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STRUCTURE OF GERANIIN IN THE EQUILIBRIUM STATE

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Structure of geraniin, the main tannin of *Geranium thunbergii* Sieb. et Zucc., was reported to have a dehydrohexahydroxydiphenoyl group bonded to O-2 and O-4 of D-glucopyranose in corilagin[1]. The ester carbonyl on cyclohexenetrione was tentatively assigned to the one bonded to O-2 of glucose. Partial hydration of the ketone groups was also presumed[1]. We have now obtained evidences which determine the orientation of the dehydrohexahydroxydiphenoyl group in geraniin, and the equilibrium state induced by hydration of ketones and by epimerization in the solution of geraniin.

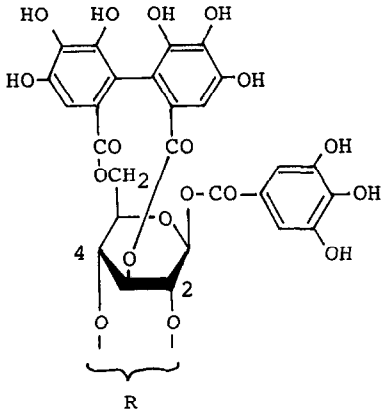
Phenazine B (1) produced *via* phenazine A which was obtained by condensation of geraniin with *o*-phenylenediamine was methylated with diazomethane to yield tetradecamethyl derivative 2, $C_{61}H_{60}O_{25}N_2$, which shows m/e 1009 [MH − tri-*O*-methylgallic acid]$^+$ and m/e 479 (base peak, 3) ions by chemical ionization mass spectrum. This derivative 2 yielded monoacetate 4, $C_{63}H_{62}O_{26}N_2$ [PMR(90 MHz, $CDCl_3$), δ 2.36 (acetyl)]. In the PMR spectrum of 2 ($CDCl_3$), H-4 (δ 5.11) of glucose indicates esterification at C-4. Although H-2 in 2 is hidden by other protons, it shows downfield shift to δ 5.32 (coupled with H-1 at δ 6.56) in the PMR spectrum of 4. The cleavage of one of the ester linkages in phenazine B upon the methylation with diazomethane, therefore, occurred at O-2 of glucose. Hydrolysis of 2 in refluxing 10% HCl for 2 hours yielded the phenylphenazine residue 5 having a carboxyl group, which was purified by preparative thin-layer chromatography. This product gave M^+ (m/e 478) ion, and yielded upon methylation with diazomethane,

dimethyl ester 6 which was identified with methyl 4-methoxy-3-(4,5,6-trimethoxy-2-methoxycarbonylphenyl)-phenazine-2-carboxylate[1]. The PMR spectra of monoester 5, diester 6, and dicarboxylic acid 7, showed significant downfield shifts of the protons presumably located *ortho* to the free carboxyl group, upon addition of pyridine-d_5 to the solution of these compounds in chloroform-d. This presumption was supported by the comparison of PMR spectra of tri-*O*-methylgallic acid and methyl tri-*O*-methylgallate, between which only the former showed significant downfield shift of the aromatic protons upon addition of pyridine-d_5 (Table 1). These data indicate that the free carboxyl group in 5 is located *ortho* to H_A. The structure of tetradecamethyl derivative of phenazine B is therefore exhibited as 2, and the ester linkages in phenazine B and geraniin are shown as 1 and 8, respectively. The molecular model shows that the upfield shift of H-1 of glucose upon the formation of 1 is attributable to stereostructure 9 of phenazine B.

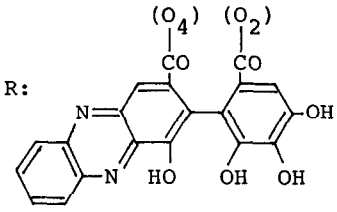
Geraniin was equilibrated in acetone-d_6 containing D_2O (ca. 10%) at 35°C, in 6 hours to yield a mixture whose PMR spectrum shows two peaks of almost equal area for each of the protons in the region of aromatic and vinyl protons, and for the methine proton. Transformations of the sugar protons were also observed. The complete equilibration in anhydrous acetone-d_6 required longer than 12 hours. Singlets of the methine proton and the vinyl proton, which were exhibited at δ 5.16 and 6.56 in acetone-d_6 before the equilibration, were

Table 1. Shifts of H_A and H_B in the PMR spectra

compounds	$CDCl_3$		5% C_5D_5N in $CDCl_3$		Shift value	
	H_A	H_B	H_A	H_B	H_A	H_B
5	8.20	7.26	8.29	7.28	-0.09	-0.02
6	8.70	7.47	8.71	7.48	-0.01	-0.01
7	8.10	7.30	8.16	7.37	-0.06	-0.07
methyl tri-*O*-methylgallate	7.28		7.29		-0.01	
tri-*O*-methylgallic acid	7.38		7.43		-0.05	

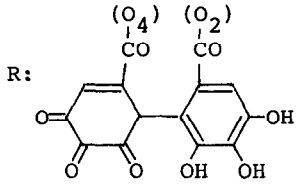


R



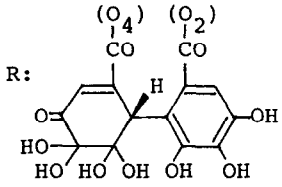
R:

1



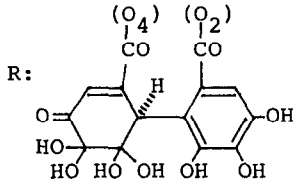
R:

$\cdot XH_2O$ 8



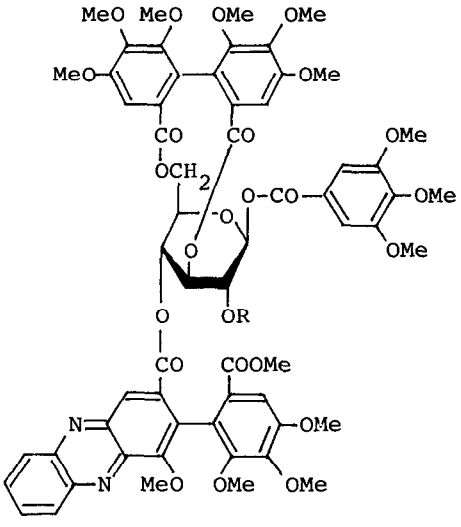
R:

10a



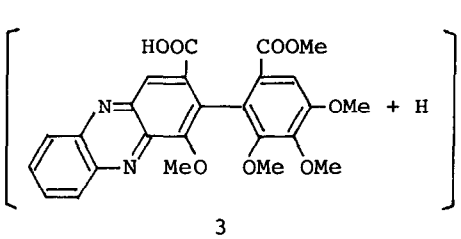
R:

10b



2 R=H

4 R=Ac



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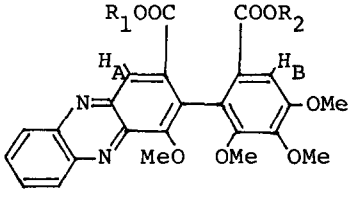
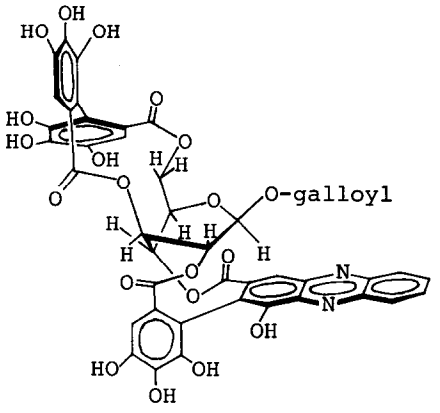


5 R_1=H, R_2=Me

6 R_1=R_2=Me

7 R_1=R_2=H



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accompanied after the equilibration, by mutually coupled doublets (J=1.5 Hz) at δ 4.72 and 6.26. The ^{13}C-NMR spectrum (25 MHz) of the equilibrated solution shows each one of the methine carbon (δ 46.0, 51.9), the six glucose carbons (δ 62.4, 63.4; 63.8, 63.9; 65.9, 66.8; 70.0, 70.5; 72.6, 73.2; 91.1, 91.9), and the ketone carbon (δ 192.0, 194.8), composed by a pair of peaks of equal area. The proportion of the peak area in a pair varied depending on the extent of equilibration, keeping equality among the pairs in a spectrum. The original crystalline geraniin was recovered upon recrystallization. This equilibration is attributable to the epimerization at the methine carbon.

The comparisons of the peak area of the carbon carrying geminal diol (δ 92.3, 92.5 and 96.3) with that of C-1 of glucose, and of that of ketone carbon with the carbonyl carbon of the ester groups, indicate that two of the three ketones in geraniin are hydrated in this equilibrium state. The shift values of the ketone peaks are attributable to the conjugated ketone in 10a and 10b. The equilibrium state of geraniin is thus shown by structural formulas 10a ⇄ 10b.

REFERENCES

1. T. Okuda, T. Yoshida and H. Nayeshiro, Tetrahedron Letters, 3721 (1976); Chem. Pharm. Bull., 25, 1862 (1977).