaHCO_3$ in refluxing CCl_4; then the (chloromethyl)oxirane was transformed to the chiral alkynol [14] **6** in 70% yield under base-induced oxirane ring opening with BuLi in dry THF. The secondary alcohol **6** was protected with (*tert*-butyl)chlorodiphenylsilane ($^tBuPh_2SiCl$) in the presence of 1*H*-imidazole to give the silyl ether in 93% yield. The latter was formylated with DMF and BuLi in dry THF to provide alkynal **7** in 65% yield. This aldehyde **7** was converted to the required (*Z*)-alkenal **8** in 85% yield by hydrogenation over *Lindlar*'s catalyst in dry CH_2Cl_2. Then alkenal **8** was converted into oxirane **9** by reaction with trimethylsulfonium iodide (1.0 equiv.) and 50% aqueous NaOH in the presence of tetrabutylammonium iodide (catalytic amount) in CH_2Cl_2 [15]. Oxirane **9** was a 1:1.3 mixture of the two diastereoisomers which could not be differentiated by TLC. The resulting diastereoselectivity was determined from ^1H- and ^{13}C-NMR data. The next step in the synthesis was to produce the diastereoisomerically pure oxirane by means of *Jacobsen*'s hydrolytic kinetic resolution (HKR). Thus, oxirane **9** was subjected to the HKR [16] with [Co(OAc){(*S*,*S*)-salen}] complex (0.5 mol-%) and H_2O (0.55 equiv.) in THF (0.55 equiv.) at room temperature to afford (*S*)-oxirane **10** in 40% yield and the diol in 52% yield.

Our next concern was the construction of the key 2*H*-pyran-2-one moiety of the target compounds. Hence, employing the *Yamaguchi* procedure [17], oxirane **10** was treated with the lithium salt of ethyl prop-2-ynate in dry THF at −78° to furnish **11** in 79%, which was then subjected to partial reduction over *Lindlar*'s catalyst in benzene to afford compound **12** in 88% yield. The latter was then subjected to lactonization with pyridinium *p*-toluenesulfonate (= pyridinium 4-methylbenzenesulfonate; PPTS) in $CHCl_3$ to afford 2*H*-pyran-2-one **13** in 95%. The $^tBuPh_2Si$ ether group of **13** was removed with triethylamine tris(hydrofluoride) in MeCN to afford the natural product (−)-deacetylumuravumbolide (**1a**) in 94% yield. The latter was acetylated with Ac_2O/pyridine to afford (+)-umuravumbolide (**1b**) in 97% yield. The physical and optical data of **1a** (optical purity 98.0%) and of **1b** (optical purity 99.0%) were in close agreement with the ones reported for the natural products **1a** and **1b**, respectively [10] (see *Exper. Part*).

Conclusions. – We accomplished the total synthesis of the umuravumbolides starting from pentanal employing *Sharpless* asymmetric epoxidation, *Jacobsen*'s hydrolytic kinetic resolution (HKR), the *Yamaguchi* oxirane-opening method, and acid-catalyzed lactonization. This synthetic sequence provides an easy access to the preparation of umuravumbolides.

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Experimental Part

General. Solvents were dried over standard drying agents and freshly distilled prior to use. The reagents were purchased from *Aldrich* and *Acros* 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). 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}, ^{1}H- and ^{13}C-NMR Spectra: *Bruker-Avance-300* instrument; at 300 and 75 MHz, resp.; in $CDCl_3$; δ in ppm rel. to $SiMe_4$ as internal standard, *J* in Hz. MS: *Agilent-Technologies-1100* spectrometer (*Agilent* Chemistation software); in *m*/*z*.

*Ethyl (2*E*)-Hept-2-enoate* (**3**). To a stirred soln. of pentanal (**2**; 1.9 g, 21.62 mmol) in CH_2Cl_2 (60 ml) was added (ethoxycarbonylmethylene)triphenylphosphorane (9 g, 25.95 mmol) at r.t. and stirred for 3 h. After completion of the reaction, the mixture was diluted with H_2O and extracted with CH_2Cl_2 (3 × 15 ml), the extract dried (Na_2SO_4), and concentrated and the crude residue purified by CC (AcOEt/hexane 1:99): pure **3** (2.5 g, 87%). Colorless liquid. IR (neat): 2925, 2854, 1724, 1655, 1465, 1366, 1127, 721. ^{1}H-NMR: 6.93 (*dt*, *J* = 15.0, 7.1, 1 H); 5.76 (*dt*, *J* = 15.0, 1.3, 1 H); 4.15 (*q*, *J* = 7.1, 2 H); 2.2 (*q*, *J* = 7.9, 2 H); 1.33–1.52 (*m*, 4 H); 1.29 (*t*, *J* = 7.1, 3 H); 0.92 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR: 165.8; 149.0; 121.0; 59.4; 31.3; 29.7; 21.7. ESI-MS: 156 (M^+).

*(2*E*)-Hept-2-en-1-ol* (**4**). To a cooled (0°) soln. of **3** (1.9 g, 12.10 mmol) in dry CH_2Cl_2 (40 ml) was added DIBAL-H (2.58 g, 18.16 mmol, 20% soln. in toluene) within 15 min, and the mixture was stired at r.t. for 2 h. After completion of the reaction, the mixture was quenched with MeOH (1ml) and sodium potassium tartrate soln. (5 ml). The mixture was passed through a short pad of *Celite*. The filtrate was concentrated and the residue purified by CC (AcOEt/hexane 1:9): **4** (1.25 g, 90%). Colorless liquid. IR (neat): 3446, 2923, 2854, 1640, 1460, 1171, 769. ^{1}H-NMR: 5.54–5.70 (*m*, 2 H); 4.04 (*d*, *J* = 4.5, 2 H); 2.01–2.07 (*m*, 2 H); 1.24–1.42 (*m*, 4 H); 0.91 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 62.98; 70.43; 73.68; 81.33; 120.61; 127.85; 127.94; 128.47; 134.57; 137.72. ESI-MS: 226 ($[M + NH_4]^+$).

*(2*R*,3*R*)-3-Butyloxirane-2-methanol* (**5**). To a cooled (−20°) suspension of 4 Å powdered activated molecular sieves in dry CH_2Cl_2 (10 ml) were added $Ti(O^iPr)_4$ (0.58 ml, 1.96 mmol) and (+)-diethyl L-tartrate (0.4 g, 1.96 mmol) in dry CH_2Cl_2 (10 ml), and the mixture was stirred for 30 min at −20°. Then **4** (1.1 g, 9.8 mmol) in dry CH_2Cl_2 (20 ml) was added and the mixture stirred for another 30 min at −20°, followed by cumene hydroperoxide (2.23 ml, 14.7 mmol) addition and subsequent stirring at −20° for 5 h. After completion of the reaction, the mixture was quenched with H_2O (1 ml) and stirred for 1 h at r.t. After that, 30% aq. NaOH soln. (5 ml) and sat. NaCl soln. (1 ml) were added, and the mixture was stirred vigorously for another 30 min at r.t. The resulting mixture was then filtered through *Celite* rinsing with CH_2Cl_2. The aq. phase was extracted with CH_2Cl_2, the combined org. phase washed with brine, dried (Na_2SO_4), and concentrated, and the residue purified by CC (AcOEt/hexane 1:9): **5** (1.14 g, 80%). Viscous liquid. $[\alpha]_D^{25} = -44.4$ (*c* = 0.25, $CHCl_3$), e.e. = 99.2% (determined by chiral HPLC (*Zorbax-SBC-3* column (150 × 4.6 mm, 20 μm), Me_3CN/H_2O 7:3)). IR (neat): 3408, 2930, 2866, 1088. ^{1}H-NMR: 3.85 (*d*, *J* = 12.8, 1 H); 3.53–3.61 (*m*, 1 H); 2.83–2.93 (*m*, 2 H); 2.15 (*s*, 1 H); 1.52–1.61 (*m*, 2 H); 1.32–1.49 (*m*, 4 H); 0.93 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 72.03; 63.30; 62.48; 32.67; 28.10; 22.66; 14.13. EI-MS: 130 (M^+).

*(3*S*)-Hept-1-yn-3-ol* (**6**). A soln. of **5** (1.43 g, 11 mmol), Ph_3P (4.66 g, 16.5 mmol), and $NaHCO_3$ (497 mg, 5.5 mmol) in CCl_4 (15 ml) under N_2 was refluxed for 3 h. After completion of the reaction, the solvent was evaporated and the residue purified by CC (5% AcOEt/hexane): (chloromethyl)oxirane (1.27 g, 78%). Yellow oil. ^{1}H-NMR: 3.60 (*dd*, *J* = 11.7, 5.9, 1 H); 3.38 (*dd*, *J* = 11.7, 5.9, 1 H); 2.92 (*td*, *J* = 5.9, 2.2, 1 H); 2.79 (*td*, *J* = 5.9, 2.2, 1 H); 1.60–1.54 (*m*, 2 H); 1.50–1.33 (*m*, 4 H); 0.93 (*t*, *J* = 6.8, 3 H).

The (chloromethyl)oxirane (1.18 g, 8 mmol) was taken up in cooled (−78°) dry THF (15 ml), 1.6M BuLi in hexane (16 ml, 24 mmol) was added dropwise, and the mixture was stirred for 10 min. After completion of the mitxture, the reaction was quenched with sat. aq. NH_4Cl soln. (15 ml) and H_2O (15 ml). The resulting soln. was extracted with Et_2O (3 × 30 ml), the extract washed with brine, dried (Na_2SO_4), and concentrated, and the crude product purified by CC (AcOEt/hexane 1:9): **6** (675 mg, 70%). $[\alpha]_D^{25} = -20$ (*c* = 0.7, $CHCl_3$). IR (neat): 3445, 2926, 1634, 1035, 761. ^{1}H-NMR: 4.31 (*td*, *J* = 6.4, 2.1,

1 H); 2.30 (*s*, 1 H); 1.71–1.62 (*m*, 2 H); 1.47–1.26 (*m*, 4 H); 0.92 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 72.8; 67.5; 62.3; 37.3; 27.8; 27.7; 13.9. EI-MS: 112 (M^+).

*(4*S*)-4-{[(*tert*-Butyl)diphenylsilyl]oxy}oct-2-ynal* (**7**). To a cooled (0°) soln. of **6** (2.5 g, 12.13 mmol) and 1*H*-imidazole (2.06 g, 30.25 mmol) in dry CH_2Cl_2 (30 ml) was added dropwise (*tert*-butyl)chlorodiphenylsilane (4.0 g, 14.55 mmol) and the mixture was stirred for 4 h. After completion of the reaction, the mixture was diluted with H_2O (20 ml) and extracted with CH_2Cl_2 (3 × 30 ml). The combined org. layer was washed with brine (10 ml), dried (Na_2SO_4), and concentrated, and the crude residue purified ny CC (AcOEt/hexane 5 : 95) to give the silyl ether of **6** (2.2 g, 93%) as yellow liquid. The silyl ether was used for the next reaction. To a cooled (−78°) soln. of this silyl ether (4.96 g, 21.85 mmol) in dry THF (50 ml) was added 2.5M BuLi in hexane (10.5 ml, 26.25 mmol), and the mixture was stirred for 10 min, followed by the addition of DMF (3.19 g, 43.7 mmol) and subsequent stirring for 1 h. After completion of the reaction, the mixture was quenched with aq. dil. (1%) HCl soln. (40 ml). The product was extracted with Et_2O (3 × 50 ml), the extract dried ($MgSO_4$) and, concentrated, and the residue subjected to CC (hexane/AcOEt 9 : 1): pure **7** (2.89 g, 65%). $[\alpha]_D^{25} = -23.5$ (*c* = 2, $CHCl_3$). IR (neat): 2956, 2932, 2859, 2208, 1670, 1109, 702. ^{1}H-NMR: 9.01 (*s*, 1 H); 7.73–7.57 (*m*, 4 H); 7.48–7.28 (*m*, 6 H); 4.52–4.45 (*m*, 1 H); 1.78–1.64 (*m*, 1 H); 1.54–1.19 (*m*, 5 H); 0.86 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 176.5; 135.9; 135.7; 132.9; 132.8; 130.0; 129.9; 127.7; 127.5; 97.8; 84.1; 63.6; 37.1; 26.8; 22.2; 19.2; 13.8.

*(2*S*,4*Z*)-4-{[(*tert*-Butyl)diphenylsilyl]oxy}oct-2-enal* (**8**). A soln. of **7** (1.88 g, 4.98 mmol) in dry CH_2Cl_2 (20ml) and *Lindlar*'s catalyst (0.5g) were stirred under H_2 (TLC monitoring). After completion of the reaction (10 h), the mixture was filtered through a silica gel pad, the solvent evaporeted, and residue purified by CC (hexane/AcOEt 98 : 2): pure **8** (1.6 g, 85%). Liquid. $[\alpha]_D^{25} = +15.1$ (*c* = 1.65, $CHCl_3$). IR (neat): 2957, 2932, 2859, 1688, 1466, 1428, 1109, 703. ^{1}H-NMR: 9.29 (*d*, *J* = 8.0, 1 H); 7.65–7.57 (*m*, 4 H); 7.42–7.30 (*m*, 6 H); 6.39 (*dd*, *J* = 11.2, 8.8, 1 H); 5.64 (*dd*, *J* = 11.2, 7.2, 1 H); 4.92 (*q*, *J* = 15.2, 6.4, 1 H); 1.75–1.45 (*m*, 2 H); 1.28–1.17 (*m*, 4 H); 1.06 (*s*, 9 H); 0.86 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 190.4; 153.1; 135.7; 135.6; 133.3; 133.2; 130.8; 129.9; 129.4; 128.1; 127.6; 127.5; 68.8; 37.4; 26.8; 22.3; 19.1; 13.8.

*(*tert*-Butyl){[(1*S*,2*Z*)-1-butyl-3-(oxiran-2-yl)prop-2-en-1-yl]oxy}diphenylsilane* (**9**). To a soln. of **8** (1.9 g, 5 mmol) and (Bu_4N)(0.065mmol) in CH_2Cl_2 (25 ml) were added 50% aq. NaOH soln. and trimethylsulfonium iodide (102 mg, 5 mol). The was heated at 50° with vigorous stirring for 48 h whereupon the originally undissolved sulfonium salt had disappeared. After completion of the reaction, the mixture was poured on ice, the org. phase washed with H_2O, dried (Na_2SO_4), and concentrated, and the residue purified by CC (hexane/AcOEt 9 : 1): 1 : 1.3 diastereoisomer mixture **9** (1.65 g, 84%). Liquid. $[\alpha]_D^{25} = +2.5$ (*c* = 0.6, $CHCl_3$). ESI-MS: 395 ($[M+1]^+$).

(*tert*-*Butyl){[(1*S*,2*Z*)-1-butyl-3-[(2*S*)-oxiran-2-yl]prop-2-en-1-yl]oxy}diphenylsilane* (**10**). To a cooled (0°) soln. of **9** (0.9 g, 2.31mmol) in THF (0.3ml) was added [Co^{III}(OAc){(*S*,*S*)-salen}] (8 mg, 0.012 mmol). The mixture was stirred for 5 min, and then dist. H_2O (22.9 µl, 1.27 mmol) was added. After stirring for 72 h, this mixture was concentrated and purified by CC (petroleum ether/AcOEt 9 : 1): liquid **10** (360 mg, 40%) and on elution with petroleum ether/AcOEt 3 : 2, liquid diol **10** (468 mg, 52%): $[\alpha]_D^{25} = -10.3$ (*c* = 0.6, $CHCl_3$). IR (neat): 2932, 2858, 1426, 1106. ^{1}H-NMR: 7.64–7.71 (*m*, 4 H); 7.31–7.43 (*m*, 6 H); 5.66–5.76 (*m*, 1 H); 4.75–4.89 (*m*, 1 H); 4.47–4.57 (*m*, 1 H); 2.87–2.93 (*m*, 1 H); 2.46 (*dd*, *J* = 5.3, 3.0, 1 H); 2.31 (*dd*, *J* = 5.3, 3.0, 1 H); 1.44–1.71 (*m*, 2 H); 1.13–1.24 (*m*, 4 H); 1.05 (*s*, 9 H); 0.82 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 138.8; 135.9; 135.8; 129.5; 129.4; 127.6; 127.5; 127.3; 127.0; 126.8; 69.6; 48.0; 47.7; 37.8; 26.9; 22.5; 19.2; 15.4; 13.9. ESI-MS: 395 ($[M+H]^+$). HR-ESI-MS: 395.2403 ($[M+H]^+$, $C_{25}H_{35}O_2Si^+$; calc. 395.2401).

*Ethyl (5*R*,6*Z*,8*S*)-8-{[(*tert*-Butyl)diphenylsilyl]oxy}-5-hydroxydodec-6-en-2-ynoate* (**11**). To cooled (−78°) soln. of ethyl prop-2-ynoate (588 mg, 6.6 mmol) in anh. THF (15 ml) was added dropwise 1.6M BuLi in hexane (4.2 ml, 6.64 mmol) and the mixture was stirred for 15 min, followed by addition of $BF_3 \cdot Et_2O$ (0.84 ml, 6.6 mmol) and subsequent stirring for an additional 15 min. Once the formation of dark black alkynyl borane was observed, a soln. of **10** (260 mg, 0.66 mmol) in anh. THF (10 ml) was added to the above soln. and stirred for 30 min at −78°. After completion of the reaction, the mixture was quenched at −78° by addition of sat. Na_2SO_4 soln. (20 ml) and AcOEt/H_2O. The mixture was extracted with AcOEt, the combined org. phase washed with brine, dried (Na_2SO_4), and concentrated, and the crude residue purified by CC (20% AcOEt/petroleum ether): pure **11** (256 mg, 79%). $[\alpha]_D^{25} = -36.0$ (*c* =

0.3, $CHCl_3$). IR (neat): 3449, 2928, 2857, 2236, 1712, 1250, 1105, 1055. ^{1}H-NMR: 7.62–7.70 (*m*, 4 H); 7.35–7.45 (*m*, 6 H); 5.64–5.75 (*m*, 1 H); 5.05–5.22 (*m*, 1 H); 4.32–4.41 (*m*, 1 H); 4.25 (*q*, *J* = 6.9, 7.2, 2 H); 3.94–4.03 (*m*, 1 H); 3.54–2.90 (*m*, 2 H); 1.46–1.63 (*m*, 2 H); 1.34 (*t*, *J* = 7.2, 3 H); 1.16–1.28 (*m*, 4 H); 1.06 (*s*, 9 H); 0.85 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 157.01; 137.6; 135.9; 135.8; 129.8; 129.7; 129.6; 127.5; 127.4; 122.6; 122.3; 88.43; 69.79; 69.15; 64.32; 61.93; 37.99; 33.87; 33.34; 29.70; 26.99; 22.62; 13.96. ESI-MS: 515 ($[M+Na]^+$). HR-ESI-MS: 515.2585 ($[M+Na]^+$, $C_{30}H_{40}NaO_4Si^+$, calc. 515.2588).

*Ethyl (2Z,5*R*,6Z,8*S*)-8-{[(*tert*-Butyl)diphenylsilyl]oxy}-5-hydroxydodeca-2,6-dienoate* (**12**). A suspension of **11** (197 mg, 0.4 mmol) and *Lindlar*'s catalyst (100 mg) in benzene (15 ml) was flushed with H_2 gas and stirred for 5 h under H_2 (TLC monitoring). After completion, the mixture was filtered (*Celite*), the filtrate concentrated, and the residue purified by CC (20% AcOEt/petroleum ether): **12** (174 mg, 88%). Oil $[\alpha]_D^{25} = -8.0$ (*c* = 0.2, $CHCl_3$). IR: 3450, 2928, 2857, 2096, 1731, 1635, 1463, 1221 1076, 771, 1388, 1251, 1045, 918, 796, 742, 618, 621. ^{1}H-NMR: 7.77–7.64 (*m*, 4 H); 7.48–7.33 (*m*, 6 H); 5.90–5.50 (*m*, 3 H); 5.10–4.94 (*m*, 1 H); 4.55–4.47 (*m*, 1 H); 4.16–3.85 (*m*, 3 H); 3.12–3.54 (*m*, 2 H); 1.52–1.60 (*m*, 2 H); 1.32 (*t*, *J* = 7.2, 3 H); 1.14–1.28 (*m*, 4 H); 1.02 (*s*, 9 H); 0.84 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 166.9; 147.9; 137.3; 135.9; 135.8; 129.5; 129.4; 127.5; 127.4; 126.0; 125.7; 121.0; 120.5; 69.9; 65.9; 60.2; 53.4; 40.6; 38.3; 29.6; 26.9; 22.6; 19.2; 13.9. ESI-MS: 517 ($[M+Na]^+$).

*(6*R*)-6-{(1Z,3*S*)-3-{[(*tert*-Butyl)diphenylsilyl]oxy}hept-1-en-1-yl}-5,6-dihydro-2*H*-pyran-2-one* (**13**). A soln. of **12** (168 mg, 0.34 mmol) and PPTS (170 mg, 0.68 mmol) in $CHCl_3$ (10 ml) was refluxed for 6 h. After completion of the reaction, the mixture was diluted with H_2O (10 ml) and extracted with $CHCl_3$ (3 × 50 ml). The combined org. layer was washed with brine, dried (Na_2SO_4), and concentrated and the resulting crude product purified by CC (20% AcOEt/petroleum ether): **13** (152 mg, 95%). Pale yellow oil. $[\alpha]_D^{25} = -11.1$ (*c* = 0.45, $CHCl_3$). IR (neat): 2929, 2857, 1735, 1464, 1225, 1078, 703. ^{1}H-NMR: 7.69–7.63 (*m*, 4 H); 7.44–7.34 (*m*, 6 H); 6.40 (*dd*, *J* = 9.8, 4.0, 1 H); 5.96 (*dd*, *J* = 9.8, 2.3, 1 H); 5.89–5.77 (*m*, 1 H); 5.71–5.62 (*m*, 1 H); 5.09–4.95 (*m*, 1 H); 4.39–4.31 (*m*, 1 H); 2.89–2.70 (*m*, 2 H); 1.60–1.53 (*m*, 2 H); 1.31–1.19 (*m*, 4 H); 1.04 (*s*, 9 H); 0.86 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR: 165.0; 148.9; 137.6; 135.9; 135.8; 129.8; 129.7; 127.6; 127.5; 123.1; 123.0; 120.1; 120.0; 70.0; 69.2; 37.9; 33.0; 29.6; 26.8; 22.6; 19.2; 13.9. ESI-MS: 471 ($[M+Na]^+$). HR-ESI-MS: 471.2345 ($[M+Na]^+$, $C_{28}H_{36}NaO_3Si^+$; calc.: 471.2326).

(−)-Deacetylumuravumbolide (=*(1*R*)-5,6-Dihydro-6-[(1Z,3*S*)-3-hydroxyhept-1-en-1-yl]-2*H*-pyran-2-one*; **1a**). To a soln. of **13** (235 mg, 0.5 mmol) in MeCN (4 ml) was added $Et_3N \cdot 3$ HF (0.6 g, 4.0 mmol) and stirred for 12 h. After completion of the reaction, the mixture was diluted with H_2O and extracted with AcOEt (3 × 25 ml). The extract was dried ($MgSO_4$) and concentrated, and the crude product subjected to CC (hexane/AcOEt 3 : 2): **1a** (98 mg 94%). $[\alpha]_D^{25} = -5.4$ (*c* = 1, $CHCl_3$), optical purity 98.0% (natural product **1a** [10]: $[\alpha]_D^{24} = -5.3$ (*c* = 1.3, $CHCl_3$); synthetic **1a** [11b]: $[\alpha]_D^{25} = -5.4$ (*c* = 1, $CHCl_3$)). IR (neat): 3429, 2924, 2855, 1726, 1377, 1243, 1082. ^{1}H-NMR: 6.88 (*m*, 1 H); 6.0 (*dd*, *J* = 9.8, 2.2, 1 H); 5.60–5.73 (*m*, 2 H); 5.25–5.36 (*m*, 1 H); 4.33–4.47 (*m*, 1 H); 2.34–2.51 (*m*, 2 H); 2.2 (*s*, 1 H); 1.45–1.70 (*m*, 2 H); 1.20–1.42 (*m*, 4 H); 0.88 (*t*, *J* = 6.9, 3 H). ^{13}C-NMR: 163.8; 144.9; 137.9; 127.4; 121.4; 73.7; 67.7; 36.8; 29.9; 27.5; 22.6; 14.0. ESI-MS: 211 ($[M+H]^+$). HR-ESI-MS: 211.1323 ($[M+H]^+$, $C_{12}H_{19}O_3^+$; calc. 211.1329).

(+)-Umuravumbolide (=*(6*R*)-6-[(1Z,3*S*)-3-(Actyloxy)hept-1-en-1-yl]-5,6-dihydro-2*H*-pyran-2-one*; **1b**). To a soln. of **1a** (52 mg, 0.25 mmol) and pyridine (80 mg, 1 mmol) in CH_2Cl_2 (1 ml) was added Ac_2O (0.05 g, 0.5 mmol) and stirred for 18 h. After completion of the reaction, the mixture was diluted with cold H_2O and extracted with CH_2Cl_2 (3 × 15 ml). The combined extract was dried (Na_2SO_4) and concentrated, and the crude residue subjected to CC (hexane/AcOEt 8 : 2): **1b** (61 mg, 97%). $[\alpha]_D^{25} = +33.4$ (*c* = 1, $CHCl_3$), optical purity 99.0% (natural product **1b** [10]: $[\alpha]_D^{20} = +30.0$ (*c* = 2.1, $CDCl_3$); synthetic **1b** [11b]: $[\alpha]_D^{25} = +33.4$ (*c* = 1, $CDCl_3$) [11b]. IR (neat): 2929, 2860, 1747, 1730, 1242. ^{1}H-NMR: 6.88 (*m*, 1 H); 6.01 (*dd*, *J* = 9.8, 2.2, 1 H); 5.71 (*dd*, *J* = 11.1, 8.0, 1 H); 5.31–5.56 (*m*, 3 H); 2.28–2.57 (*m*, 2 H); 2.02 (*s*, 3 H); 1.44–1.75 (*m*, 2 H); 1.20–1.43 (*m*, 4 H); 0.87 (*t*, *J* = 6.9, 3 H). ^{13}C-NMR: 170.1; 163.4; 144.2; 131.7; 130.0; 121.7; 74.0; 69.5; 34.3; 30.1; 27.3; 22.5; 22.2; 17.0; 14.0. ESI-MS: 253 ($[M+1]^+$).

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