Optical Rotatory Dispersion and Absolute Configuration of Flavanones, 3-Hydroxyflavanones, and Their Glycosides

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THE Cotton effect of flavanones and 3-hydroxyflavanones due to the low intensity $n \rightarrow \pi^*$ transition (320—330 mμ) may be correlated with the relationship between the chirality of $\alpha\beta$-unsaturated ketones and the sign of their high wavelength Cotton effect derived by Snatzke.[1] Of more significance, the lower wavelength $\pi \rightarrow \pi^*$ Cotton effect centred at approximately 280—290 mμ, which is easier to characterize than the weaker Cotton effect at 325 mμ, further confirmed configurational assignment to flavanones and 3-hydroxyflavanones.

(+)-Naringenin (Ia), of unknown configuration, was obtained from (—)-naringin‡ (Ib) by enzymic hydrolysis. Since the 2-aryl group of (+)-(Ia) is equatorial ($J_{2,3a}$ = 12·5 Hz.), the negative Cotton effect (Figure) observed near 325 mμ allows assignment[1] of configuration (*R*) at C-2 in both (+)-(Ia) and (—)-(Ib).

Therefore, the (—)-naringenin obtained[2] from

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‡ Our sample of (—)-naringin was of unknown origin from Calbiochem, Los Angeles. Hydrolysis was conducted at pH 4·7 using fungal hemicellulase. Optically active naringenin has not been previously obtained from naringin. (R. M. Horowitz, "Biochemistry of Phenolic Compounds," ed., J. R. Harborne, Academic Press, New York, 1964, p. 546).

Helichrysin A may be assigned the 2(*S*)-configuration. Examination of other flavanones and 3-hydroxyflavanones of known[3] configuration (Table), having equatorial 2-aryl substituents in the former or diequatorial 2,3-substituents in the latter, has led to the following conclusions. Flavanones of 2(*S*)-configuration and 3-hydroxyflavanones of 2(*R*) : 3(*R*) configuration exhibit a positive Cotton effect due to the $n \rightarrow \pi^*$ transition and a negative Cotton effect in the $\pi \rightarrow \pi$ region.[4]

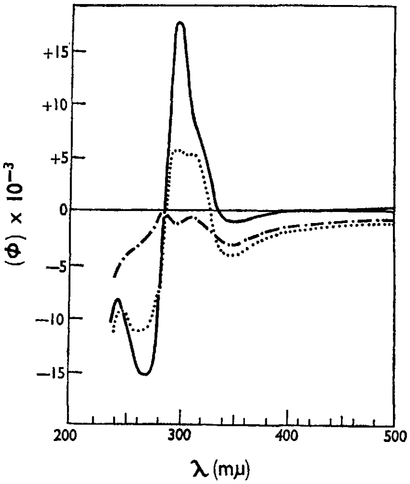


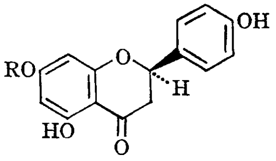
FIGURE. *O.r.d. curves of naringin (natural),* • • •; *naringin (cyclized from chalcone),* — • — • —; *naringenin (from natural naringin),* ——.

Since a flavanone or 3-hydroxyflavanone glycoside will possess optical activity due to the carbohydrate moiety, in addition to the chiral centres of the aglycone, we have examined the o.r.d. of glycosides in which the aglycone asymmetric centres are optically active on one hand and racemic on the other. The aglycones (+)-(Ia) and (−)-hesperetin were obtained by hydrolysis of their respective glycosides and in each case the o.r.d. of the glycoside was similar to that of the related aglycone (Figure). (−)-Liquiritin (II) and (−)-liquiritigenin were obtained separately and similarly (−)-astilbin (III) and (+)-dihydroquercetin were isolated independently. Since the sign and magnitude of the Cotton effects of glycosides (II) and (III) were similar to their corresponding aglycones, the absolute configuration of the chiral centre(s) in the dihydropyrone ring is identical in the related compounds. It is noteworthy that the D-line rotations§ of glycosides (−)-(Ib), (−)-(II), and (−)-hesperidin (IV) are quite similar but that examination of the Cotton effect region showed (−)-(Ib) to be of opposite configuration to (−)-(II) and (−)-(IV) at C-2.

TABLE

Cotton effects of flavanones and 3-hydroxyflavanones

	$n \rightarrow \pi^*$	$\pi \rightarrow \pi^*$
Flavanones		
(−)-Liquiritigenin	+	−
(−)-Eriodictyol	+	−
(−)-Hesperetin	+	−
(+)-Sakuranetin	−	+
3-Hydroxyflavanones		
(+)-Dihydroquercetin	+	−
(+)-Dihydrorobinetin	+	−
(−)-Dihydrofisetin	−	+



(Ia) R=H
(Ib) R=2-*O*-L-rhamnosyl-D-glucosyl

Chemical cyclization[5] of hesperidin chalcone and naringin chalcone gave hesperidin and naringin, respectively, in which C-2 of the aglycone was racemic. Examination of the o.r.d. of synthetic naringin (Figure) showed marked changes in comparison to (+)-(Ia) and natural (−)-(Ib). While Cotton effects were still present in the 250—350 mμ region, they were greatly reduced in magnitude and are probably related to asymmetric perturbation of the aromatic ring by the optically active carbon atoms of the glycoside. A similar result was obtained with (−)-(IV). Enzymic hydrolysis of synthetic naringin gave optically inactive naringenin showing that there was no asymmetric induction upon chalcone cyclization. Thus, examination of the Cotton effect region of flavanone or 3-hydroxyflavanone glycosides is

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§ (−)-Naringin, $[\alpha]_D^{27}$ −84·4 (50% acetone–water); (−)-liquiritin, $[\alpha]_D^{27}$ −70·5 (methanol); (−)-hesperidin, $[\alpha]_D^{27}$ −99·1 (methanol).

diagnostic of the optical activity of the aglycone portion of the molecule.

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[1] G. Snatzke, *Tetrahedron*, 1965, **21**, 413, 439.

[2] R. Hänsel and D. Heise, *Arch. Pharm.*, 1959, **292**, 398.

[3] For formulae and absolute configuration references see: J. W. Clark-Lewis, *Rev. Pure Appl. Chem.*, 1962, **12**, 96; F. M. Dean, "Naturally Occurring Oxygen Ring Compounds," Butterworths, London, 1963, p. 333; W. B. Whalley, "The Chemistry of Flavonoid Compounds," ed. T. A. Geissman, Macmillan, New York, 1962, p. 441.

[4] The sign of the $\pi \rightarrow \pi^*$ Cotton effect agrees with the results of C. Djerassi, R. Records, E. Bunnenberg, K. Mislow, and A. Moscowitz, *J. Amer. Chem. Soc.*, 1962, **84**, 870.

[5] M. Shimokoriyama, *J. Amer. Chem. Soc.*, 1957, **79**, 4199.