Chiroptical Differentiation of 6- and 8-C-Glycosylflavones

By WILLIAM GAFFIELD*
(*Western Regional Research Laboratory*,† *Berkeley, California* 94710)
and R. M. HOROWITZ
(*Fruit and Vegetable Chemistry Laboratory*,† *Pasadena, California* 91106)

Summary C.d. studies of *C*-glycosylflavones have shown that a positive Cotton effect at 250—275 nm indicates that the glycosyl residue is linked to C-6 (*e.g.* isovitexin) while a negative Cotton effect at 250—275 nm indicates it is linked to C-8 (*e.g.* vitexin).

A RECURRING problem in the structure determination of *C*-glycosylflavones is assignment of the position of attachment of the glycosyl residue to the aglycone. Mass spectra,[1] n.m.r. spectra of acetyl derivatives,[2] and R_F values[2] have been used to distinguish C-6 and C-8 in glycosylflavones. We report here the differentiation of individual isomeric glycosylflavones by c.d. measurements. This is an absolute method which requires neither formation of derivatives nor the presence of both isomers.

The u.v. absorption maxima of *C*-glycosylflavones generally fall in the regions 300—340 (log ϵ *ca.* 4·3), 250—275 (*ca.* 4·3), and 213—217 nm (*ca.* 4·5). In the c.d. spectra of various *C*-glycosylflavones and their derivatives at least one Cotton effect was observed in each of the three absorption regions. The sign of the dominant Cotton effect at 250—275 nm is diagnostic of the position of the *C*-glycosyl residue on the flavone. A positive Cotton effect at 250—275 nm indicates that the sugar is linked to C-6 of the flavone, as in isovitexin (**8**), while a negative Cotton effect indicates it is linked to C-8, as in vitexin (**1**). These conclusions refer to the β-D-glucopyranosyl flavones which are the most common naturally occurring derivatives. Examples are shown in the Figure and listed in the Table. The c.d. spectrum of (**15**) (– – – in Figure), a 6,8-di-*C*-β-glycosyl derivative of the

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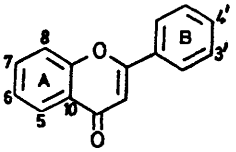
† Laboratories of the Western Marketing and Nutrition Research Division, Agricultural Research Service, U.S. Department of Agriculture.

flavone luteolin, is instructive. The 250—275 nm Cotton effect is essentially cancelled compared to those of the mono-substituted *C*-glycosylflavones although the high- and low-wavelength Cotton effects are of similar magnitude for mono- and di-*C*-glycosylflavones [see also (**14**) in Table].

Cotton effect[a] *of substituted* 6- *and* 8-C-*glycosylflavones*



Compound	5	6	7	8	C.d.[c] $[\theta] \times 10^{-3}(\lambda)$
	Substituents[b]				
(**1**)	OH	—	OH	Glu[d]	−15·6(272)
(**2**)	OAc	—	OAc	Ac$_4$Glu[d]	−17·9(261)
(**3**)	OMe	—	OMe	Me$_4$Glu[d]	−20·4(263)
(**4**)	OMe	—	OMe	Glu[d]	−13·0(260)
(**5**)	OH	—	OH	Xyl-Glu[e]	−20·2(273)
(**6**)	OH	Br	OH	Glu[d]	−10·6(270)
(**7**)	OAc	—	OAc	Ac$_4$Glu[d]	−18·0(265)
(**8**)	OH	Glu[d]	OH	—	+8·7(265)
(**9**)	OAc	Ac$_4$Glu[d]	OAc	—	+24·3(258)
(**10**)	OMe	Me$_4$Glu[d]	OMe	—	+21·0(263)
(**11**)	OMe	Glu[d]	OMe	—	+15·1(263)
(**12**)	OMe	Ac$_4$Glu[d]	OMe	—	+25·7(258)
(**13**)	OAc	Ac$_4$Glu[d]	OAc	—	+26·8(252)
(**14**)	OMe	Me$_4$-β-Gly[f]	OMe	Me$_4$-β-Gly[f]	+3·1(263) −1·1(255)
(**15**)	OMe	Ac$_4$-β-Gly[f]	OMe	Ac$_4$-β-Gly[f]	−2·3(270)

[a] Cotton effect referred to is at 250—275 nm; [b] B-ring substituents are: (**1**), (**5**), (**6**), and (**8**), 4′-OH; (**2**) and (**9**), 4′-OAc; (**3**), (**4**), (**10**), (**11**), and (**12**), 4′-OMe; (**7**) and (**13**), 3′,4′-di-OAc; (**14**) and (**15**), 3′-4′-di-OMe. [c] Recorded in MeOH at 27 °C. [d] Glu = β-D-glucosyl. [e] Xyl-Glu = 2″-*O*-β-D-xylosylglucosyl. [f] Gly is probably D-glucosyl.

The c.d. spectrum of 6-bromovitexin (**6**) is closely similar to that of vitexin (**1**) (Table). Thus, a 6-substituent does not greatly affect the c.d. of an 8-*C*-glycosylflavone when the substituent is symmetrical with respect to the plane of the A-ring. The Cotton effects at 250—275 nm given by vitexin hepta-acetate (**2**) and isovitexin hepta-acetate (**9**) differ in magnitude but not in sign from those of the parent flavones, (**1**) and (**8**), respectively. This implies that the Cotton effects with opposite signs of the 6- and 8-*C*-β-D-glucosylflavones are due to some factor other than intramolecular hydrogen bonding differences between the 6- and 8-isomers. A possible explanation for the dissimilar chiroptical properties of the C-6 and C-8 isomers is that the carbohydrate group resides on opposite sides of a symmetry plane of the substituted benzoyl chromophore. The results presented herein may be rationalized to an extent by a quadrant rule based empirically upon the c.d. data listed in the Table using the plane of the A-ring and a plane perpendicular to the A-ring passing through C-7 and C-10 as symmetry planes.

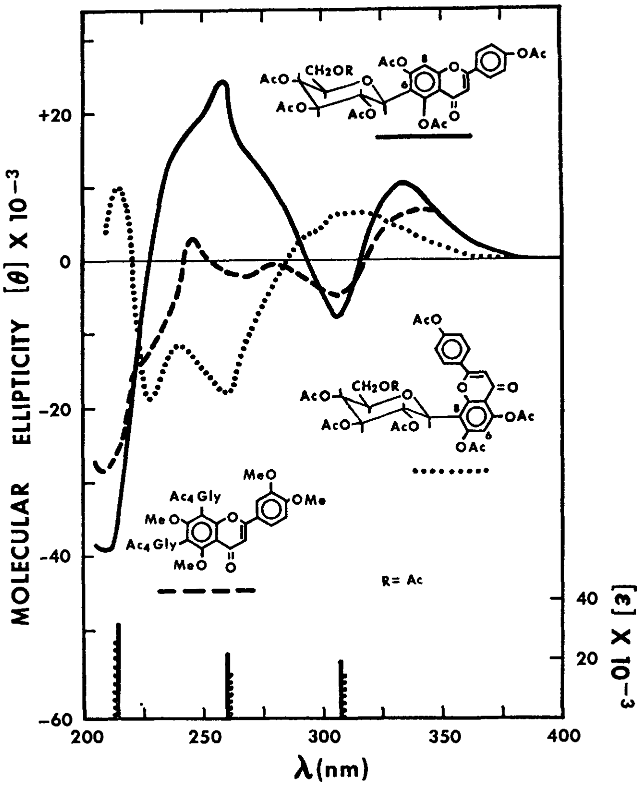


Figure. *C.d. and u.v. data in* MeOH: ——— *isovitexin hepta-acetate* (**9**), · · · · · *vitexin hepta-acetate* (**2**), – – – – *tetra*-O-*methyl-octa*-O-*acetyl-lucenin* (**15**).

It seems clear that c.d. provides a useful and sensitive method for determining whether *C*-glucosylflavones contain 6-*C*, 8-*C* or 6,8-di-*C*-glycosyl residues.

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[1] A. Prox, *Tetrahedron*, 1968, **24**, 3697.

[2] B. Gentili and R. M. Horowitz, *J. Org. Chem.*, 1968, **33**, 1571.