The Two Bitter Principles of *Isodon shikokianus* Kudo

Takashi Kubota and Isao Kubo

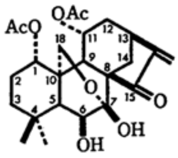
Faculty of Science, Osaka City University, Sugimoto-cho, Sumiyoshi-ku, Osaka

(Received March 24, 1969)

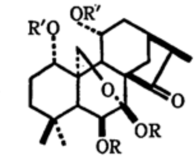
Chromatography of the ether extract of *Isodon shikokianus* Kudo yielded two crystalline bitter diterpenoid compounds, (I) $C_{20}H_{28}O_6$, mp 258—262 °C(decomp.), $[\alpha]_D^{18°}$ $-45.0°$ (pyridine), λ_{max}^{EtOH} 238 mμ (log ε 4.04) and (II) $C_{24}H_{32}O_8$ (*m*/*e* 448), mp 286—288°C (decomp.), $[\alpha]_D^{22°}$ $-38.6°$ (pyridine).

Compound I, according to its physical constants and spectral properties, is identical with the known oridonin[1] which is present in *I. trichocarpus* Kudo and *I. japonicus* Hara.

Compound II, which is found to be new and designated as shikokianin, exhibits in UV and IR spectra λ_{max}^{EtOH} 237 mμ (log ε 3.98) and ν_{max} 1720 and 1645 cm^{-1}. The IR spectrum indicated also the presence of hydroxyl groups (ν_{max}^{Nujol} 3600 and 3350 cm^{-1}, $\nu_{max}^{CHCl_3}$ 3600 and 3350 cm^{-1}) and chelated five membered ketone (1720 cm^{-1}).*1 The NMR spectrum in $CDCl_3$ showed the presence of two acetoxyl groups (8.10 and 7.90 τ, each 3H, s.), an exocyclic methylene group (4.02 and 4.54 τ, each 1H, s.), an ether type methylene group (5.60 and 6.10 τ, AB-type $J=12$ cps, $-CH_2-O-$), two tertiary methyl groups (8.84 τ, 6H, s., $(CH_3)_2C\langle$) and two hydroxyl groups (4.02 and 4.21 τ, disappeared on addition of D_2O). Catalytic hydrogenation of II on Pd-C yielded dihydroshikokianin (III), $C_{24}H_{35}O_8$, mp 266—267°C (decomp.), $[\alpha]_D^{20°}$ $-61.2°$ (pyridine), which exhibits no UV and IR band due to double bond or NMR signal due to a secondary methyl group. Although II and III could not be acetylated with acetic anhydride and pyridine,*1 on treatment with acetic anhydride and BF_3-etherate III gave tetraacetate (IV), $C_{28}H_{38}O_{10}$, mp 187—192°C (decomp.) which exhibits no IR band due to hydroxyl group. In NMR spectrum



(II)



(III) R′=H, R=Ac
(IV) R=R′=Ac
(V) R=R′=H

IV shows four acetoxyl groups (7.86, 7.95, 7.96 and 7.99 τ, each 3H, s.) and this suggests the presence of two hydroxyl groups in III and also II itself. Dihydroshikokianin III was hydrolysed with 0.05N 50% methanolic potassium hydroxide or 1N 50% ethanolic hydrochloric acid to give the tetraol (V), $C_{20}H_{30}O_6$, mp 256—261°C (decomp.) which exhibits no signal in NMR spectrum due to acetoxyl group and reverted to III on treatment with acetic anhydride and pyridine. This indicated that the change of carbon skeleton did not take place during hydrolysis with alkali or acid. Finally, tetraol V on oxidation with periodic acid gave dihydronodosin, $C_{20}H_{28}O_6$, mp 250—252°C (decomp.) which was obtained from nodosin[2] by catalytic hydrogenation on Pd-C.

As the results of the foregoing experiments, the structural formula II including its absolute configuration is proposed for shikokianin. The assignment of α-configuration of C(11) in II was also supported by an observation that the signal of the proton attached to C(11) appeared as double doublet at 6.20 τ ($J_{ax}=9$ cps and $J_{bx}=18$ cps), as in the case of isodonal[3] (6.27 τ, d. d. $J_{ax}=7$ cps and $J_{bx}=15$ cps).

---

*1 These results indicated the presence of a chelated five membered ketone. Therefore the 6-hydroxyl group must be of β-configuration as oridonin.[1]

[1] E. Fujita, T. Fujita, H. Katayama and M. Shibuya *Chem. Commun.*, **1967**, 252.

[2] E. Fujita, T. Fujita and M. Shibuya, *Chem. Pharm. Bull.*, **16**, 509 (1968).

[3] T. Kubota and I. Kubo, *Tetrahedron Letters*, **1967**, 3781.