Efficient Synthesis of Novel Jolkinolides and Related Derivatives Starting from Stevioside

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Abstract: Jolkinolides are naturally occurring tetracyclic diterpene from Euphorbia genus, which exhibit promising antitumor and other biological activity. Efficient syntheses of the 19-carboxy derivative of jolkinolide A and 19-hydroxyjolkinolide E have been accomplished in 13 steps with a total yield of 7.8% starting from the easily available and low-cost sweetener stevioside, and some related derivatives have also been synthesized.

Key words: jolkinolides, Euphorbiaceae, stevioside, antitumor

Natural products are interesting sources of novel leading compounds for the design of new drugs. ‘Lang-du’ serving as a kind of traditional Chinese medicine with various biological activity was first described ~2,000 years ago. It is the root of dried Euphorbia Fischieriana Steud (Euphorbiaceae) and has been used in folk medicine for the treatment of cancer, edema, inflammation, tuberculosis, and ascites. Many scientists have paid close attention to the active components of this herb, and many investigations have reported that it mainly contained diterpenoids, triterpenoids, tannins, and steroids. Abietane lactone-type have reported that it mainly contained diterpenoids, triterpenoids, and some oxidation function groups in ring C, such as an cyclic with a nus, and this kind of carbon skeleton is commonly tetra-

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Figure 1 Structures of jolkinolides A, B, D, and E

starting material, and developed a facile access to obtain the target compounds (Scheme 1).

Stevioside was hydrolyzed by a literature method 7 to give the steviol 4 in 70% yield (Scheme 2). Selective esterification of 4 with chloromethyl methyl ether and N,N-diisopropylethylamine gave 5 in good yield (95%). Treatment of 5 with selenium oxide and tert-butyl hydroperoxide led to 6 (85%), which was subsequently oxidized with pyridinium dichromate to afford 7 (75%). Ozone oxidation of 7 at –78 °C gave a mixture of 8 and 9.10 In normal ozonolysis, only the double bond is cleaved, but during this reaction, the C13–C16 and C15–C16 single bonds are both cleaved. We proposed that the Criegee rearrangement may have occurred.11

As shown in Scheme 3, during the ozone oxidation process, the C16–C17 double bond of 7 was transformed to 1,2,3-trioxacyclopentane intermediate I, which then rearranged to the more stable ozonide intermediate II, and further rearrangement of intermediate III with the loss of methanal provided 8, some of which was decarboxylated to afford compound 9. We attempted to modify the reaction conditions (e.g., time, temperature, ozone quantity) to increase the yield of 9, but the products of ozonolysis were still a mixture of 8 and 9. Next we examined the transformation of 8 to 9, several conventional decarboxylation methods [e.g., Pb(OAc)4, NaOCl] were attempted, but failed. However, when we treated 8 with pyridinium
dichromate at room temperature, it gave the desired compound 9. We also attempted ozone oxidation of 6 to give compound 9 directly, but because of the extremely poor solubility of 6 in various solvents, the yield of oxidation products was very low. At this point, since compound 7 was very soluble in all kinds of solvents, we attempted the ozone oxidation of 7 and found the reaction was smoothly accomplished in good yield. Decarboxylation of 9 with lead tetraacetate in refluxing benzene provided enone 10 (60%). Epoxidation of 10 with hydrogen peroxide afforded the C8–C14 epoxy 11 in moderate yield (61%). Treatment of 11 with tert-butoxybis(dimethylamino)methane in N,N-dimethylformamide gave 12 (90%). Then, using Wasserman oxidation, we transformed 12 into 13 in moderate yield (70%). Esterification of 13 with 2-(diethoxyphosphoryl)propanoic acid in the presence of 4-(dimethylamino)pyridine and N,N'-dicyclohexylcarbodiimide provided 14, which was treated with sodium hydride to afford lactone 1d. Then, deprotection of MOM ester 1d with 10% hydrochloric acid in tetrahydrofuran at room temperature gave the acid 1a.

The synthetic strategy for preparation of 19-hydroxyjolkinolide E is shown in Scheme 4, treatment 4 with excess chloromethyl methyl ether provided 15. Reduction of 15 with lithium aluminum hydride in refluxing tetrahydrofuran led to 16, which was acetylated with acetic anhydride and gave acetate 17 in high yield (95%). Using the same preparative procedures en route to 10, acetate 17 was transformed to enone 23. Deprotection of 23 with 10% hydrochloric acid in refluxing methanol gave C15-hydroxy enone 24 in high yield (96%). Chloromethyl methyl ether was used to protect the C15-hydroxy of 24 to afford compound 25 in 97% yield. Application of Rubottom oxidation and treatment of 25 with lithium diisopropylamide and trimethylsilyl chloride gave a silyl enol ether, which was treated with 3-chloroperbenzoic acid and followed by

**Scheme 1** Synthetic strategy for the preparation of novel jolkinolides and related derivatives

**Scheme 2** Reagents and conditions: (a) NaIO4, KOH, H2O, 70%; (b) MOMCl, DIPEA, DMF, r.t., 95%; (c) SeO2, r-BuOOH, THF, r.t.; (d) PDC, DMF, r.t., 75%; (e) O2, CH2Cl2, –78 °C; (f) PDC, DMF, 77%; (g) Cu(OAc)2, H2O, Pb(OAc)4, pyridine, benzene, reflux, 60%; (h) 30% H2O2, 6 M NaOH, MeOH, r.t., 61%; (i) r-BuOCH(NMe)2, DMF, 80 °C; (j) O2, tetraphenylporphine, CH2Cl2, iodo-halogen lamp, –78 °C, 70%; (k) 2-(diethoxyphosphoryl)propanoic acid, DCC, DMAP, CH2Cl2, r.t., 61%; (l) 60% NaH, THF, r.t., 82%; (m) 10% HCl, THF, H2O, r.t., 97%.
desilylation with tetrabutylammonium fluoride to afford \( \beta \)-hydroxy ketone 26 overall in 51% yield.\textsuperscript{15} We attempted to use the same method with 23 as the substrate to obtain the \( \beta \)-hydroxy ketone directly, but this was unsuccessful, we thought that perhaps excess \( n \)-butyllithium may have decomposed the C15-acetyl protecting group. Esterification of 26 with 2-(diethoxyphosphoryl)propanoic acid gave 27, which was treated with sodium hydride to afford 3b.\textsuperscript{17}

From the NOESY spectrum of target compound 3b (Figure 2), H12 (\( \delta_H = 4.87 \)) shows correlations to 20-CH\(_3\) (\( \delta_H = 0.93 \)), which suggests that C12-hydroxy and 20-CH\(_3\) bear the opposite configuration. According to the literature,\textsuperscript{16} 20-CH\(_3\) is \( \alpha \)-orientated, so we could identify the configuration of the C12-hydroxy of 26 as \( \beta \)-orientated. Deprotection of 3b (10% HCl in THF–MeOH, r.t.) gave 3a. The physical data of compound 3a is in agreement with the naturally occurring compound 19-hydroxyjolkinolide E, which was isolated from the roots of \textit{Phlogacanthus curviflorus}.\textsuperscript{18}

Several related derivatives of jolkinolide A, B were prepared from compound 1a as outlined in Scheme 5. Esterification of 1a with halogenated compounds, such as benzyl chloride provided 1b. Epoxidation of 1b with 3-chloroperbenzoic acid gave 2a (70%). The NOESY spectrum of 2a (Figure 2) was used to identify the configurat...
tion of the C8–C14 epoxy and C11–C12 epoxy groups, while both H11 (δH = 3.65 ppm) and H14 (δH = 3.15 ppm) show correlations to 20-CH3 (δH = 0.54 ppm). It suggests that H11, H14, and 20-CH3 bear the same configuration. As 20-CH3 is α-orientated, therefore H11, H14 are also α-orientated, while the C8–C14 and C11–C12 epoxy groups are β-orientated. Compounds, such as 1c, 2b, and 2c were also prepared with the same procedure.

<table>
<thead>
<tr>
<th>Scheme 5</th>
<th>Reagents and conditions: (a) RX, DMF, r.t., 93%; (b) 85% MCPBA, CH2Cl2, r.t., 70%.</th>
</tr>
</thead>
</table>

In summary, the syntheses of the 19-carboxy-derivative of jolkinolide A 1a and 19-hydroxyjolkinolide E (3a) have been accomplished in 13 steps with an overall yield of 7.8%. Some related derivatives, such as 1b-d, 2a-c, 3b have also been synthesized. Since stevioside is an easily available and low-cost material, this preparation serves a available and low-cost material, this preparation serves a

1H and 13C NMR spectra were recorded at 300 MHz and 75 MHz, respectively; relative to internal TMS standard. LRMS and HRMS were recorded in ESI mode. IR spectra were recorded either on neat samples (KBr disks) or as thin film. The melting points of the compounds were measured on a Kofler-type Reichert Thermovar micro hot stage microscope and were uncorrected. Petroleum ether = PE.


To a soln of 4 (2 g, 6.29 mmol) in DMF (20 mL) were added MOMCl (0.5 mL, 6.22 mmol) and DIPEA (1.8 mL, 10.88 mmol), and the mixture was allowed to stir at r.t. for 2 h. The mixture was neutralized with 10% HCl and extracted with EtOAc. The EtOAc layer was washed with brine, dried (anhdy Na2SO4), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 6:1) to give 5 (2.2 g, 95%) as a white amorphous solid; mp 234–236 °C.

**IR (KBr):** 3406, 2979, 2949, 2837, 1732, 1715, 1655, 1461, 1445, 1375, 1337, 1251, 1167, 1141, 1130, 1102, 1078, 1009, 938, 927, 906, 886, 771 cm−1.

**1H NMR (300 MHz, CDCl3):** δ = 5.22 (d, J = 5.98 Hz, 1 H), 5.14 (d, J = 5.98 Hz, 1 H), 4.93 (s, 1 H), 4.77 (s, 1 H), 3.45 (s, 3 H), 2.13–2.18 (m, 2 H), 1.99–2.07 (m, 3 H), 1.68–1.99 (m, 6 H), 1.35–1.70 (m, 6 H), 1.22–1.25 (d, J = 11.1 Hz, 1 H), 1.17 (s, 3 H), 0.91–1.06 (m, 3 H), 0.84 (s, 3 H).

**13C NMR (75 MHz, CDCl3):** δ = 176.6, 155.6, 102.7, 90.2, 79.7, 57.6, 56.6, 53.5, 47.2, 46.5, 43.8, 41.3, 41.1, 40.4, 39.1, 39.02, 37.6, 28.5, 21.6, 20.1, 18.8, 15.3.

**HRMS:** m/z calculated for C20H23O5 362.2457; found: 362.2473.

**Methoxymethyl ent-8-Carboxy-13-oxopodocarpan-15-oate (9)**

To a soln of 6 (1.5 g, 3.97 mmol) in DMF (15 mL) was added PDC (1.64 g, 4.37 mmol). The mixture was allowed to stir at r.t. for 3 h and then neutralized with 10% HCl, and extracted with EtOAc. The EtOAc layer was washed with brine, dried (anhdy Na2SO4), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 2:1) to give 7 (1.05 g, 75%) as a white amorphous solid; mp 187–189 °C.

**IR (KBr):** 3451, 2953, 2923, 2868, 1733, 1717, 1651, 1479, 1375, 1337, 1251, 1167, 1141, 1130, 1102, 1078, 1009, 938, 927, 906, 886, 771 cm−1.

**1H NMR (300 MHz, CDCl3):** δ = 6.02 (s, 1 H), 5.44 (s, 1 H), 5.27 (d, J = 5.98 Hz, 1 H), 5.18 (d, J = 5.98 Hz, 1 H), 3.49 (s, 3 H), 2.51 (d, J = 11.21 Hz, 1 H), 2.21 (d, J = 14.3 Hz, 1 H), 1.74–2.04 (m, 9 H), 1.40–1.51 (m, 4 H), 1.24 (s, 3 H), 1.17–1.21 (m, 2 H), 1.04–1.05 (m, 1 H), 0.96 (s, 3 H).

**13C NMR (75 MHz, CDCl3):** δ = 208.5, 176.7, 151.4, 114.9, 90.4, 76.7, 57.8, 55.9, 55.0, 50.1, 44.5, 44.0, 40.0, 39.7, 39.0, 37.6, 32.8, 28.7, 20.6, 20.0, 18.7, 15.5.

**HRMS:** m/z calculated for C20H23O5 399 [M + Na]+.

**Methoxymethyl ent-8-Carboxy-13-oxopodocarpan-15-oate (9)**

To a soln of 7 (2 g, 5.32 mmol) in CH2Cl2 (30 mL), the mixture was subjected to O3 for 30 min before the addition of Et3N (1.5 mL, 10.39 mmol) at −78 °C. The mixture was stirred and allowed to warm to r.t. over 3 h and then neutralized with 10% HCl, washed with brine, dried (anhdy Na2SO4), filtered, and evaporated to dryness. The resulting 1:1 mixture of 8 and 9 was treated with PDC (2 g, 5.32 mmol) in DMF (20 mL) at r.t. over 2 h and then neutralized with 10% HCl, washed with brine, dried (anhdy Na2SO4), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 2:1) to give 9 as a white amorphous solid; mp 119–121 °C.

**IR (KBr):** 3386, 3026, 2985, 2937, 2849, 2819, 1717, 1463, 1446, 1375, 1348, 1327, 1283, 1207, 1184, 1135, 1091, 1062, 1030, 992, 954, 934, 913, 809, 788 cm−1.

**1H NMR (300 MHz, CDCl3):** δ = 5.28 (d, J = 5.94 Hz, 1 H), 5.18 (d, J = 5.94 Hz, 1 H), 3.49 (s, 3 H), 2.58 (m, 1 H), 2.23 (d, J = 13.15 Hz, 2 H), 1.69–2.05 (m, 11 H), 1.48–1.53 (m, 1 H), 1.25 (s, 5 H), 1.03 (m, 1 H), 0.92 (s, 4 H).

**13C NMR (75 MHz, CDCl3):** δ = 176.7, 90.5, 57.9, 55.7, 44.0, 43.4, 39.8, 37.6, 33.2, 28.7, 20.1, 19.6, 18.8, 15.0.  

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MS (ESI): \( m/z = 389 \) [M + Na]+.
HRMS: \( m/z = [M]^{+} \) calcd for C_{3}H_{3}O_{6}: 366.2042; found: 366.2048.

Methoxymethyl 13-Oxopodocarp-8(14)-en-15-oate (10)
To a soln of (9 (1 g, 3.4 mmol) in anhyd benzene (30 mL) were added Cu(OAc)_{2}·H_{2}O (0.1 g, 0.4 mmol) and pyridine (2 mL, 25.3 mmol); the mixture was purged with N_{2} for 15 min. After the addition of Pb(OAc)_{4} (4.5 g, 10.14 mmol), the soln was stirred at r.t. for 1 h and then refluxed for 1 h. The soln was then filtered through a pad of silica gel under vacuum, the mixture was neutralized with 10% HCl and extracted with diethylether. The organic layer was washed with brine, dried (anhyd Na_{2}SO_{4}), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 4:1) to give 10 (0.57 g, 60%) as a colorless oily product.

IR (film): 3427, 2955, 1728, 1667, 1566, 1366, 1258, 1236, 1172, 1136, 1078, 1027, 932 cm\(^{-1}\).

HRMS: \( m/z = 321 \) [M + H]+.

MS (ESI): \( m/z = 373 \) [M + Na]+.
HRMS: \( m/z = [M]^{+} \) calcd for C_{19}H_{26}O_{6}: 350.1729; found: 350.1741.

Methoxymethyl 13-epi-12-Oxopodocarp-8(14)-en-15-oate (11)
To a soln of 10 (1 g, 3.4 mmol) in MeOH (20 mL) were added 60% NaH at 0 °C, the mixture was stirred at r.t. for 3 h. The mixture was neutralized with 10% HCl and then PURIFIED by flash chromatography (silica gel, PE–EtOAc, 4:1) to give 11 (0.64 g, 61%) as a white amorphous solid; mp 194–196 °C.

IR (KBr): 3452, 2931, 2851, 1769, 1728, 1655, 1466, 1381, 1275, 1260, 1227, 1128, 1077, 939, 765, 750 cm\(^{-1}\).

HRMS: \( m/z = [M]^{+} \) calcd for C_{22}H_{28}O_{6}: 388.1886; found: 388.1898.

Methoxymethyl 12-(Dimethylamino)methylene-14-epoxy-13-oxopodocarp-15-oate (12)
To a soln of 11 (0.67 g, 1.75 mmol) in DMF (3 mL) was added t-BuOCH(NMe_{2}) (0.78 mL, 3.21 mmol) and stirring for 1 h at 120 °C. The mixture was neutralized with sat. NaHCO_{3} soln, and then extracted with EtOAc. The EtOAc layer was washed with brine, and dried (anhyd Na_{2}SO_{4}). Evaporation of the organic solvent gave the crude oil 12 (0.70 g), which was used for the next reaction without further purification.

To a soln of 12 (0.6 g, 1.37 mmol) in CH_{2}Cl_{2} (30 mL) was added tetraethyl orthoformate (2 mg, 0.003 mmol); the mixture was irradiated with a 300-W iodo-halogen lamp while O_{2} was bubbling for 0.5 h at –78 °C. Then the mixture was concentrated in vacuo and puri-
2.23 (m, 4 H), 1.73–1.89 (m, 6 H), 1.52–1.70 (m, 7 H), 1.22 (s, 3 H), 0.72–0.91 (m, 4 H).  

IR (KBr): 3465, 2935, 2871, 1738, 1461, 1390, 1371, 1461, 1390, 1372, 1285, 1250, 1160, 1109, 1096, 1037, 980, 964, 951, 930 cm⁻¹.

MS (ESI): \( m/z = 345 \) [M + H]⁺.

HRMS: \( m/z = 345 \) [M⁺] calcd for C₁₉H₂₄O₃: 344.1624; found: 344.1632.

Methoxymethyl ent-13-(Methoxymethoxy)kauren-18-oate (15) Following the typical procedure for 5, treatment of 4 (2.0 g, 6.29 mmol) gave 15 as a colorless oily product (1.24 mg, 97%).

HRMS: \( m/z = 380.2301 \) found: 360.2303.

ent-18-Hydroxy-13-(methoxymethoxy)kaurene (16)

To a soln of 15 (0.6 g, 1.66 mmol) in anhyd THF (15 mL) was added LiAlH₄ (0.2 g, 5.26 mmol) at 0 °C and the mixture was refluxed for 40 min. The mixture was diluted with sat. NH₄Cl and extracted with EtOAc. The organic layer was washed with brine, dried (anhyd Na₂SO₄), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 3:1) to give 16 (0.44 g, 85%) as a colorless oily product.

HRMS: \( m/z = 333 \) [M + Na]⁺.

ent-15-Hydroxypodocarp-8(14)-en-13-one (24)

To a soln of 23 (200 mg, 0.48 mmol) in MeOH (15 mL) was added 10% HCl (3 mL); the mixture was stirred and refluxed for 30 min. The mixture was neutralized with sat. NaHCO₃ soln, and then extracted with EtOAc, the EtOAc layer was washed with brine, dried (anhyd Na₂SO₄), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 3:1) to give 24 (165 mg, 96%) as a white amorphous solid; mp 183–186 °C.

IR (KBr): 3361, 2928, 2869, 1734, 1656, 1608, 1453, 1375, 1261, 1059, 1028, 749, 649 cm⁻¹.

HRMS: \( m/z = 291 \) [M⁺] calcd for C₁₇H₂₆O₂: 262.1933; found: 262.1935.

ent-18-Acetoxy-13-hydroxy-15-oxokaurene (20)

To a soln of 19 (0.5 g, 1.24 mmol) in THF (10 mL) was added 10% HCl (2 mL); the mixture was stirred for 30 min. The mixture was neutralized with sat. NaHCO₃ soln, and then extracted with EtOAc, the EtOAc layer was washed with brine, dried (anhyd Na₂SO₄), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 3:1) to give 20 (0.43 g, 97%) as a white amorphous solid; mp 191–193 °C.

IR (KBr): 3488, 2947, 2932, 2865, 1723, 1643, 1482, 1433, 1392, 1372, 1285, 1250, 1160, 1096, 1037, 980, 964, 951, 930 cm⁻¹.

HRMS: \( m/z = 383 \) [M⁺] calcd for C₂₀H₂₆O₅: 360.2301; found: 360.2303.


To a soln of 24 (1.65 g, 6.29 mmol) in CH₂Cl₂ (20 mL) was added MOMCl (0.5 mL, 6.22 mmol) and DIPEA (2 mL); the mixture was allowed to stir at 60 °C for 2 h. The mixture was neutralized with 10% HCl, extracted with CH₂Cl₂. The organic layer was washed with brine, and dried (anhyd Na₂SO₄), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 3:1) to give 25 (165 mg, 96%) as a white amorphous solid; mp 183–186 °C.

IR (film): 3465, 2935, 2781, 1738, 1461, 1390, 1371, 1371, 1240, 1151, 1109, 1034, 996, 972, 907 cm⁻¹.

HRMS: \( m/z = 383 \) [M⁺] calcd for C₂₃H₃₆O₃: 348.2464; found: 348.2664.


To a soln of 17 (0.7 g, 1.79 mmol) in THF (15 mL) were added SeO₂ (0.12 g, 1.08 mmol) and t-BuOOH (2 mL); the mixture was stirred at r.t. for 3 h. The mixture was diluted with distilled H₂O and extracted with EtOAc, the EtOAc layer was washed with brine, dried (anhyd Na₂SO₄), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 4:1) to give 18 (0.62 g, 85%) as a colorless oily product.

IR (film): 3465, 2935, 2871, 1738, 1461, 1390, 1371, 1371, 1240, 1151, 1109, 1034, 996, 972, 907 cm⁻¹.

HRMS: \( m/z = 200 \) [M⁺] calcd for C₁₉H₂₈O₃: 263.1935; found: 263.1935.


To a soln of 24 (1.65 g, 6.29 mmol) in CH₂Cl₂ (20 mL) was added MOMCl (0.5 mL, 6.22 mmol) and DIPEA (2 mL); the mixture was allowed to stir at 60 °C for 2 h. The mixture was neutralized with 10% HCl, extracted with CH₂Cl₂. The organic layer was washed with brine, and dried (anhyd Na₂SO₄), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc, 3:1) to give 25 (1.85 g, 97%) as a colorless oily product.

IR (film): 3299, 2882, 1767, 1616, 1446, 1275, 1259, 1145, 1106, 1046, 750 cm⁻¹.

**ent-12-Hydroxy-15-(methoxymethoxy)podocarp-8(14)-en-13-one (26)**

To a solution of i-PrNH (0.47 mL, 3.5 mmol) in THF (2 mL) was added 1.3 M BuLi in hexane soln (2.2 mL, 3.5 mmol) at –78 °C and the mixture was stirred for 30 min at the same temperature. To the generated LDA soln was added a soln of 25 (0.2 g, 0.65 mmol) in THF (5 mL) at −78 °C and the mixture was stirred for 1 h at the same temperature. To the above mixture was added TMSCl (0.6 mL, 3.4 mmol) and the mixture was stirred at r.t. for 2 h. The mixture was diluted with EtOAc and the organic layer was washed with water, NaHCO₃ and brine, dried (Na₂SO₄). Evaporation of the organic solvent gave crude oily product, which was used for the next reaction without further purification.

To a soln of 1H NMR (300 MHz, CDCl₃): δ = 6.26 (s, 1 H), 4.87 (d, J = 4.8 Hz, 1 H), 4.57 (s, 2 H), 3.59 (d, J = 9.4 Hz, 1 H), 3.33 (s, 3 H), 3.32 (d, J = 9.4 Hz, 1 H), 2.48–2.61 (m, 2 H), 2.11–2.22 (m, 2 H), 1.90 (s, 3 H), 1.83–1.97 (m, 3 H), 1.38–1.56 (m, 5 H), 1.20–1.31 (m, 2 H), 1.02 (s, 3 H), 0.88 (s, 3 H).

13C NMR (75 MHz, CDCl₃): δ = 175.2, 156.0, 151.7, 116.3, 140.4, 96.7, 77.4, 77.0, 76.6, 75.9, 70.4, 56.1, 55.1, 52.0, 41.5, 39.6, 37.9, 37.5, 36.3, 29.7, 28.2, 27.5, 24.0, 18.8, 17.7, 8.2.

**MS (ESI):** m/z = 345 [M + Na⁺].

HRMS: m/z [M⁺] for C₃₂H₃₂O₃: 434.2144; found: 434.2108.

**19-Benzylxylo-19-oxojolkinolide B (2a)**

To a soln of 1b (30 mg, 0.069 mmol) in CH₂Cl₂ (7 mL) was added NaN₃ (80 mg, 1.21 mmol) and the mixture was stirred at r.t. for 4 h. The mixture was neutralized with 10% HCl and then extracted with EtOAc, the EtOAc layer was washed with brine, dried (Na₂SO₄), filtered, and evaporated to dryness. The residue was purified by flash chromatography (silica gel, PE–EtOAc: 2:1) to give 2a (21 mg, 70%) as a white amorphous solid; mp 149–151 °C.

**IR (KBr):** 3024, 2926, 2849, 1776, 1720, 1458, 1384, 1316, 1275, 1260, 1226, 1207, 1155, 1132, 1036, 1014, 971, 883, 850, 766, 761, 750, 745, 698 cm⁻¹.

**[M⁺] calcd for C₂₇H₃₀O₆: 450.2042; found: 450.2063.**

**HRMS: m/z [M⁺] for C₂₇H₃₀O₆: 450.2042; found: 450.2063.**

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References and Notes


