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NEW CONSTITUENTS OF RHODODENDRON JAPONICUM SURINGER, RHODOJAPONIN-V AND -VI

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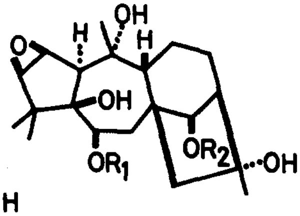
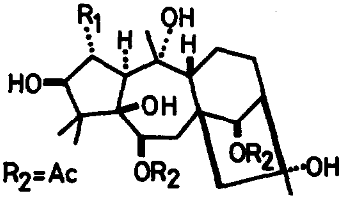
The toxic constituents of Rhododendron japonicum Suringer (Japanese Azalea) (Ericaceae) were classified Rhodojaponin (abbreviated to R) -I (1), -II (2), -III (3)[1] and -IV (5)[2] by T. Takemoto. We investigated hot water and ether extractions of the dry flowers of this plant and isolated two new constituents, R-V*(4), mp 232°, $[\alpha]_D^{18}$ -34.1° (c 0.22, ethanol), and R-VI, amorphous, $[\alpha]_D^{18}$ -20.2° (c 0.28, ethanol), in addition to R-I (1), mp 237°, R-II (2), mp 261°, and R-III (3), mp 274° (decomp). The respective yield of the constituents were 0.015, 0.026, 0.005, 0.006 and 0.003%. R-V (4) gave the empirical formula, $C_{22}H_{34}O_7$, and showed an IR absorption at 3400 (OH), 1720 and 1250 cm^{-1} (CH_3COO). On alkaline hydrolysis with 3% NaOH-Methanol, the acetate (4) gave an alcohol identical with R-III (3) (92% yield). The carbon bearing the acetoxyl group was confirmed as follows: The NMR spectrum (C_5D_5N) of R-V (4) showed the presence of four methyl groups as singlets (δ 1.30, 1.41, 1.50, 1.81), one acetyl group (δ 1.96) and several methyne groups (δ 2.89 s C_1-H, 3.19 d J=3 C_3-H, 4.00 q J_{AX}=9 J_{BX}=7 C_6-H, 4.16 d J=3 C_2-H, 6.08 s C_{14}-H). The signal of the C_{14}-proton of R-V (4) was 1.26 ppm down field from the corresponding signal of the C_{14}-proton of R-II (2), while the C_6-proton signal of R-V (4) appeared at 1.46 ppm up field from that of R-II (2). Therefore, the ester group of R-V (4) is



1 $R_1=R_2=Ac$
2 $R_1=Ac, R_2=H$
3 $R_1=R_2=H$
4 $R_1=H, R_2=Ac$



5 $R_1=H, R_2=Ac$
6 $R_1=OH, R_2=H$
7 $R_1=OAc, R_2=Ac$

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* Private communication: Dr. H. Hikino (Tohoku University) has also isolated this compound from this plant and elucidated the structure. He also named this R-V.

assigned to the C_{14}-position. This estimation is supported by the fact that R-V (4) consumed one equimole of lead tetraacetate in acetic acid, while R-I (1) and R-II (2) did not under similar conditions. R-VI (6) gave the empirical formula, $C_{20}H_{34}O_7 \cdot 1/2\ CH_3COOC_2H_5$ (purified from ethyl acetate), showed an IR absorption at 3400 cm^{-1} (OH) and consumed two equimoles of lead tetraacetate in acetic acid. The NMR spectrum of R-VI (6) showed signals for four methyl groups as singlets (δ 1.56 6H, 1.58, 1.87) and several methyne groups (δ 2.98 d J=8 C_1-H, 4.02 d J=3 C_3-H, 4.68 q J_{AX}=10 J_{BX}=4 C_6-H, 4.96 s C_{14}-H, 5.10 dd J=8 and 3 C_2-H). Irradiation at δ 5.10 caused each of the signals at δ 2.98 and 4.02 to change to singlets. The alkaline treatment (0.3N KOH-85% DMSO at 100° for 3 hrs.)[3] of R-III (3) gave an alcohol identical with R-VI (6) (36% yield). Thus, R-VI is determined to be a heptaol like 6. The stereochemistry of R-VI (6) at C_2 and C_3 was elucidated as follows: When R-I (1) was treated with acetic acid in ether containing small amounts of boron trifluoride at -10° for 1.5 hrs., a 92% yield of the triacetate (7), $C_{26}H_{40}O_{10}$, mp 238°, $[\alpha]_D^{18}$ -46.3° (c 0.43, ethanol), was obtained. Hydrolysis of the triacetate (7) (3% NaOH-MeOH) gave a 96% yield of R-VI (6). The oxide ring of R-I (1) is cleaved by acetolysis. The NMR spectrum of the triacetate (7) showed signals of C_1-, C_2- and C_3-protons at δ 3.40 (d J=3), 6.05 (d J=3) and 3.90 (d J=5), respectively. With the addition of D_2O, the doublet peak at δ 3.90 changed to a singlet, while the doublet at δ 7.50 (J=5) disappeared. On irradiation at δ 6.05, the signal at δ 3.40 changed to a singlet and vice versa. Since the C_2-proton signal of the triacetate (7) is 0.95 ppm down field from that of R-VI (6), the acetoxyl group was assigned the C_2-position. The C_3-proton must be coupled with the C_3-hydroxyl proton. Since the substituents at C_2 and C_3 of the triacetate (7) must be trans[4] and the oxide ring of R-I (1) is β-oriented[1], the C_2-acetoxyl group of the triacetate (7) was ascertained to be α-oriented and the C_3-hydroxyl β-oriented. Thus, the C_2-hydroxyl group of R-VI (6) was determined as α-oriented and the C_3-hydroxyl as β-oriented.

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