

Synthesis of 6(*E*)-Geranylgeraniol-19-oic Acid

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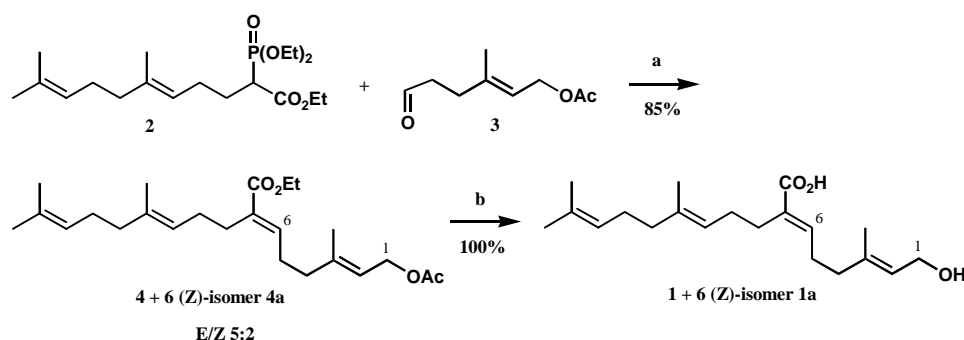
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Abstract: Facile synthesis of 6(*E*)-geranylgeraniol-19-oic acid **1**, a naturally occurring alicyclic diterpene acid, by a Horner–Wadsworth–Emmons olefination of two readily available fragments **2** and **3**, is described.

Keywords: Horner–Wadsworth–Emmons reaction, 6(*E*)-geranylgeraniol-19-oic acid, synthesis.

The title compound **1** is a novel oxidative metabolite of the class of alicyclic diterpene acid derived from geranylgeraniol¹. Its structure was characterized¹ *via* the corresponding methyl ester of 6 (*E*)-geranylgeraniol-19-oic acid by extensive spectroscopic analysis. Biological activities of **1** and other members of this class of natural products are unknown². Herein, we report a convenient chemical synthesis of **1** and its geometrical 6 (*Z*) isomer **1a** (Scheme 1).

Scheme 1



Reagents and conditions: (a) $\text{LiN}(\text{TMS})_2$, DME, $-50\text{ }^\circ\text{C}$, 16 h. (b) KOH, EtOH–H₂O (v/v 1:1), reflux, 2 h.

The key reaction is the stereoselective Horner–Wadsworth–Emmons olefination³ of **2** and **3**. These two fragments can be readily prepared as described in lit.⁴ The desired coupling product **4** (*E*-form) was produced predominately⁵ along with its 6 (*Z*) isomer **4a** in a ratio of 5:2 as determined by ¹H NMR⁶ in a combined yield of 85%. The two isomers were separated by column chromatography on silica gel eluting with 2% (v/v) ethyl acetate in petroleum ether (60–90 °C). After saponification of ester **4** and **4a**

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with KOH in 50% aqueous EtOH under reflux, the title compound **1** and its 6(*Z*) isomer **1a** were obtained in quantitative yield respectively. The spectral data (^1H NMR, IR and MS) of the synthetic **1**⁷ are fully identical with those of reported¹. The ^1H NMR signal of H-6 of **1a** was shifted upfield to 6.00 ppm.

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References and Notes

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(b) *ibid*, *Hecheng Huaxue* (Synthetic chemistry) (in Chinese), **1996**, 4, 128.
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6. Characteristic chemical shifts: **4**, $\delta_{\text{H(C-6)}}$ 6.71 (t); **4a**, $\delta_{\text{H(C-6)}}$ 5.83 (t) ppm.
7. Spectral data: **1**, IR (film): ν 3339(br), 1686(vs), 1442, 1380, 1275, 992 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , δ ppm): 1.60 (br s, 6 H, 2 CH_3), 1.69 (s, 3 H, CH_3), 1.70 (s, 3 H, CH_3), 1.97~2.18 (m, 8 H, 4 CH_2), 2.31~2.39 (m, 4 H, 2 CH_2), 4.15 (d, 2 H, $J = 6.8$ Hz, CH_2O), 5.10 (t, 1 H, $J = 7.2$ Hz, $\text{CH}=\text{}$), 5.15 (t, 1 H, $J = 7.2$ Hz, $\text{CH}=\text{}$), 5.45 (t, 1 H, $J = 7.3$ Hz, $\text{CH}=\text{}$), 6.87 (t, 1 H, $J = 7.4$ Hz, $\text{CH}=\text{}$); ^{13}C NMR (100 MHz, CDCl_3 , δ ppm): 172.3, 144.4(2C), 138.3, 136.3, 131.6, 124.3(2C), 123.3, 59.3, 39.7, 38.3, 27.5, 27.0, 26.8, 26.7, 25.6, 17.7, 16.3, 16.0; EIMS m/z 302 (7.6%, M- H_2O), 287 (6), 275 (25), 259 (46), 233 (41), 215 (32), 187 (11), 105 (20), 69 (100); Anal. calcd for $\text{C}_{20}\text{H}_{32}\text{O}_3$: C, 74.96; H, 10.06; found: C, 74.88; H, 10.11. **1a**, IR (film) ν 3328(br), 1687(vs), 1443, 1379, 1259, 992 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , δ ppm): 1.59 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 1.69 (br s, 6 H, CH_3), 1.96~2.17 (m, 8 H, 4 CH_2), 2.26~2.31 (m, 4 H, 2 CH_2), 4.15 (d, 2 H, $J = 7.0$ Hz, CH_2O), 5.11 (m, 2 H, 2 $\text{CH}=\text{}$), 5.43 (t, 1 H, $J = 6.8$ Hz, $\text{CH}=\text{}$), 6.00 (t, 1 H, $J = 7.3$ Hz, $\text{CH}=\text{}$); ^{13}C NMR (100 MHz, CDCl_3 , δ ppm): 172.7, 144.4(2C), 138.8, 136.0, 131.2, 124.3, 124.1, 123.2, 59.3, 39.7, 38.9, 28.0, 27.7, 26.8, 25.7, 23.3, 17.7, 16.2, 16.0.

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