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Synthesis of 7,8-*epi*-Valtrate from (+)-Genipin

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Valepotriates are natural products of a large number of plant families. They belong to the iridoids, which are cyclopentan-*c*-pyran monoterpenoids, often in the form of glycosides[1], with a 10-carbon basic skeleton.[2] Based on their chemical structure, valepotriates can be separated into diene (**1**), the monoene (**2**), the valtrate-hydrine (**3**), and the desoxy monoene groups (**4**) (Fig. 1).[3] The roots and rhizomes of some Valeriana species have been used for centuries in traditional medicine for epilepsy, hysteria, and nervous disorders.[4-7] Physicians have used valerian root as a diuretic, pain reliver, and spasmolytic agents.[8,9] Today, valerian preparationsare used primarily as a mild sedative to treat light forms of neurasthenia and emotional stress.[10,11] In addition, valepotriates possess alkylating properties, for which the epoxy group is mainly responsible. Several studies have reported on the cytotoxicity and mutagenicity of valepotriates in *in vitro* cell systems, and inhibition of DNA and protein synthesis in *in vitro* cultured mammalian cells have been described.[12] Newly discovered iridoid compounds were reported to be cytotoxic in HeLa S3[13] cells and valtrate (**5**) exhibits *anti*-HIV activity by inhibiting nuclear export of Rev.[14,15] Thus, because valepotriates with diverse chemical structures have useful biological properties they are potential lead compounds for disease treatments.

Drug discovery in natural products and mimetic synthetics, identifies drug candidates with anticancer activity by assessing them for cytotoxicity against cancer cells and inhibition of angiogenesis. For example, sulfonyl and sulfidyl artemisinin derivatives strongly inhibit tumor angiogenesis.[16,17] The 10-substituted triazolyl artemisinin derivative exhibited potent cytotoxicity against various cancer cells.[18] Pyridine- and thiophene-linked symmetrical bis-alkynyl curcumin derivatives inhibit proliferation and tube formation of human umbilical vein endothelial cells (HUVECs).[19] Curcumin mimics with asymmetric alkyl and aryl amide functional groups are antiangiogenic[20] and reverse multidrug resistance (MDR).[21] Substituted triazolyl curcumin mimics strongly inhibit osteoclastogenesis induced by the receptor activator of NF-jB ligand (RANKL).[22] An efficient drug discovery process includes synthesizing the natural product and naturomimetic library, then assessing their biological properties with diverse screening systems.

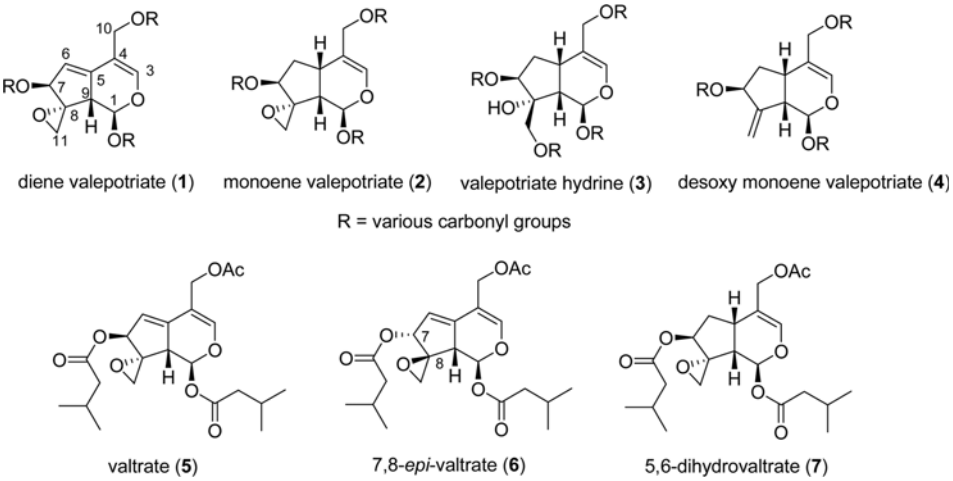


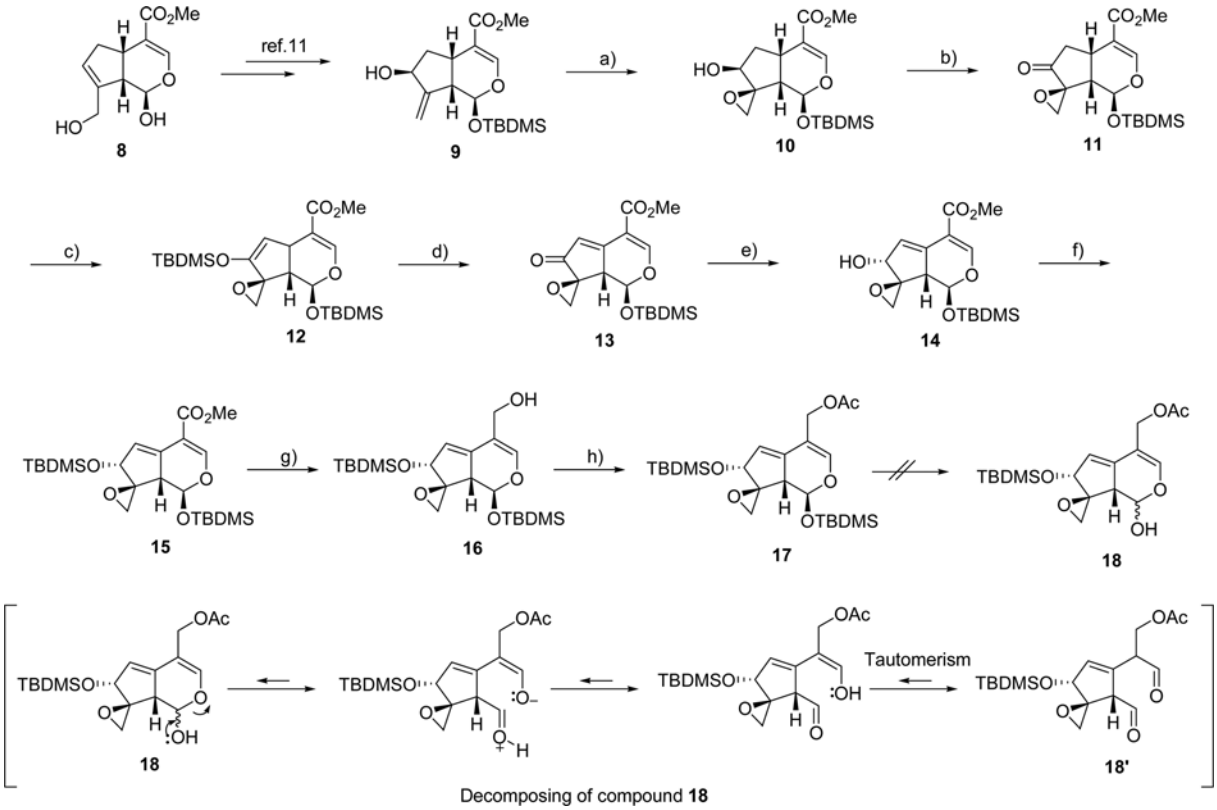
Figure 1. Chemical structures of valepotriates.

[a]These authors contributed equally to this work.

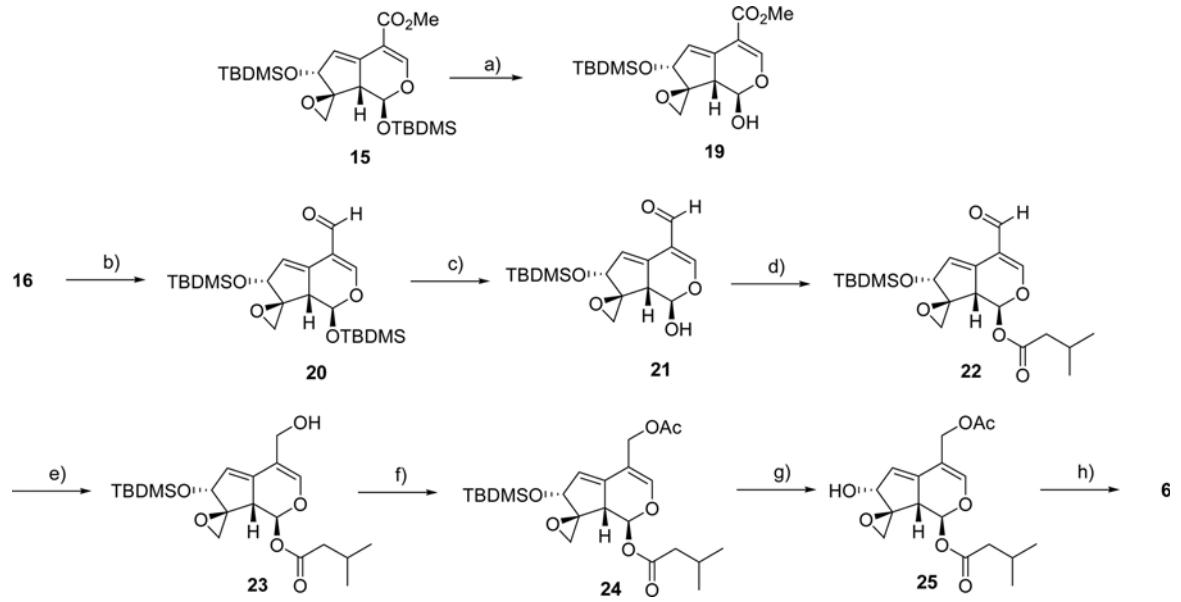
In this paper, we will describe the trial synthesis of valtrate (**5**), although we obtained 7,8-*epi*-valtrate (**6**). Before our submission of this independent report on the synthesis of 7,8-*epi*-valtrate (**6**), Tamura, *et al.* reported the synthesis and biological properties[23] of 5,6-dihydrovaltrate (**7**) from (+)-genipin (**8**), a monotype derivative of monoene valepotriate (**2**). They have not reported synthesis of diene-type valepotriate derivatives. Therefore, this report describes the key step in the synthesis of diene-type valepotriates (**1**) such as valtrate (**5**).

To synthesize of 7,8-*epi*-valtrate (**6**), an important synthetic intermediate **9** was synthesized from the commercially available natural chiral building block (+)-genipin (**8**), by a previously described method.[23] Stereoselective epoxidation of the adjacent hydroxyl group using *tert*-butyl hydroperoxide (TBHP) and vanadium oxyacetyl acetonate $[VO(acac)_2]$[24] yieled epoxy alcohol **10**. Swern oxidation of **10** with oxalyl chloride and dimethylsulfoxide (DMSO) yield ketone **11**, which was reacted with LDA and TBDMSOTf in THF at −78 °C to produce TBDMS-protected enol compound **12**, an important intermediate in forming the structure of diene-type valepotriate (**1**). After reaction of **12** with 2,3-dichloro-5,6-dicyanoquinone (DDQ) in pyridine, 5,6-unsaturated ketone **13** was obtained with trace amounts of starting material **13**, which was stereoselectively reduced using $NaBH_4$ and $CeCl_3{\cdot}7H_2O$[25] to produce 7α-alcohol **14**. The stereochemistry of C-7 and C-8 of **14** are the opposite of that of the natural product valtrate (**5**) in the NMR spectrum.[26] The hydroxyl group of **14** was protected as a TBDMS ether to give the desired silyl ester **15**. In order to introduce an acyl group on the 11-hydroxyl, the 4-methyl ester of **15** was reduced with diisobutylaluminum hydride (DIBAL) to obtain **16**, which was reacted with acetic anhydride to form the precursor of our target compound, **6**. However, the deprotection reaction with TBAF to remove two TBDMS protective groups at the 1,7-position of **17** was not successful. We have no products because compound **17** was entirely decomposed. We have tried to remove the TBDMS groups with various deprotection reaction conditions but have not succeeded.[27] After 3,4-unsaturated methyl ester is reduced to the allyl alcohol group, the temporarily formed C-1 hemiacetal group is hydrolyzed to dialdehyde compound **18**, then reacted with 2 aldehydes to yield an undefined mixture.

To confirm recovery of the stable hemiacetal group at C-1 and add an isovaleryl group to maintain the 3,4-unsaturated methyl ester, we treated compound **15** with TBAF in THF and obtained product **19** without decomposition of functionality. Based on this preliminary reaction for deprotection of the C-1 TBDMS group, we can proceed with the synthetic steps for the final target, 7,8-*epi*-valtrate (**6**), shown in Scheme 2. The allyl alcohol compound **16** was produced and then was successively oxidized by TPAP and NMO to produce conjugated aldehyde **20**. Selective deprotection of the silyl acetal **20** with TBAF at 0 °C gave hemiacetal **21**, which was reacted with isovaleryl chloride in the presence of pyridine to produce isovaleryl ester **22**. Reduction of **22** by



Scheme 1. Reagents and conditions: (a) TBHP, $VO(acac)_2$, C_6H_6, rt, 89%; (b) oxalyl chloride, DMSO, CH_2Cl_2, −78 °C, 97%; (c) LDA, TBDMSOTf, THF, −78 °C, 75%; (d) DDQ, pyridine, C_6H_6, 50 °C, 56%; (e)$NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, 0 °C, 94%; (f) TBDMSCl, imidazole, CH_2Cl_2, rt, 92%; (g) DIBAL-H, CH_2Cl_2, −78 °C, 78%; (h) acetyl chloride, pyridine, CH_2Cl_2, −78 °C, 84%.



Scheme 2. Reagents and conditions: (a) TBAF, THF, 0 °C, 82%; (b) TPAP, NMO, CH_2Cl_2, rt, 62%; (c) TBAF, THF, 0 °C, 83%; (d) isovaleryl chloride, pyridine, CH_2Cl_2, −78 °C, 46%; (e) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH, 0 °C, 67%; (f) acetyl chloride, pyridine, CH_2Cl_2, −78 °C, 78%; (g) TBAF, THF, rt, 70%; (h) isovaleryl chloride, pyridine, CH_2Cl_2, rt, 60%.

$NaBH_4$ in the presence of $CeCl_3 \cdot 7H_2O$ provided alcohol and then acetylation of the primary hydroxyl group with acetic anhydride gave **24**. In order to add isovaleryl at position C-7, compound **24** was deprotected with TBAF and 7,8-*epi*-valtrate **6** was obtained by reacting isovaleryl chloride with final precursor **25**.[28]

In conclusion, we synthesized 7,8-*epi*-valtrate (**6**) from (+)-genipin (**8**). Although final product **6** has the opposite stereochemistry at C-7 and 8 compared to natural valtrate (**5**), this is the first synthesis of a diene-type valepotriate epimeric structure by an efficient synthetic pathway. We screened the compounds for proliferation inhibition of various cancer cell lines and HUVEC and discovered 7,8-*epi*-valtrate (**6**) and its synthetic intermediates showed strong inhibitory activity; these results will be published elsewhere.

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27. Reagent and conditions: TBAF, THF, 0 °C; AcBr, CH_2Cl_2; aq. HF, CH_3CN. AcOH, H_2O, THF; BF_3Et_2O, $CHCl_3$; pyridine-HF, THF;

TsOH, THF, H_2O; TFA, H_2O, CH_2Cl_2; NBS, DMSO, H_2O.

28. Analytical data for **9**: white solid, mp 48-50 °C; $[\alpha]_D$ −16.1 (*c* 0.0006, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.48 (d, 1H, *J* = 0.7 Hz, H-3), 5.45 (s, 1H, H-10α), 5.40 (s, 1H, H-10β), 4.79 (d, 1H, *J* = 7.3 Hz, H-1), 4.47 (br, 1H, H-7), 3.73 (s, 3H, -OMe), 3.23 (q, 1H, *J* = 7.1 Hz, 9.7 Hz, H-5), 2.71 (t, 1H, *J* = 7.3 Hz, H-9), 2.26 (m, 1H, H-6α), 1.77 (br, 1H, -OH), 1.64 (m, 1H, H-6β), 0.92 (s, 9H, Si-*t*Bu), 0.13 (s, 3H, Si-Me), 0.11 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 167.7, 152.9, 152.4, 114.7, 109.7, 94.8, 73.3, 51.2, 45.9, 41.5, 32.9, 25.6, 18.0, –4.38, –5.15; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.41 (d, 1H, *J* = 1.1 Hz, H-3), 5.03 (d, 1H, *J* = 5.3 Hz, H-1), 4.04 (m, 1H, H-7), 3.74 (s, 3H, OMe), 3.26 (m, 2H, H-10α, H-5), 2.89 (d, 1H, *J* = 4.6 Hz, H-10β), 2.34 (m, 1H, H-9), 2.20 (m, 3H, H-6, OH), 0.88 (s, 9H, Si-*t*Bu), 0.12 (s, 3H, Si-Me), 0.11 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 167.2, 151.9, 110.3, 92.7, 70.0, 65.1, 51.2, 49.8, 45.4, 38.8, 29.2, 25.5, 17.7, –4.5, –5.4; for **11**: white solid, mp 119-120 °C; $[\alpha]_D$ −147.0 (*c* 0.00035, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.46 (d, 1H, *J* = 1.5 Hz, H-3), 5.17 (d, 1H, *J* = 3.1 Hz, H-1), 3.74 (s, 3H, OMe), 3.47 (m, 1H, H-5), 3.26 (d, 1H, *J* = 6.2 Hz, H-10α), 2.98 (d, 1H, *J* = 6.2 Hz, H-10β), 2.81 (m, 3H, H-9, H-6), 0.88 (s, 9H, Si-*t*Bu), 0.14 (s, 3H, Si-Me), 0.12 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 212.3, 166.8, 152.6, 108.5, 90.9, 59.5, 51.4, 51.3, 41.8, 25.5, 25.3, 17.8, –4.5, –5.4; for **12**: colorless oil; $[\alpha]_D$ −78.5 (*c* 0.00001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40 (d, 1H, *J* = 1.4 Hz, H-3), 5.30 (d, 1H, *J* = 2.6 Hz, H-6), 4.99 (d, 1H, *J* = 5.1 Hz, H-1), 3.74 (s, 3H, OMe), 3.71 (m, 1H, H-5), 3.15 (d, 1H, *J* = 5.1 Hz, H-10α), 2.98 (d, 1H, *J* = 5.0 Hz, H-10β), 2.43 (dd, 1H, *J* = 5.1 Hz, 7.3 Hz, H-9), 0.90 (s, 9H, Si-*t*Bu), 0.89 (s, 9H, Si-*t*Bu), 0.16 (s, 3H, Si-Me), 0.15 (s, 3H, Si-Me), 0.11 (s, 6H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 167.4, 151.6, 150.4, 111.6, 110.5, 93.4, 65.0, 51.2, 48.2, 44.4, 32.6, 25.6, 25.5, 18.1, 17.8, –4.5, –4.9, –5.0, –5.2; for **13**: colorless oil; $[\alpha]_D$ −271.7 (*c* 0.001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1H, H-3), 6.71 (d, 1H, *J* = 2.4 Hz, H-6), 5.81 (d, 1H, *J* = 10.4 Hz, H-1), 3.82 (s, 3H, OMe), 3.77 (d, 1H, *J* = 11.0 Hz, H-10α), 3.64 (d, 1H, *J* = 10.8 Hz, H-10β), 3.11 (m, 1H, H-6), 0.98 (s, 9H, Si-*t*Bu), 0.25 (s, 3H, Si-Me), 0.24 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 204.7, 164.4, 162.7, 160.4, 122.0, 106.0, 97.9, 77.3, 51.8, 43.1, 25.5, 17.7, –3.9, –5.2; for **14**: colorless oil; $[\alpha]_D$ −96.2 (*c* 0.0005, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.60 (s, 1H, H-3), 6.28 (t, 1H, *J* = 2.0 Hz, H-6), 5.15 (d, 1H, *J* = 9.3 Hz, H-1), 4.90 (d, 1H, *J* = 5.9 Hz, H-7), 3.77 (s, 3H, OMe), 3.13 (dd, 2H, *J* = 5.7 Hz, 7.7 Hz, H-10), 2.86 (m, 1H, H-9), 1.97 (d, 1H, *J* = 7.3 Hz, OH), 0.92 (s, 9H, Si-*t*Bu), 0.16 (s, 3H, Si-Me), 0.16 (s, 3H, Si-Me). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 165.6, 156.7, 131.2, 125.7, 105.4, 98.8, 76.6, 68.7, 51.4, 46.6, 45.8, 25.5, 17.7, –3.8, –5.0; for **15**: white solid, mp 156-157 °C; $[\alpha]_D$ −159.1 (*c* 0.00045, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H, H-3), 6.21 (t, 1H, *J* = 2.0 Hz, H-6), 5.14 (d, 1H, *J* = 9.2 Hz, H-1), 4.93 (s, 1H, H-7), 3.77 (s, 3H, OMe), 3.03 (q, 2H, *J* = 5.85 Hz, 8.43 Hz, H-10), 2.82 (m, 1H, H-9), 0.91 (s, 9H, Si-*t*Bu), 0.90 (s, 9H, Si-*t*Bu), 0.16 (s, 3H, Si-Me), 0.15 (s, 3H, Si-Me), 0.10 (s, 3H, Si-Me), 0.08 (s, 3H, Si-Me). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 165.7, 156.4, 129.9, 126.5, 105.5, 98.6, 76.5, 69.0, 51.3, 45.9, 45.8, 25.8, 25.5, 18.2, 17.7, –3.7, –4.9, –5.0, –5.1; for **16**: colorless oil; $[\alpha]_D$ −23.5 (*c* 0.00001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.59 (s, 1H, H-3), 5.64 (t, 1H, *J* = 2.0 Hz, H-6), 5.03 (d, 1H, *J* = 9.3 Hz, H-1), 4.95 (s, 1H, H-7), 4.24 (q, 2H, *J* = 13.9 Hz, 10.3 Hz, H-11), 3.03 (q, 2H, *J* = 5.7 Hz, 6.1 Hz, H-10), 2.85 (m, 1H, H-9), 0.91 (s, 9H, Si-tBu), 0.90 (s, 9H, Si-*t*Bu), 0.14 (s, 3H, Si-Me), 0.12 (s, 3H, Si-Me), 0.09 (s, 3H, Si-Me), 0.08 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 145.6, 134.8, 121.8, 112.2, 97.6, 76.4, 69.5, 66.4, 60.1, 46.0, 45.9, 29.7, 25.8, 25.6, 18.3, 17.7, –3.5, –4.9, –4.9, –5.1; for **17**: colorless oil; $[\alpha]_D$ −13.3 (*c* 0.0015, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.65 (s, 1H, H-3), 5.52 (t, 1H, *J* = 1.8 Hz, H-6), 5.04 (d, 1H, *J* = 9.3 Hz, H-1), 4.94 (s, 1H, H-7), 4.66 (q, 2H, *J* = 12.3 Hz, 9.5 Hz, H-11), 3.03 (q, 2H, *J* = 5.7 Hz, 5.0 Hz, H-10), 2.84 (d, 1H, *J* = 9.3 Hz, H-9), 2.07 (s, 3H, COMe), 0.91 (s, 9H, Si-*t*Bu), 0.90 (s, 9H, Si-*t*Bu), 0.14 (s, 3H, Si-Me), 0.13 (s, 3H, Si-Me), 0.09 (s, 3H, Si-Me), 0.08 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 171.1, 147.7, 134.8, 121.7, 107.8, 97.5, 76.3, 69.5, 61.1, 45.9, 45.8, 25.7, 25.5, 21.1, 18.3, 17.7, –3.6, –4.9, –5.0, –5.1; for **19**: colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.30 (s, 1H, H-3), 6.58 (t, 1H, *J* = 2.0 Hz, H-6), 5.57 (t, 1H, *J* = 5.9 Hz, H-1), 4.96 (s, 1H, H-7), 3.75 (s, 3H, OMe), 3.24-2.80 (m, 6H, H-10, H-9), 0.90 (s, 9H, Si-tBu), 0.10 (s, 3H, Si-Me), 0.09 (s, 3H, Si-Me); for **20**: white solid, mp 107-108 °C; $[\alpha]_D$ −68.2 (*c* 0.00045, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 9.38 (s, 1H, CHO), 7.30 (s, 1H, H-3), 6.46 (t, 1H, *J* = 2.0 Hz, H-6), 5.23 (d, 1H, *J* = 9.2 Hz, H-1), 4.96 (s, 1H, H-7), 3.03 (q, 2H, *J* = 5.7 Hz, 8.3 Hz, H-10), 2.84 (m, 1H, H-9), 0.93 (s, 9H, Si-*t*Bu), 0.89 (s, 9H, Si-*t*Bu), 0.19 (s, 3H, Si-Me), 0.17 (s, 3H, Si-Me), 0.10 (s, 3H, Si-Me), 0.08 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 187.8, 164.2, 128.2, 127.9, 116.0, 100.0, 76.6, 45.9, 45.5, 25.8, 25.5, 18.2, 17.7, –3.7, –4.9, –5.1, –5.2; for **21**: colorless oil; $[\alpha]_D$ −18.0 (*c* 0.00001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 9.40 (s, 1H, CHO), 9.39 (s, 1H, CHO), 7.32 (s, 1H, H-3), 7.24 (s, 1H, H-3), 6.58 (s, 1H, *J* = 2.0 Hz, H-6), 6.46 (t, 1H, *J* = 2.0 Hz, H-6), 5.57 (d, 1H, *J* = 3.1 Hz, H-1), 5.20 (d, 1H, *J* = 9.5 Hz, H-1), 4.98 (s, 1H, H-7), 4.92 (s, 1H, H-7), 3.24-2.80 (m, 6H, H-10, H-9), 0.90 (s, 9H, Si-*t*Bu), 0.10 (s, 3H, Si-Me), 0.09 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 187.5, 164.1, 128.6, 127.9, 116.2, 95.8, 76.6, 45.9, 45.5, 25.7, 18.2, -4.9, –5.2; for **22**: colorless oil; $[\alpha]_D$ +62.5 (*c* 0.00016, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 9.41 (s, 1H, CHO), 7.26 (s, 1H, H-3), 6.53 (t, 1H, *J* = 1.8 Hz, H-6), 6.09 (d, 1H, *J* = 9.9 Hz, H-1), 4.99 (s, 1H, H-7), 3.05 (m, 2H, H-10α, H-9), 2.67 (d, 1H, *J* = 5.0 Hz, H-10β), 2.32-2.10 (m, 3H), 1.00 (d, 6H), 0.89 (s, 9H, Si-*t*Bu), 0.10 (s, 3H, Si-Me), 0.07 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 187.5, 171.0, 162.9, 129.5, 126.3, 116.1, 93.8, 76.6, 69.1, 46.1, 43.0, 41.9, 25.7, 25.6, 22.3, 22.3, 18.2, –4.8, –5.1; for **23**: colorless oil; $[\alpha]_D$ −34.5 (*c* 0.00001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.58 (s, 1H, H-3), 5.92 (d, 1H, *J* = 9.9 Hz, H-1), 5.73 (t, 1H, *J* = 2.0 Hz, H-6), 4.97 (s, 1H, H-7), 4.27 (q, 2H, *J* = 12.3 Hz, 13.9 Hz, H-11), 3.09 (m, 1H, H-9), 3.02 (d, 1H, *J* = 5.1 Hz, H-10α), 2.68 (d, 1H, *J* = 5.1 Hz, H-10β), 2.28-2.03 (m, 3H), 0.98 (d, 6H, *J* = 6.6 Hz, Me), 0.89 (s, 9H, Si-*t*Bu), 0.09 (s, 3H, Si-Me), 0.08 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 171.4, 144.8, 133.0, 123.2, 112.5, 92.4, 77.2, 76.0, 69.5, 59.8, 45.9, 43.2, 42.4, 31.9, 29.7, 29.4, 25.8, 25.6, 22.7, 22.4, 22.3, 14.1, –4.9, –5.0; for **24**: colorless oil; $[\alpha]_D$ −13.0 (*c* 0.00001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.64 (s, 1H, H-3), 5.94 (d, 1H, *J* = 9.9 Hz, H-1), 5.62 (t, 1H, *J* = 1.8 Hz, H-6), 4.95 (s, 1H, H-7), 4.67 (q, 2H, *J* = 12.6 Hz, 9.4 Hz, H-11), 3.09 (m, 1H, H-9), 3.02 (d, 1H, *J* = 5.1 Hz, H-10α), 2.68 (d, 1H, *J* = 5.1 Hz, H-10β), 2.28-2.03 (m, 3H), 2.07 (s, 3H, OAc), 0.98 (d, 6H, *J* = 6.6 Hz, Me), 0.89 (s, 9H, Si-*t*Bu), 0.09 (s, 3H, Si-Me), 0.08 (s, 3H, Si-Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 171.5, 145.2, 133.6, 126.7, 111.4 92.7, 77.2, 76.2, 49.3, 44,5, 43.6, 25.8, 25.7, 22.4, 14.2; for **25**: colorless oil; $[\alpha]_D$ −68.5 (*c* 0.00001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.66 (s, 1H, H-3), 5.95 (d, 1H, *J* = 10.1 Hz, H-1), 5.74 (t, 1H, *J* = 1.8 Hz, H-6), 4.95 (s, 1H, H-7), 4.69 (q, 2H, *J* = 11.7 Hz, 19.1 Hz, H-11), 3.12 (d, 1H, *J* = 4.6 Hz, H-10α), 3.10 (m, 1H, H-9), 2.75 (d, 1H, *J* = 4.6 Hz, H-10β), 2.28-2.03 (m, 3H), 2.17 (s, 3H, OAc), 0.98 (d, 6H, *J* = 6.6 Hz, Me); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 171.4, 171.0, 149.3, 137.2, 131.3, 111.8, 88.3, 69.9, 64.1, 63.4, 50.0, 43.2, 42.1, 25.6, 22.3, 22.3, 21.0; for **6**: colorless oil; $[\alpha]_D$ −34.5 (*c* 0.00001, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.67 (s, 1H, H-3), 5.95 (d, 1H, *J* = 8.2 Hz, H-1), 5.79 (m, 1H, H-7), 5.35 (m, 1H, H-6), 4.69 (m, 2H, H-11), 3.65 (m, 1H, H-9), 3.01 (d, 1H, *J* = 4.6 Hz, H-10α), 2.75 (d, 1H, *J* = 4.6 Hz, H-10β); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 172.6, 171.4, 171.0, 147.5, 141.6, 137.2, 111.0, 87.9, 71.9, 63.5, 62.2, 50.3, 43.2, 43.2, 41.7, 33.6, 29.3, 22.4, 22.3, 22.3, 21.0.