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The Structure of Rubescensin C: A New Minor Diterpenoid isolated from *Rabdosia rubescens*

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A new diterpenoid, rubescensin C, was isolated from the leaves of *Rabdosia rubescens* (HEMSL.) HARA (Labiateae) and its structure was established from spectral and chemical evidence.

Keywords—diterpenoid; *ent*-kaurene; *Rabdosia rubescens*; rubescensin C; structure; ¹H-NMR; ¹³C-NMR

Rabdosia rubescens, which is widely distributed in the Huanghe river valley and the southern district of China, has been used for the treatment of esophageal and cardiac carcinoma in Honan. We have reported the isolation of oridonin¹⁾ (=rubescensin A²⁾) and ponigidin³⁾ (=rubescensin B⁴⁾) from the ethereal extract of the dry leaves of this plant. The present paper describes the structural elucidation of a new diterpenoid, rubescensin C, which is a minor component isolated from the same plant.

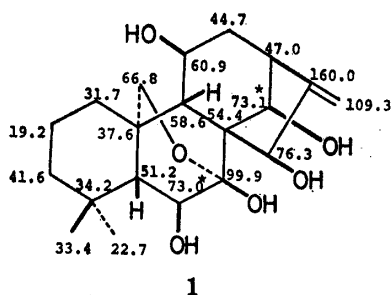


Fig. 1. Rubescensin C (1): ¹³C-NMR Data (δ /ppm) in C₅D₅N Solution

*: may be reversed.

Rubescensin C [1; C₂₀H₃₀O₆; mp 239—241°C; $[\alpha]_D^{25}$ -68.6° ($c=0.14$, C₅H₅N); IR ν_{\max} 1640 cm⁻¹ (>C=CH₂)] showed the presence of two methyl groups, five methylene groups, seven methine groups, four quaternary carbons, and two olefinic carbons in the ¹³C nuclear magnetic resonance (NMR) spectrum (Fig. 1).⁵⁾ The signals due to an acetal carbon at δ 99.9 (C-7, s), an oxygenated methyl group at δ 66.8 (C-20, t), and an exomethylene group at δ 109.3 (C-17, t) and δ 160.0 (C-16, s) were also observed. On the other hand, the signals due to an oxygenated methyl group at δ 4.14 (20-H_a, 1H, dd, $J=10$ and 2 Hz) and δ 3.87 (20-H_b, 1H, d, $J=10$ Hz), and those of an exomethylene at δ 5.21 and 5.16 (17-2H, each d, $J=2$ Hz)

were observed in the ¹H-NMR spectrum (Fig. 2). Furthermore, long-range coupling with δ 4.14 (20-H_a) and δ 2.37 (9 β -H, dd, $J=9$ and 2 Hz) was confirmed by a decoupling experiment. On irradiation at δ 2.37 (9 β -H), the doublet-doublet at δ 4.14 collapsed to a doublet ($J=10$ Hz). On treatment with 15% methanolic hydrochloric acid, rubescensin C was transformed into a saturated ketone [2; C₂₀H₃₀O₆; mp 241—243°C; CD (methanol) $\Delta\epsilon^{25}$: -1.12 (299) (negative maximum)⁶⁾] via the garryfoline-cuachichicine rearrangement,⁷⁾ indicating the presence of a 15 β hydroxyl group in an *ent*-16-kaurene skeleton. The presence of this hydroxyl group was supported by the peaks at δ 5.34 (br s) in the ¹H-NMR spectrum and at δ 76.3 (d) in the ¹³C-NMR spectrum.

Thus, these spectroscopic and chemical findings suggested that rubescensin C has an *ent*-7 α , 15 α -dihydroxy-7 β , 20-epoxykaur-16-ene as the basic structure.

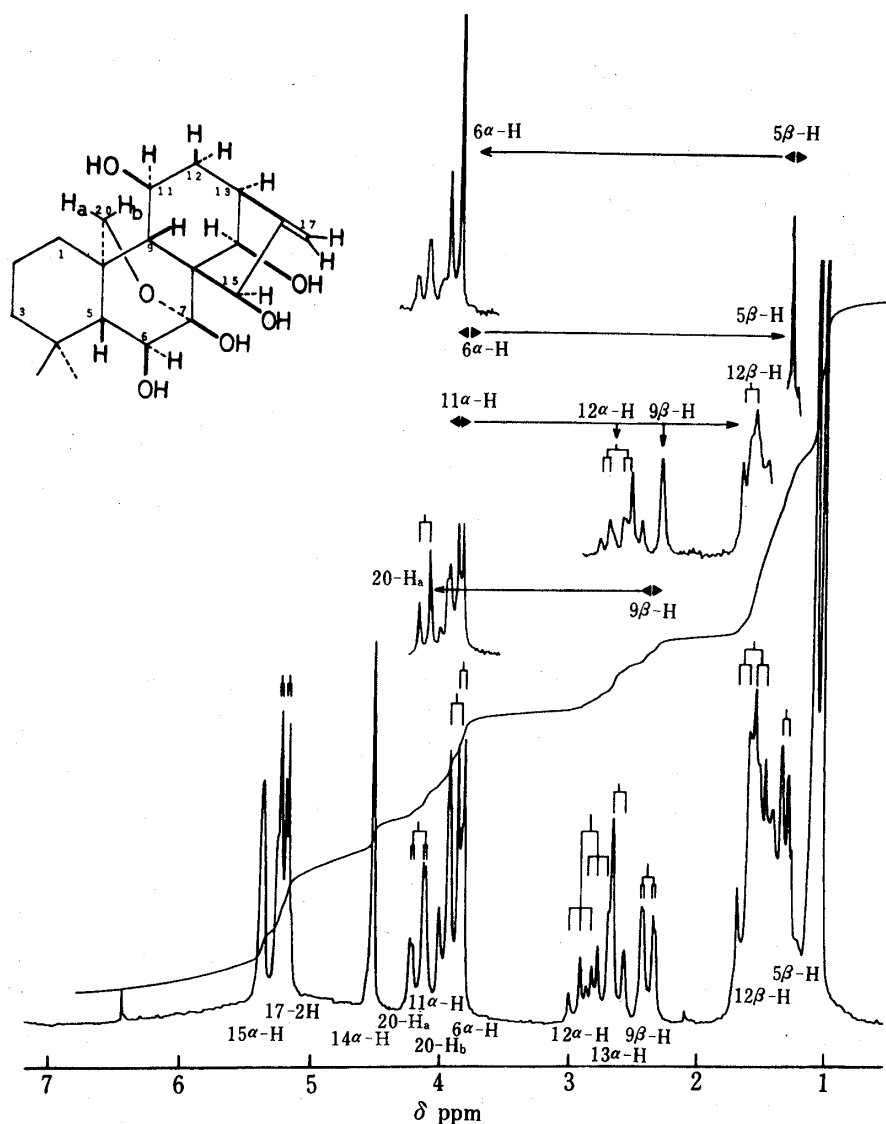
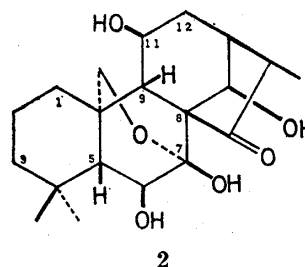


Fig. 2. The $^1\text{H-NMR}$ Spectrum of Rubescensin C in $\text{CDCl}_3 + \text{C}_5\text{D}_5\text{N}$ Solution

Rubescensin C was found to have another three hydroxyl groups: IR ν_{max} 3300 cm^{-1} ; $^1\text{H-NMR}$ δ 3.82 (1H, d, $J=5\text{ Hz}$), 3.91 (1H, m), and 4.50 (1H, s); $^{13}\text{C-NMR}$ δ 73.1, 73.0, and 60.9 (each d). The location of one hydroxyl group was elucidated as 14β from the chemical shift (δ 4.50) and coupling pattern (sharp s)¹⁾ of the 14α proton signal.

The locations of the other two hydroxyl groups at 6β and 11β were supported by the following decoupling experiments. On irradiation at δ 1.32 ($5\beta\text{-H}$, d, $J=5\text{ Hz}$), the doublet at δ 3.82 ($6\alpha\text{-H}$) changed into a singlet. On the other hand, on irradiation at δ 3.82, the doublet at δ 1.32 changed into a singlet. Further, on irradiation at δ 3.91 ($11\alpha\text{-H}$), the doublet-doublet at δ 2.37 ($9\beta\text{-H}$, $J=9$ and 2 Hz) collapsed to a broad singlet and the sextet at δ 2.83 ($12\alpha\text{-H}$, $J=9$, 9 , and 14 Hz) changed into a doublet-doublet ($J=9$ and 14 Hz); further, the doublet-doublet at δ 1.57 ($12\beta\text{-H}$, $J=9$ and 14 Hz) changed into a doublet ($J=14\text{ Hz}$). These results indicate that the signal of $11\alpha\text{-H}$ couples with $9\beta\text{-H}$, $12\alpha\text{-H}$, and $12\beta\text{-H}$, having



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a J value of 9 Hz. In addition, the signal pattern at δ 2.71 (13 α -H) indicates that 13 α -H only couples with 12 α -H.

Consequently, the structure of rubescensin C can be represented as 1.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Infrared (IR) absorption spectra were taken on a Hitachi 285 spectrometer, circular dichroism (CD) spectra on a Jasco J-500 instrument, and specific rotations on a Jasco DIP-180 automatic polarimeter. ^1H - and ^{13}C -NMR spectra were measured with a JEOL JNM-FX-100 machine and chemical shifts are given in δ (ppm) values with TMS as the internal standard. Mass spectra were recorded on a JEOL JMS-D-300 spectrometer.

Rubescensin C (1)—Extraction procedures have been reported⁹⁾ previously. Recrystallization from MeOH afforded plates. mp 239–241°C. $[\alpha]_D^{25}$ -68.6° ($c=0.14$, pyridine). *Anal.* Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_6$: C, 65.55; H, 8.25. Found: C, 65.29; H, 8.23. MS m/e : 366 (M^+). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3300, 1640. NMR ($\text{CDCl}_3 + \text{C}_6\text{D}_6\text{N}$) δ : 1.03, 1.09 (each 3H, C-4 Me_2), 1.32 (1H, d, $J=5$ Hz, C-5-H), 1.57 (1H, dd, $J=9$ and 14 Hz, C-12 β -H), 2.37 (1H, dd, $J=9$ and 2 Hz, C-9-H), 2.71 (1H, d, $J=9$ Hz, C-13-H), 2.83 (1H, ddd, $J=9, 9,$ and 14 Hz, C-12 α -H), 3.82 (1H, d, $J=5$ Hz, C-6-H), 3.87 (1H, d, $J=10$ Hz, C-20- H_a), 3.91 (1H, m, C-11-H), 4.14 (1H, dd, $J=10$ and 2 Hz, C-20- H_b), 4.50 (1H, s, C-14-H), 5.16 and 5.21 (each 1H, br s, C-17- H_2), 5.34 (1H, br s, C-15-H).

Preparation of a Saturated Ketone (2)—A solution of rubescensin C (14.4 mg) in MeOH (1 ml) and 20% HCl (3 ml) was stirred for 67 h at room temperature. The reaction mixture was extracted with AcOEt and the organic layer was washed with water and dried over MgSO_4 . After evaporation it gave a crystalline residue (13 mg). Recrystallization from MeOH afforded a ketone (2). mp 241–243°C. MS (high resolution) Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_6$: M^+ 366.204. Found: 366.208. CD (methanol) $\Delta\epsilon^{25}$: -1.12 (299) (negative maximum). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3350, 1710. NMR ($\text{C}_6\text{D}_6\text{N}$): 1.09, 1.21 (each 3H, s, C-4- Me_2), 1.16 (3H, d, $J=8$ Hz, C-16- H_3).

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