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STRUCTURE OF SCUTERIVULACTONE D DETERMINED BY TWO-DIMENSIONAL NMR SPECTROSCOPY.
 A NEW DITERPENOID FROM A CHINESE CRUDE DRUG "BAN ZHI LIAN"
 (SCUTELLARIA RIVULARIS WALL.)

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A new clerodane-type diterpenoid lactone, scuterivulactone D, has been isolated from the whole plants of Scutellaria rivularis Wall. and the structure has been determined by means of 2-D NMR spectroscopy including the ¹H-¹³C long-range shift correlation spectrum.

KEYWORDS — Ban Zhi Lian; Scutellaria rivularis; Labiatae; diterpenoid; clerodane; scuterivulactone D; 2-D NMR; ¹H-¹³C long-range shift correlation spectrum

The ether extract from a Chinese crude drug "Ban Zhi Lian (半枝蓮)" (dried whole plants of Scutellaria rivularis Wall., Labiatae) was separated by silica gel column chromatography followed by repeated recrystallization to give five clerodane-type diterpenoid lactones, named scuterivulactone A, B, C₁ (2), C₂ (3) (isolated as the acetate) and D, together with fourteen flavonoid constituents. The structures of the flavonoid constituents and scuterivulactone C₁ (2) and C₂ (3) were reported.^{1,2)} This paper deals with the structure of scuterivulactone D.

Chart 1

Scuterivulactone D (1a), $C_{27}H_{34}O_7$, was obtained as colorless needles (from acetone), mp 260 – 262°C, $[\alpha]_D^{26} + 57.5^\circ$ (MeOH), $UV_{\lambda_{max}}^{MeOH}$ nm (log ϵ): 236.5 (4.30), 263 (4.44). The IR spectrum of 1a showed absorption bands at 3518 (OH), 1747 (lactone) and 1725 (sh) cm^{-1} (ester) and the EIMS exhibited the M^+ peak at m/z 470 and fragment ion peaks at m/z 452 ($M^+ - H_2O$), 434 ($M^+ - 2H_2O$), 416 ($M^+ - 3H_2O$), 348 ($M^+ - C_6H_5COOH$), 330 ($M^+ - H_2O - C_6H_5COOH$), 312 ($M^+ - 2H_2O - C_6H_5COOH$), 122 (C_6H_5COOH) and 105 (C_6H_5CO). The 1H - and ^{13}C -NMR and 1H - 1H COSY spectra³ (in pyridine- d_5 and DMSO- d_6) suggested the presence of partial structures A, B and C (Fig. 1) in addition to two tert-hydroxy (δ_H 6.06 and 6.29) and four tert-methyl groups (δ_C 26.6, 25.9, 15.8 and 13.4; δ_H 1.30, 1.86, 1.26 and 1.94) and four quaternary carbons (δ_C 76.1, 74.8, 48.8 and 46.8). The 1H - 1H COSY spectrum of 1a in pyridine- d_5 is shown in Fig. 2. Each carbon signal, except for quaternary one, was assigned based on the 1H - ^{13}C COSY spectral data.³

Fig. 1 Partial Structures in 1a (δ -Values in Pyridine- d_5)
($\curvearrowright$: Long-range Coupling in 1H - 1H COSY)

Fig. 2 1H - 1H Shift Correlation Spectrum of Scuterivulactone D (1a) in Pyridine- d_5

Fig. 3 ^1H - ^{13}C Long-Range Shift Correlation Spectrum of Scuterivulactone D (1a) in $\text{DMSO}-d_6$:
 a) Whole Region, b) High Field Region (Sample: 80 mg, 40°C , $J_{\text{CH}} = 12 \text{ Hz}$, 12 h run)
 Multiplicities of the carbon signals were determined by the off-resonance and DEPT methods and are indicated as s, d, t and q. Open circles indicate the correlation peaks, which are significant but weak at this threshold level.

Next, the ^1H - ^{13}C long-range COSY spectrum of 1a was measured in order to clarify the connectivities of the partial structures and substituents groups. As shown in Fig. 3, the carbon atoms corresponding to the signals at δ 38.8 (10-C) and at δ 45.1 (5-C) are correlated with the protons corresponding to the signals at δ 1.04 (20- H_3), 1.39 (19- H_3), 1.43 (2-H) and 6.40 (11-H) and at δ 0.95 (1-H), 1.19 (18- H_3), 1.39 (19- H_3), 1.82 (7-H), 2.61 (10-H) and 3.34 (3-H), respectively. Similarly, quarternary carbons corresponding to the signals at δ 47.7 (9-C), 73.8 (8-C) and 74.6 (4-C) can be correlated with the protons indicated by arrows in the formula (Fig. 3). Also, some of significant ^1H - ^{13}C long-range correlations observed are illustrated by arrows. These data show that the gross structure of this compound is represented by the formula 1a.

The relative stereochemistry of 1a was determined on the basis of the coupling constant of each proton and the results of NOE experiments (in benzene- d_6) using the 3-O-acetate (1b), ⁴ mp 242-244°C, $[\alpha]_D^{22} + 21.8^\circ$ (CHCl_3), which was derived from 1a by the usual method. Irradiation at the 20- H_3 and 18- H_3 caused the increase of signal intensity of the 1α -, 7α (axial)-, 11 and 19-protons and the 3- and 19-protons, respectively, and irradiation at the 17- H_3 and 19- H_3 enhanced the signal intensity of the 7α - and 7β -protons and the 7α -, 18- and 20-protons, respectively.

On the basis of these findings, the structure of scuterivulactone D was determined to be as represented by the formula 1a. Absolute configurations of scuterivulactone C_1 (2), C_2 (3) and D (1a) and the structures of scuterivulactone A and B are currently under investigation.

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- 4) 1b: ^1H -NMR (CDCl_3) δ : 1.09, 1.15, 1.20, 1.44 (each 3H, s, 20-, 17-, 18- and 19- H_3), 1.62 (1H, qd, $J = 13, 3$ Hz, 1α -H), 1.96 (1H, dd, $J = 13, 5$ Hz, 7β -H), 2.09 (3H, s, OAc), 2.10 (1H, dd, $J = 13, 11$ Hz, 7α -H), 4.72 (1H, m, 3-H), 6.37, 6.42 (each 1H, d, $J = 17$ Hz, 11- and 12-H), 5.98 (1H, dd, $J = 11, 5$ Hz, 6-H); ^1H -NMR (C_6D_6) δ : 0.83, 0.88, 1.25, 1.44 (each 3H, s, 20-, 17-, 18- and 19- H_3), 1.56 (1H, qd, $J = 13, 3$ Hz, 1α -H), 1.74 (3H, s, OAc), 1.80 (1H, dd, $J = 13, 11$ Hz, 7α -H), 1.94 (1H, dd, $J = 13, 5$ Hz, 7β -H), 4.91 (1H, m, 3-H), 5.91, 6.18 (each 1H, d, $J = 17$ Hz, 11- and 12-H), 6.23 (1H, dd, $J = 11, 5$ Hz, 6-H).

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