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CIRCULAR DICHROISM SPECTRA OF FLAVANOLS

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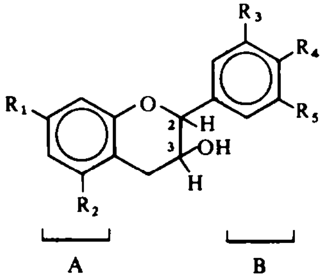
Abstract—CD spectra of the flavanols (+) catechin, (−) robinetinidol, (+) afzelechin, (−) epiafzelechin, (−) epicatechin, (−) epigallocatechin, (+) fisetinidol and (+) epifisetinidol are reported at 25° and −185°. At −185° the contributions of the two aromatic chromophores to the $'L_b$ transition can be separated. The chroman chromophore gives a negative CD band if the absolute configuration at C_2 is R and its aryl substituent is in an equatorial position, which is in contrast to the situation in the tetralin chromophore.

INTRODUCTION

Optical activity and ORD measurements have been used to elucidate the stereochemistry of flavanoids.[1] CD measurements, however, which give much more information on the individual chromophores and therefore on the conformation, have only been used in a systematic way in a study of flavanones.[2]

Table 1. Formulae of the investigated flavanols



Number	Compound	Stereochemistry		Chromophore A		Chromophore B		
		at C_2	at C_3	R_1	R_2	R_3	R_4	R_5
1	(+) catechin	R	S	OH	OH	OH	OH	H
2	(−) robinetinidol	R	S	OH	H	OH	OH	OH
3	(+) afzelechin	R	S	OH	OH	H	OH	H
4	(−) epiafzelechin	R	R	OH	OH	H	OH	H
5	(−) epicatechin	R	R	OH	OH	OH	OH	H
6	(−) epigallocatechin	R	R	OH	OH	OH	OH	OH
7	(+) fisetinidol	S	R	OH	H	OH	OH	H
8	(+) epifisetinidol	S	S	OH	H	OH	OH	H

The availability of a series of flavanols and our interest in the chrioptical behaviour of the aromatic chromophore[3] led us to investigate the CD spectra of the compounds listed in Table 1. The absolute configuration at the asymmetric centres is known.[4]

Two aromatic chromophores are present in the molecule. viz. chromophore A in two substitution patterns:

$$R_1 = R_2 = OH \text{ and } R_1 = OH.\ R_2 = H.$$

and chromophore B in three substitution patterns:

$$R_3 = R_4 = OH.\ R_5 = H;\ R_3 = R_5 = H.\ R_4 = OH \text{ and } R_3 = R_4 = R_5 = OH.$$

Absorption bands of these aromatic chromophores are found in two regions: around 280 nm (^1L_b transition) and at about 240 nm (^1L_a transition). Because of the presence of two aromatic chromophores in the flavanols, two bands are expected in each region. UV absorption data of the compounds listed have been reported.[4]

TABLE 2. CD DATA OF FLAVANOLS IN EPA (ETHANOL/ISOPENTANE/DIETHYL ETHER 2:5:5) AT 25° AND −185°

Number	Solvent Compound	EPA +25°				EPA −185°[a]			
		^1L_a		^1L_b		^1L_a		^1L_b	
		λ	Δε	λ	Δε	λ	Δε	λ	Δε
1	(+) catechin	245	+0·06	282	−0·36	233	−1·66	272	+0·09
								283	−0·24
2	(−) robinetinidol	—	—	284	−1·50	232	−4·04	274	+0·45
						237·5	−4·18	291	+0·12
3	(+) afzelechin	240	+0·80	272	−0·44	240	+1·32	276	+0·19
4	(−) epiafzelechin	239	+1·32	273	−1·04	239	+2·32	272·5	−1·28
5	(−) epicatechin	239	+1·18	278	−1·00	238	+3·72	279	−1·44
6	(−) epigallocatechin	240	+0·92	278	−0·78	239	+0·74	276	+0·42
7	(+) fisetinidol	—	—	271	−0·44	—	—	276	−1·72
				288	+2·46			290	+1·20
8	(+) epifisetinidol	240	−0·4	285·5	+1·90	240	−0·26	275	−0·41
								285	+0·72

[a] Δε values have been corrected for shrinkage of solvent

TABLE 3. CD DATA OF FLAVANOLS IN METHANOL

Number	Compound	^1L_a		^1L_b	
		λ	Δε	λ	Δε
1	(+) catechin	227	−1·52	280	−0·52
		242·5	+0·23		
2	(−) robinetinidol	236	+0·80	285	−1·86
3	(+) afzelechin	236	+1·25	273	−0·49
4	(−) epiafzelechin	238	+1·81	271	−0·95
5	(−) epicatechin	240	+0·81	272	−0·90
6	(−) epigallocatechin	238	+0·89	260	−1·10 (s)
				278	−0·23
7	(+) fisetinidol	—	—	290	+2·74
8	(+) epifisetinidol	—	—	286	+0·45

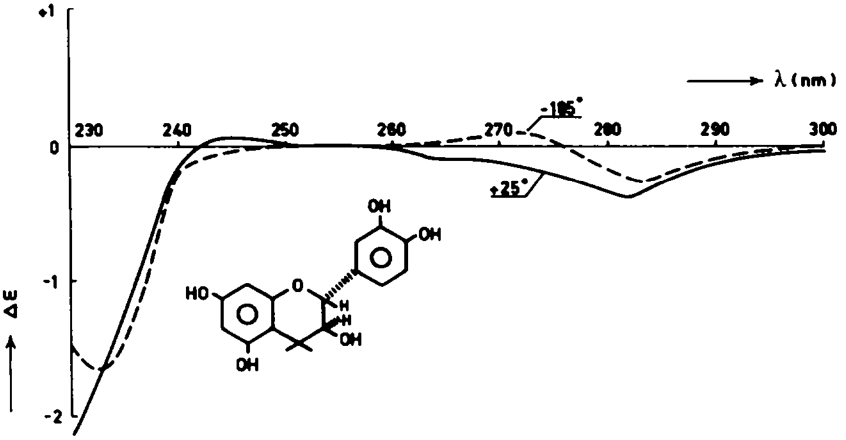


FIG 1. CD spectrum of (+) catechin in EPA at 25° and −185°.

RESULTS

CD results are given in Table 2 (EPA at 25° and −185°). Table 3 (MeOH) and Figs. 1–6 (EPA 25° and −185°). In the 240 nm region the Δε/ε ratio is unfavourable in some cases. which leads to less accurate Δε values than in the 280 nm region. Δε values at −185° have been corrected for shrinkage of the solvent.[5]

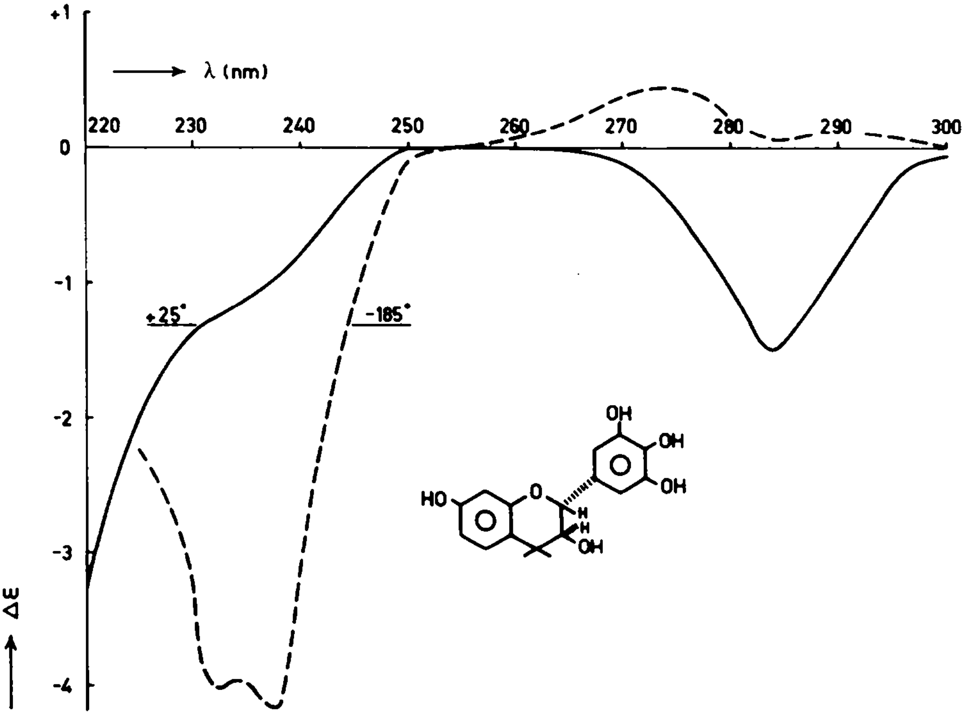
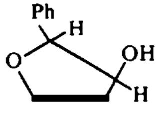


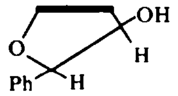
FIG 2. CD spectrum of (−) robinetinidol in EPA at 25° and −185°.

DISCUSSION

'L_b transition. It is reasonable to assume that the sign of the CD band of chromophore A is determined by the chirality of the heterocyclic ring attached to it, analogously to the situation described for tetralins by Dornhege and Snatzke,[6] *i.e.* the nearest chiral sphere determines the sign of the Cotton effect, so that the absolute configuration at C_3 has only minor influence. The chirality of the heterocyclic ring in its turn is determined by the preference of chromophore B for an equatorial position (as proved by NMR).[7] Inspection of Dreiding models shows that for absolute configuration R at C_2 (compounds 1–6) the situation depicted in **1a** exists. and for configuration S that of **1b**. Moreover. it is reasonable to assume that temperature and solvent variations will influnce the CD band of the freely rotating chromophore B much more than that of chromophore A. because the heterocyclic ring is already held in its most stable conformation at room temperature. It is clear that where two bands appear at −185°



1a



1b

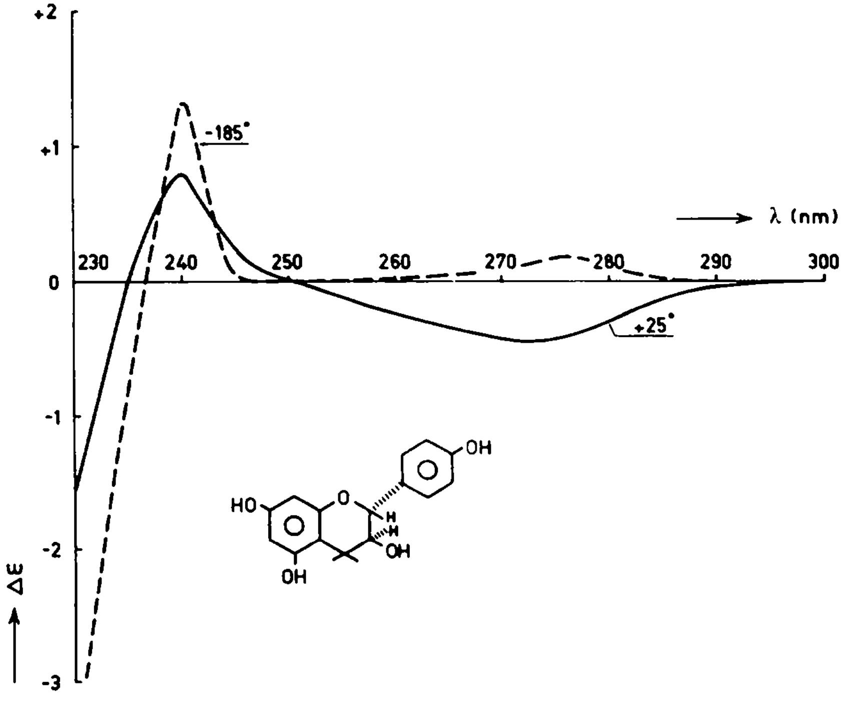


Fig 3. CD spectrum of (+) afzelechin in EPA at 25° and −185°.

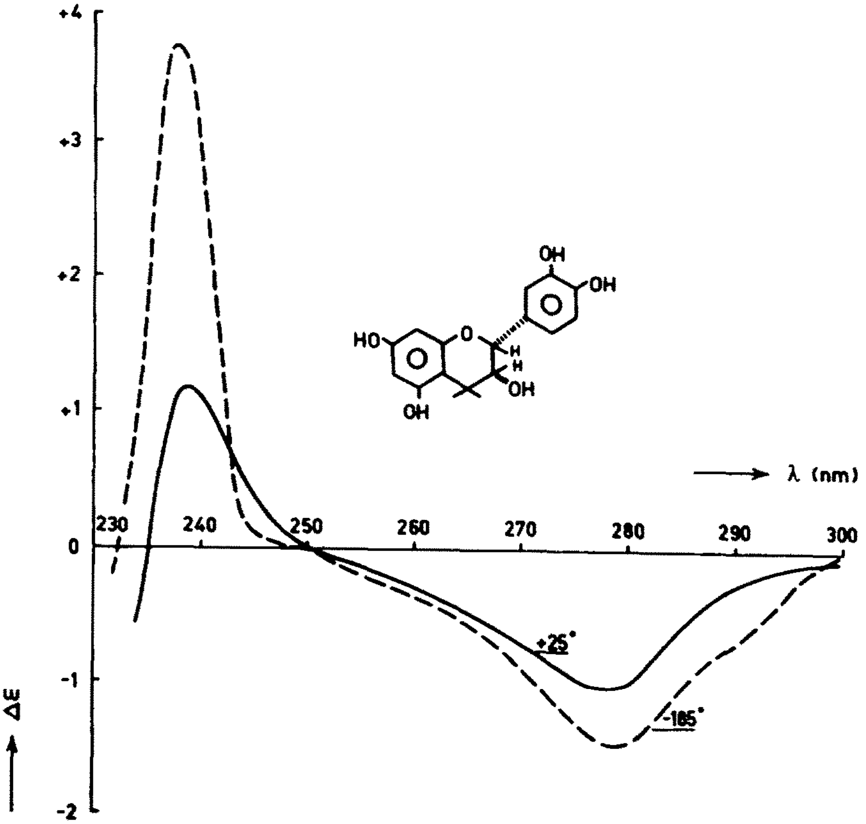


FIG 4. CD spectrum of (−) epicatechin in EPA at 25° and −185°.

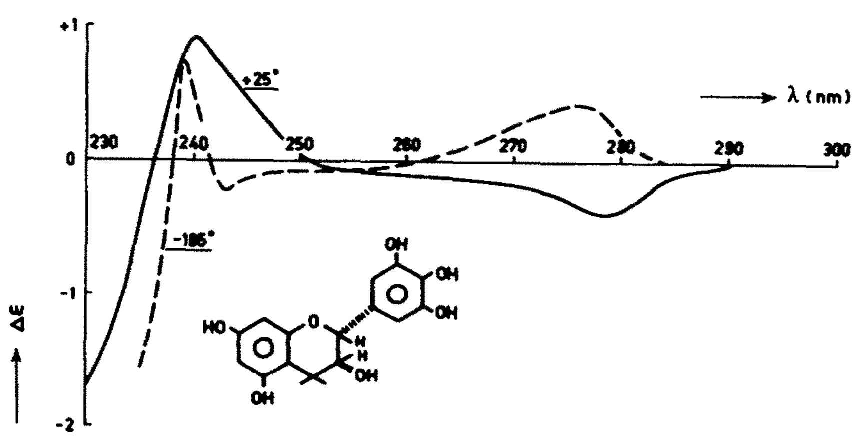


FIG 5. CD spectrum of (−) epigallocatechin in EPA at 25° and −185°.

in the $'L_b$ region (Table 2. compounds 1. 2. 7 and 8). the shorter wavelength band shows the larger temperature dependence. For this reason we ascribe the longer wavelength band to chromophore A and the shorter wavelength band to chromophore B—a similar allocation of bands to individual aromatic chromophores in a related compound has been made earlier[8]—and we conclude that an R-configuration at C_2 (**1a**) gives rise to a negative CD band for chromophore A (compounds 1–6) and an S-configuration at C_2 (**1b**) to a positive one (compounds 7 and 8). This is opposite to the relationship found in the tetralins.[6] It must be noted. however. that the C_{2v} symmetry of the tetralin chromophore has been lost in the chroman chromophore. Moreover. an $n \rightarrow \pi^*$ transition from the p_z-orbital of the chroman oxygen to the π^*-orbital of the fused benzene ring might be involved.*

For the interpretation of the band arising from chromophore B. it must be realized that two asymmetric centres (at C_2 and C_3) may contribute. Because the substitution pattern of chromophore B is not identical in all compounds. the contributions of an S- or R-configuration cannot be calculated exactly. A qualitative interpretation, however, can be given in the following terms: The shorter wavelength band is negative and of relatively low intensity for compounds 1–6. A decrease in temperature changes the sign

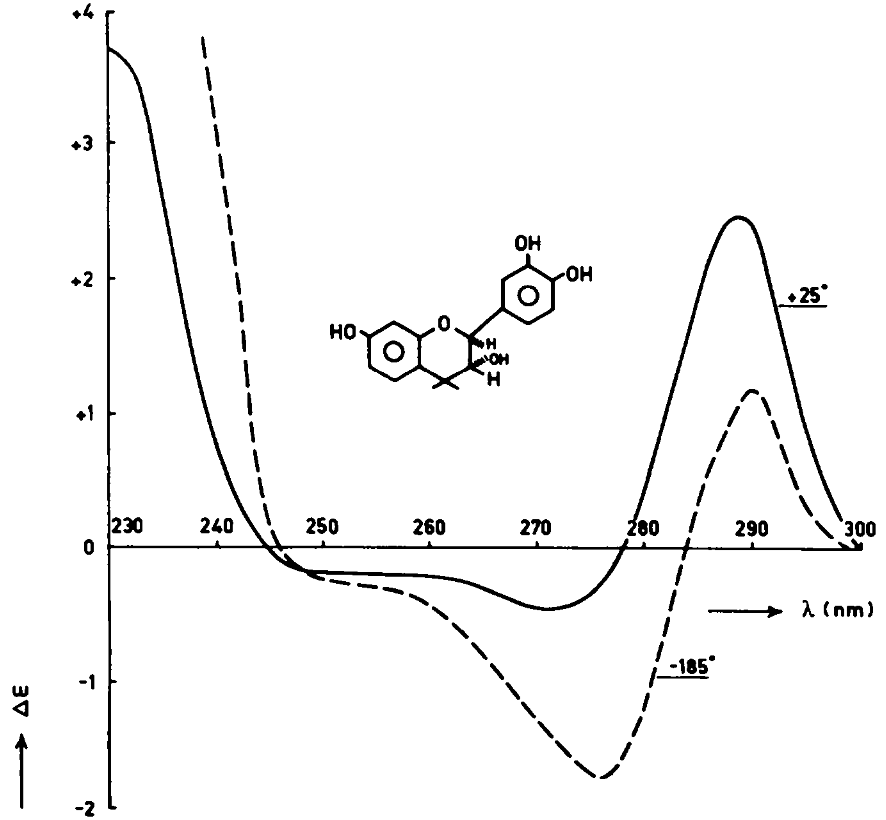


Fig 6. CD spectrum of (+) fisetinidol in EPA at 25° and −185°.

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* We thank Dr. L. Verbit for this suggestion.

in compounds 1, 2, 3 and 6. Apart from compound 6, they have the S-configuration at C_3 and also show a lower intensity than compounds 4 and 5. It appears that an S-configuration at C_3 contributes positively to the CD band of chromophore B, and an R-configuration negatively. The contribution of the C_2 asymmetric centre to the CD band of chromophore B is apparently negative for the R-configuration (compounds 1–6) and positive for the S-configuration (compounds 7 and 8). In this way the behaviour of the band arising from chromophore B in compounds 7 and 8 can be explained as follows.

In compound 7 the S-configuration at C_2 gives a positive contribution which is overcompensated by the negative contribution of the R-configuration at C_3. In compound 8 both contributions are positive. At low temperature, apparently, the contribution of C_2 changes the sign to negative, analogously to the situation in compounds 1, 2 and 3 with configuration R at C_2, where at low temperature the contribution of C_2 changes from negative to positive. In compounds 4 and 5 the changes in the relative contributions upon lowering the temperature are more or less compensated.

It remains to be explained why compound 6, which is stereochemically identical and structurally closely related to compound 5, shows such a different CD spectrum at low temperature. In this respect it must be noted that the CD spectra consist of overlapping bands of different signs. If the chromophores of compounds 5 and 6 absorb at different wavelengths, the appearance of the spectrum may be quite different. Another point might be that the substitution pattern of the freely rotating aromatic chromophore directly influences the sign of the $'L_b$ CD band as it does in mandelic acids.[3]

$'L_a$ *transition.* The CD bands of the $'L_a$ transition cannot be observed distinctly in every case. Generally speaking, however, the sign in the CD spectrum at about 240 nm is opposite to that in the $'L_b$ region.

EXPERIMENTAL

Materials. (+) Catechin hydrate (pure) and (−) epicatechin (pure) were purchased from Koch-Light Ltd, Colnbrook, England. (−) Epigallocatechin was isolated from green tea.[9] Samples of other compounds were gifts.

CD measurements were carried out on a Jouan Dichrograph 185^{II} with a Jouan low-temperature accessory.

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