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Supporting Information

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Access to Guaianolides: Highly Efficient Stereocontrolled Total Synthesis of (±)-Geigerin

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Experimental Procedure

Solvents were dried by distillation over standard reagents and stored under argon or with an apparatus (MP SPD BRAUN). ^{1}H, and ^{13}C NMR spectra were recorded on a Brucker AV 300 spectrometer.

Chemical shifts are given in δ relative to tetramethysilane (TMS) for ^{1}H NMR and to $CDCl_3$ (77.16) for ^{13}C NMR. IR spectra were recorded on a Nicolet 400 spectrometer.

Experimental procedure for the preparation of **9** from **4**: To a stirred solution of **4** (200 mg, 1.03 mmol) and $LiClO_4$ (10 mg, 0.096 mmol) in ahnydrous dichloromethane (15 mL) was added a solution of (*E*)-*tert*-butyldimethylsilyl ketene acetal derived from methyl propionate (420 mg, 2.08 mmol) in dichlomethane (3 mL) at room temperature and then the reaction mixture was stirred for a further 14 h. The reaction mixture was treated with a saturated solution of acqueous $NaHCO_3$ and the crude product **7** was isolated with ether/pentane (1:1) in the usual manner. To a solution of isolated silyl enol ether **7** in acetone at – 90°C was added a freshly prepared solution of DMDO[21b] (15.8 mL, 1.55 mmol, ca. 0.1 M in acetone). After 5 min, the stirred resulting mixture was treated with water and the alcohol 10 was isolated with EtOAc/pentane (2:1). The crude alcohol **8** was then directly treated with a catalytic amount of TSA in THF (8 mL) and the reaction mixture was stirred at room temperature for 14 h. The isolated lactone **9** (mixture of diastereomers (C11 dr = 2:1-4:1)) was purified by column chromatography on dry silica gel with EtOAc/pentane (30:70 then 40:60) to afford 135 mg (49% from **4**) of **11** as a mixture of C11 diastereomers (white solid, 151-152°C). Recrystallization from dichloromethane/EtOAc/petroleum ether 65-95 gave **9** as a white solid. M.p. 176-178°C (decomposition); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 1.25 (d, J = 7.0 Hz, 3H), 1.36 (d, J = 7.6 Hz, 3H), 2.15-2.29 (m, 1H), 2.35-2.42 (dd, J = 18.7, 1.9 Hz, 1H), 2.55-2.67 (m, 1H), 2.69-2.79 (dd, J = 18.7, 6.8 Hz, 1H), 2.85-3.00 (m, 1H), 3.24-3.35 (m, 1H), 4,75 (d, J = 10.7 Hz, 1H), 5.74-5.80 (m, 1H), 5.89-5.94 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 21.8, 37.4, 37.9, 38.6, 43.3, 44.8, 80.2, 125.5, 130.8, 140.4, 165.6, 177.9, 198.7 ppm; FTIR: $\bar{\nu}$ = 1783, 1723, 1621 cm^{-1}; MS (DCI): *m*/*z*: 284 $[M+NH_4]^+$; HRMS: calcd for $[C_{14}H_{15}O_3Cl+Na]^+$: 289.06074; found: 289.06077.

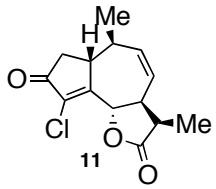
Data for selected compounds: (±)-Geigerin (**1**): M.p. 167°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.12 (d, J = 6.2 Hz, 3H), 1.18-1.30 (m, 1H), 1.48 (d, J = 6.7 Hz, 3 H), 1.75-1.92 (m, 2H), 1.95 (br s, 3H), 2.03 (d, J = 3.1 Hz, 1H), 2.12 (d, J = 18.3Hz, 1H), 2.38 (m, 1H), 2.57-2.73 (m, 3H), 4.36-4.45 (m, 1H), 4.62 ppm (dd, J = 9.2, 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.2, 16.6, 22.8, 38.1, 40,3, 40,7, 42.2, 48.6, 49.4, 75.4, 78.7, 138.4, 171,6, 178.5, 208.3 ppm; FTIR: $\bar{\nu}$ 3440, 1770, 1699, 1644 cm^{-1}; MS (DCI): *m*/*z*: 282 $[M+NH_4]^+$; HRMS: calcd for $[C_{15}H_{20}O_4+H]^+$: 265.1439; found: 265.1434.

(±)-Geigerin acetate (**2**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (d, J = 6.3 Hz, 3H), 1.18-1.30 (m, 1H), 1.40 (d, J = 7.0 Hz, 3H), 1.82 (br s, 3H), 1.85-1.94 (m, 2H), 2.08-2.14 (m, 1H), 2.14 (s, 3H), 2.54-2.80 (m, 4H), 4.38-4.48 (m, 1H), 5.42 ppm (d, J = 10.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.0, 16.2, 20.5, 22.7, 38.0, 39.7, 41.0, 42.3, 47.0, 48.3, 76.3, 78.5, 137.7, 167.9, 169.9, 185.5 ppm; FTIR: $\bar{\nu}$ 1774, 1745, 1704, 1654, 1234 cm^{-1}; MS (DCI): *m*/*z*: 324 $[M+NH_4]^+$.

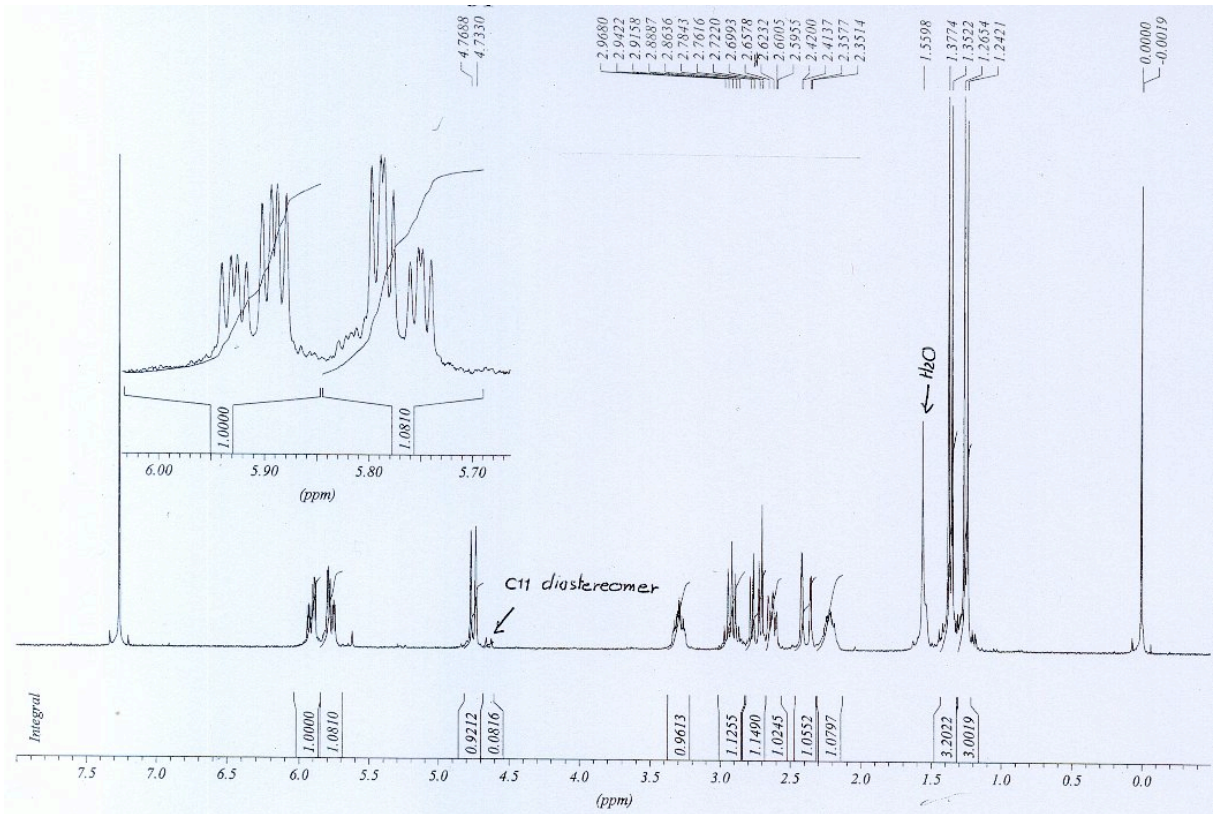
(±)-6-Deoxygeigerin (**3**): M.p. 120-121°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (d, J = 6.4 Hz, 3H), 1.23-1.34 (m, 1H), 1.35 (d, J = 6.8 Hz, 3H), 1.72 (d, J = 1.7 Hz, 3H), 1.88-1.99 (m, 2H), 2.07 (dd, J = 18.5, 1.7 Hz, 1H), 2.18-2.48 (m, 4H), 2.64 (dd, J = 18.5, 1H), 6.4 Hz, 3.05 (dd, J = 12.3, 4.9 Hz, 1H), 4.38-4.48 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.9, 14.4, 22.9, 31.3, 37.1, 39.7, 40.9, 42.1, 43.0, 50.4, 80.8, 137.7, 170.1, 178.0, 207.9 ppm; FTIR: $\bar{\nu}$ 1771, 1698, 1649 cm^{-1}; MS (DCI): *m*/*z*: 266 $[M+NH_4]^+$; HRMS: calcd for $[C_{15}H_{20}O_3+H]^+$ 249.1491; found: 249.1585.

Specrums

^{1}H NMR and ^{13}C NMR of guaian-6,12-olide **11**



11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7.0
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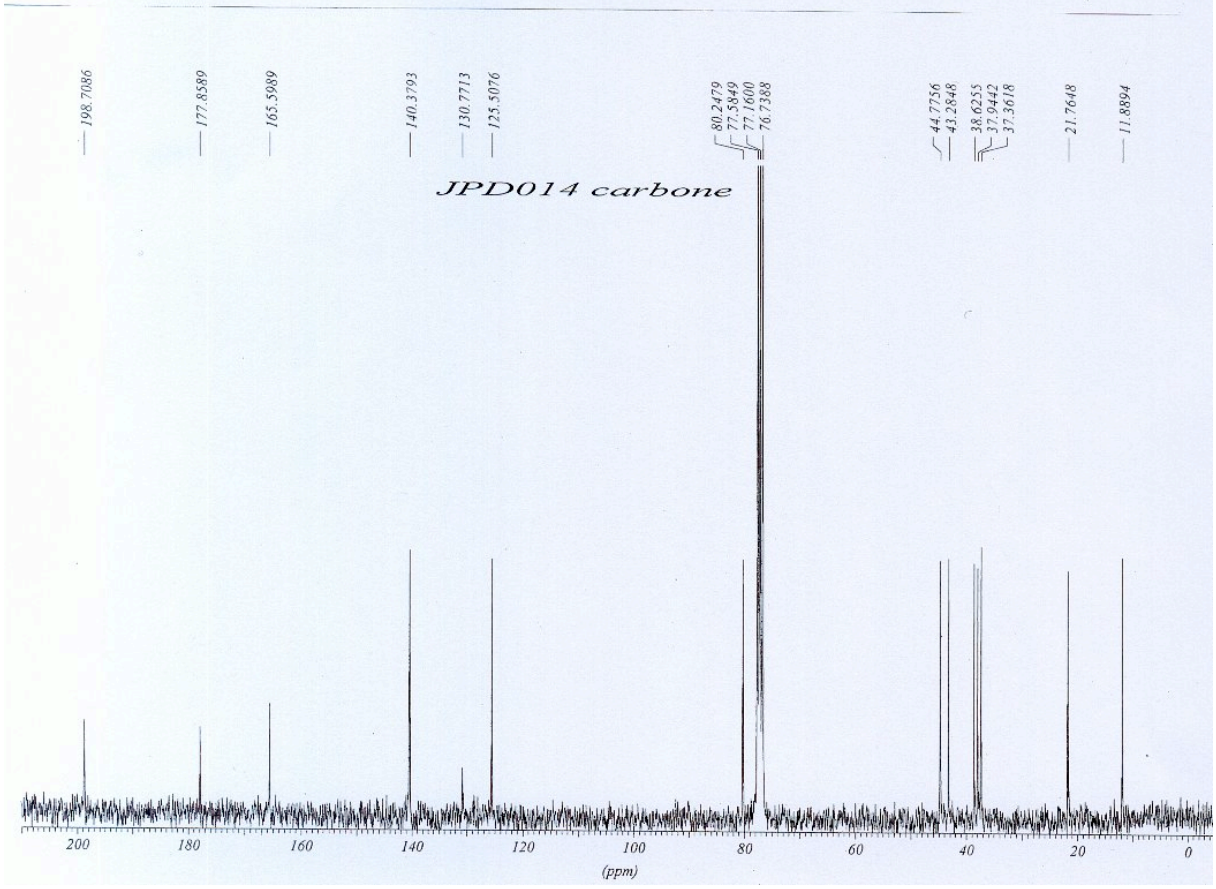
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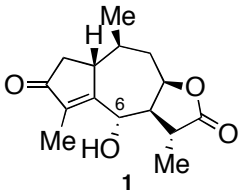
^{1}H NMR and X-ray structure analysis of (±)-geigerin (**1**)



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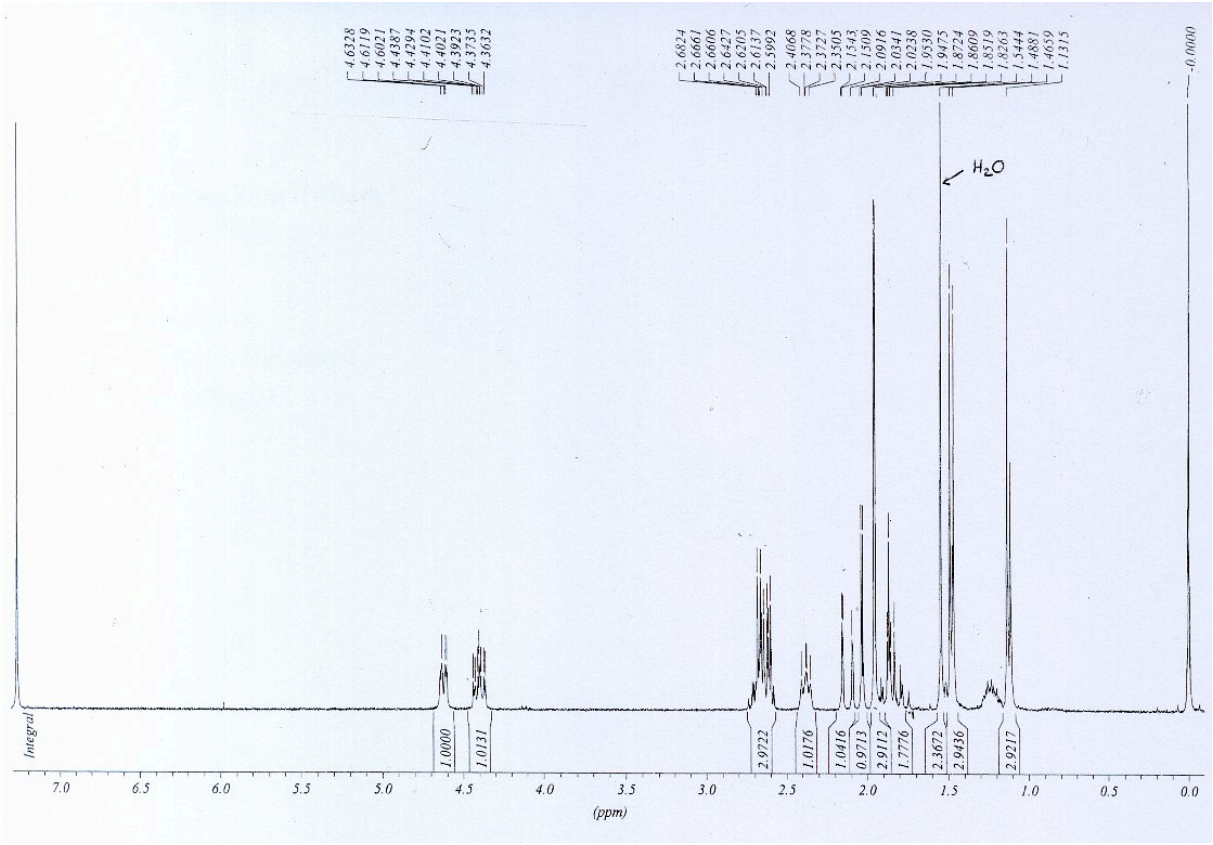
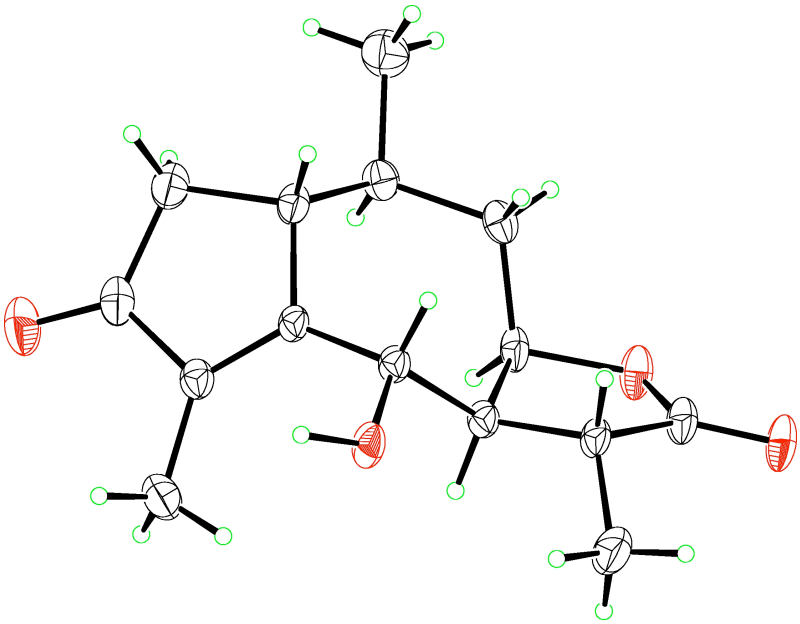
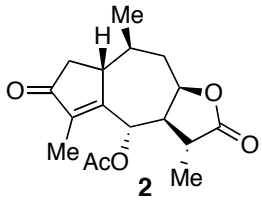




^{1}H NMR of (±)-geigerin acetate (**2**)



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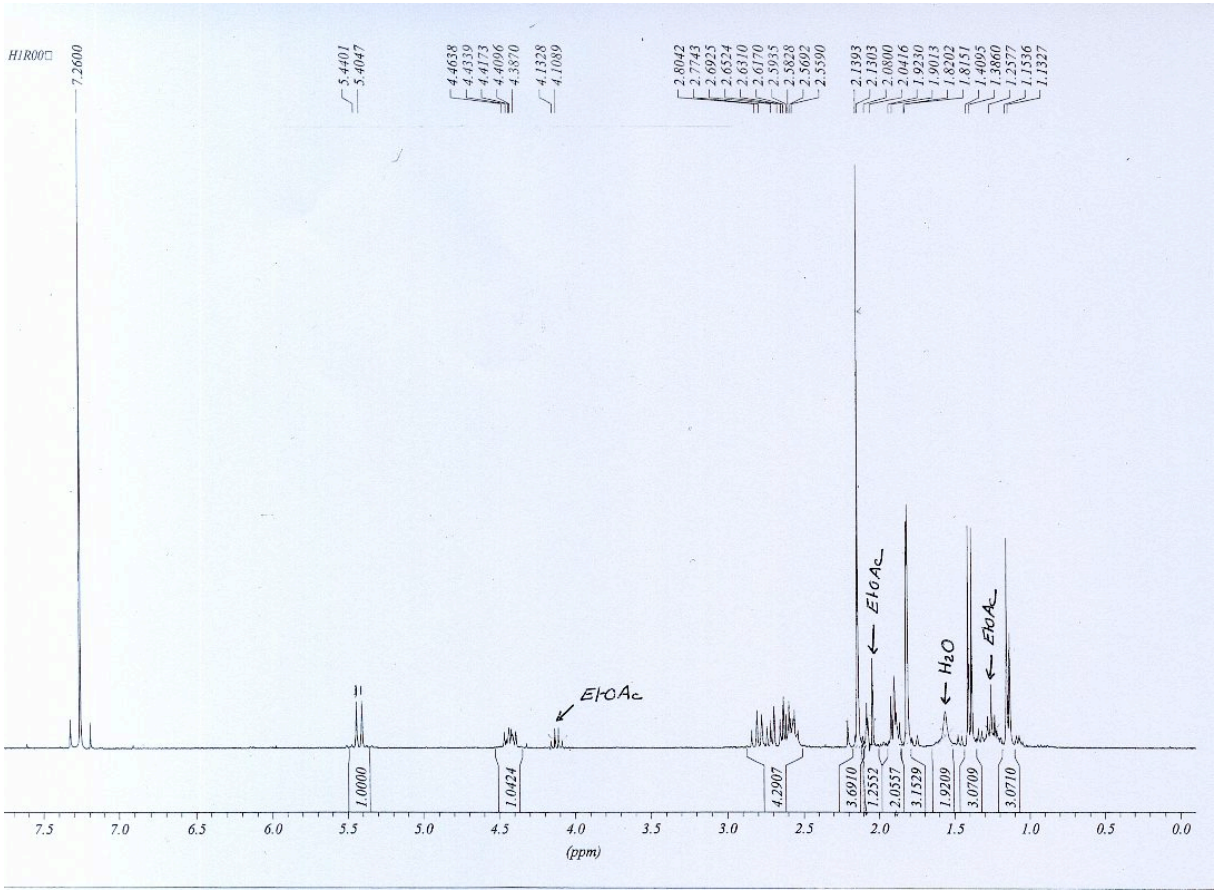
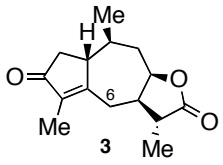


^{1}H NMR and ^{13}C NMR of (±)-6-deoxygeigerin (**3**)



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