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UTILIZATION OF THE CHIROPTICAL SPECTROSCOPIES FOR THE STRUCTURE ELUCIDATION OF FLAVONOIDS AND RELATED BENZOPYRAN DERIVATIVES†

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Abstract

Chiroptical stpectroscopies, mainly the optical rotatory dispersion (ORD) and the circular dichroism (CD) played an important role for the structure elucidation of various naturally occurring organic compounds, with the flavonoids among them, during the last four decades. The aim of the present review article is to provide characteristic examples on the utilization of these techniques in the flavonoid chemistry.

Introduction

Flavonoids are well known natural products of the plant kingdom [1-3]. Several groups of the naturally occurring flavonoids, e.g. flavans, flavanones, isoflavans, isoflavanones, etc. are chiral molecules and are isolated in enantiopure form as optically active substances. Numerous flavonoid glycosides are optically active plant products as well. For this reason, the chiroptical techniques are very convenient and efficient tools

†Dedicated to the late Prof. Dr. Günther Snatzke on the occasion of his 70th birth anniversary

for their structure elucidation mainly for the determination of the absolute configuration of their stereogenic centres.

Of the chiroptical techniques, the optical rotatory dispersion (ORD) was utilized first by using the commercially available spectropolarimeter manufactured and marketed by the Rudolph company since 1953. According to Djerassi [4], this instrument "undoubtedly represented the prince who awoke the sleeping beauty of the rotatory dispersion". This prince offered a new opportunity for the flavonoid chemistry by the determination of the absolute configuration of the optically active flavonoids (vide infra). However, because of an easier and more convenient correlation of the structure or stereochemistry and the circular dichrosim (CD) spectra if compared to the ORD properties of a particular molecule, the circular dichroism (CD) spectroscopy came to the front since the middle of the sixties [5]. Owing to the fact that a successful measurement of a CD spectrum requires less than one milligram substance, this technique is especially convenient and helpful method for the structure elucidation of naturally occurring optically active organic compounds. Reference substances with established absolute configuration or the so-called empirical rules like the octant rule [6] and sector rules [7] help to correlate the stereochemistry and the chiroptical properties of optically active flavonoids.

In our present review article, we plan to summarize the most important results of the utilization of the chiroptical spectroscopies in the flavonoid chemistry. One of the aims of this account is to direct the attention of chemists engaged in optically active flavonoids to the utility of the chiroptical techniques.

Flavanones

Since flavanones (2-phenylchromanones) are the first representatives of the known naturally occurring optically active flavonoids, it seems to be expedient to start the discussion of the application of the so-called chiroptical techniques in the flavonoid chemistry with the flavanones. Optically active flavanones, *viz.* (-)-matteucinol and (-)-demethoxymatteucinol were isolated by Fujise and Kubota [8] already in 1934. Data

relating to the determination of the absolute configuration of the stereogenic centre of optically active flavanones were, however, published only in 1960. The absolute configuration of (-)-hesperetin (**1**), (-)-liquiritigenin (**2**) and (+)-sakuranetin (**3**) (Fig. 1)

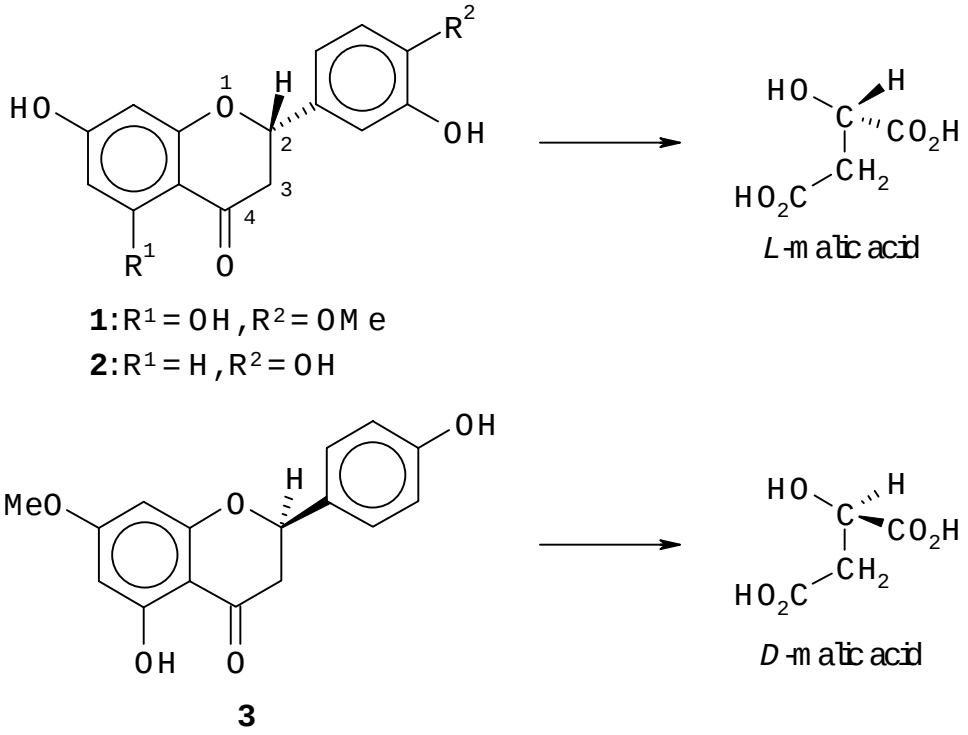


Figure 1

was established by chemical degradation by Arakawa and Nakazaki [9]. These compounds were subjected to ozonization and subsequent oxidation in order to obtain malic acid of known absolute configuration (Fig. 1, L-malic acid from the (-)-flavanones **1** and **2** and D-malic acid from the (+)-flavanone **3**) which gave unequivocally the absolute configuration of the investigated flavanones. Moreover, these results can be used as reference data for the determination of the absolute configuration of other flavanones with the help of chiroptical spectroscopies, e.g. optical rotatory dispersion (ORD) or circular dichroism (CD).

First utilization of a chiroptical spectroscopic method, *viz.* optical rotatory dispersion (ORD) in the flavonoid chemistry was published by Gaffield and Waiss [10]. They reported that (-)-flavanones **1** and **2** with *2S* absolute configuration [8] showed a

positive Cotton effect between 320-330 nm due to the n→π* transition. However, the dextrorotatory (+)-sakuranetin (**3**) of *2R* absolute configuration displayed a negative Cotton effect in the same wavelength region assigned to an n→π* transition as well. Circular dichroism (CD) spectra of flavanones including compounds **1**-**3** were measured fist by Arakawa and Masui [11]. Later, the CD spectra of a series of naturally occurring flavanones were studied by Gaffield [12] and the CD spectra of the unsubstituted flavanone enantiomers by Snatzke et al. [13], respectively. Very recently, Kojima et al. [14] applied the CD spectroscopy for the determination of the absolute configuration of optically active flavanones isolated from *Iris tenuifolia*. All these CD measurements reveal that the sign of the n→π*-band CD maximum of flavanones are independent on the substitution pattern of the aromatic rings. For this reason, the sign of the n→π*-band CD maximum can be utilized for the determination of the absolute configuration of the stereogenic centre of flavanones. Thus, the negative n→π*-band CD maximum proves the absolute configuration to be *2R*, while a positive sign of this CD maximum reveals a *2S* absolute configuration (Fig. 2). Of course, additional Cotton effects appear at shorter wavelengths, but it is not necessary to correlate their signs with the absolute

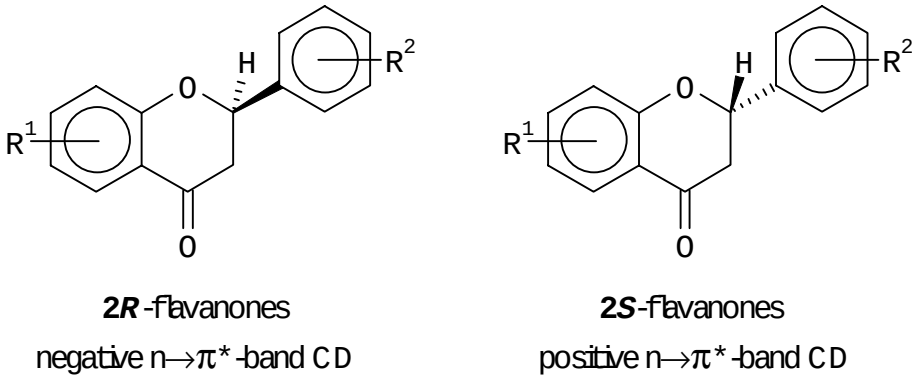


Figure 2

configuration of the molecule. Consideration of the sign of the n→π*-band CD is enough for this purpose. It is worth mentioning that Gaffield [10] attempted to apply the Snatzke's modified octant rule [15] for the prediction of the sign of the n→π*-band CD maximum as well.

Although it is not the aim of this review article to discuss the utility of the chiroptical techniques for related heterocyclic compounds with heteroatom other than oxygen, we mention that the CD spectroscopy was successfully applied for the determination of the absolute configuration of optically active 1-thioflavanones and the so-called "azaflavanones" by Antus et al. [16].

3-Hydroxyflavanones (dihydroflavonols) are well known and important natural products isolated from numerous plants [1-3]. Owing to their two stereogenic centres,

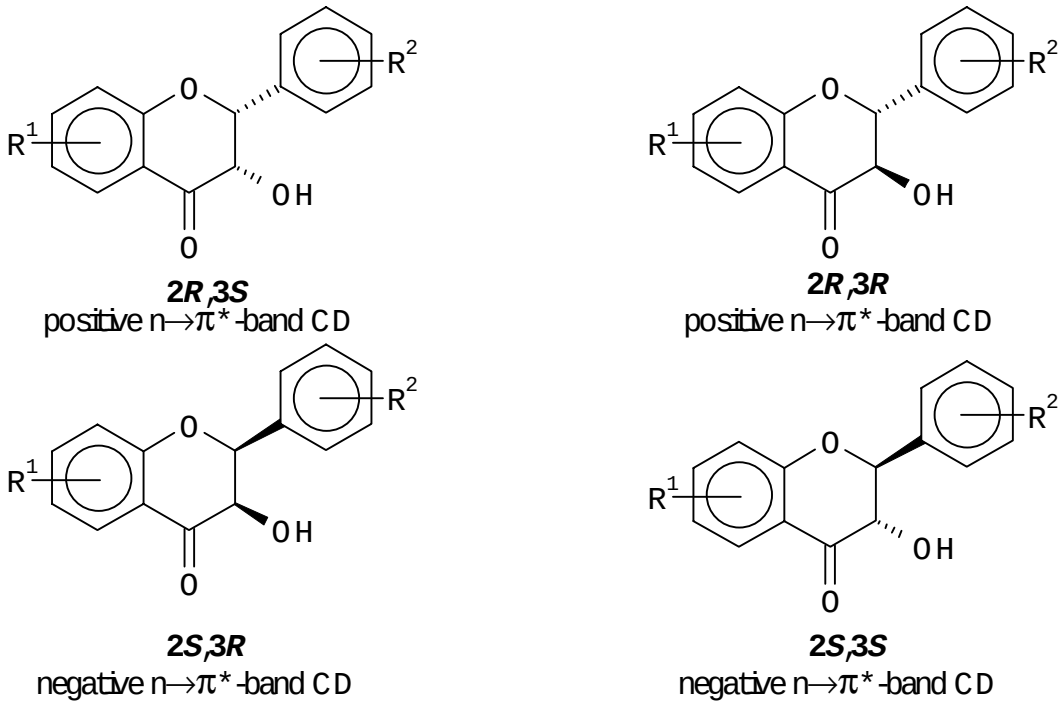


Figure 3

they can exist in four optically active stereoisomers (Fig. 3). CD spectroscopy was successfully used for the determination of their absolute configuration [10,12,14,17,18]. A positive n→π*-band CD maximum in the 330-340 nm wavelength region proves the *2R* corfiguration for both the *cis* and *trans* isomers. However, a negative CD maximum belonging to a similar wavelength value reveals a *2S* absolute configuration for the other two stereoisomers. Configuration at the C-3 atom can then be deduced from these data (Fig. 3). As in the case of flavanones (vide supra), although several CD maxima are generally measured, it is enough to use the sign of the n→π*-band CD maximum around

330-340 nm to determine the absolute configuration of both stereogenic centres of the 3-hydroxyflavanones.

Isoflavanones

Recently, opticaly active isoflavanones (3-phenylchromanones) have also been isolated from various plant sources [19,20]. First utilization of a chiroptical spectroscopy for synthetic isoflavanones was described by Farkas et al. [21] in 1969. They measured the ORD spectra of some isoflavanone glycosides and determined the absolute configuration of the aglycone of the (-)-5-acetoxy-7-methoxy-4'-(tetra-O-acetyl-β-D-glucosyloxy)isoflavanone by this method. CD spectroscopy was used to determine the absolute configuration of the recently isolated isoflavanones [19,20]. A positive $n\rightarrow\pi^*$-band CD maximum in the 325-352 nm wavelength region reveals a *3R* absolute configuration on the basis of the modified octant rule [15] (Fig. 4).

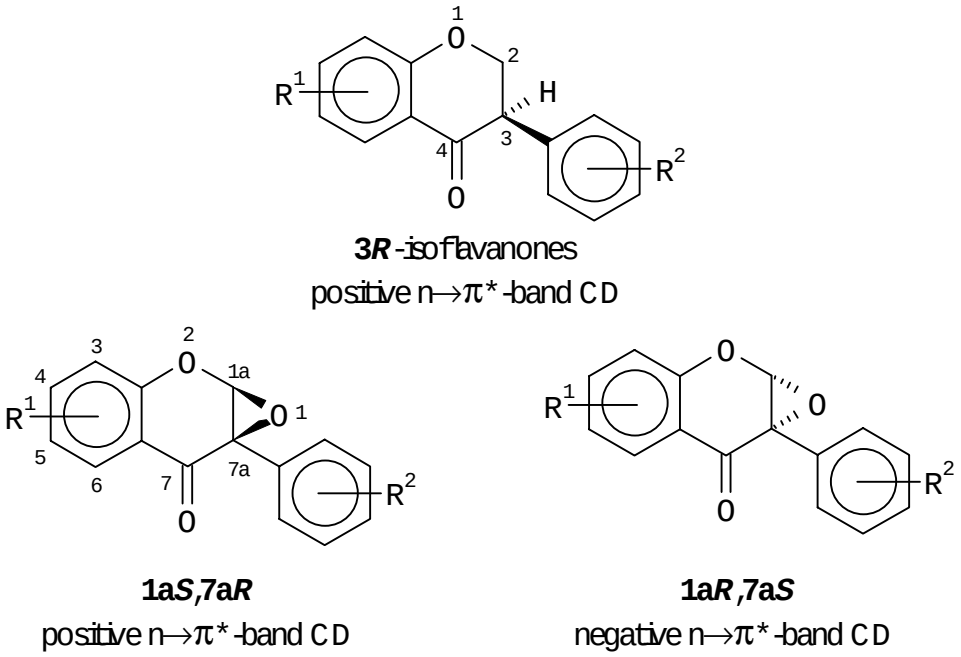


Figure 4

A newest development in the application of the CD spectroscopy for the determination of the absolute configuration of isoflavanone derivatives is our own study

on optically active isoflavone epoxides [22] (Fig. 4). It has been found that a negative $n\rightarrow\pi^*$ CD maximum of the (-)-compounds uniquivocally proves the *1aR,7aS*, while a positive sign of the same CD band of their (+)-enantiomers reveals the *1aS,7aR* absolute configuration by using the Snatzke's "inverse octant rule" [15]. These results are in full harmony with those determined by X-ray diffraction analysis [23]. Thus, it can be concluded that in the case of the optically active isoflavanones or 3,4-epoxyisoflavanones the knowledge of the sign of their $n\rightarrow\pi^*$-band CD maximum is enough to determine the absolute configuration of their stereogenic centres by using the modified octant rule or the inverse octant rule both introcuded by Snatzke [15].

Flavans

In the present review two groups of flavan derivatives, *viz.* 3-hydroxyflavans and 4-substituted flavans are discussed, the available CD data of which make possible some general considerations.

3-Hydroxyflavans

The stereochemical problems of the 3-hydroxyflavans (catechins and epicatechins) have been summarized in a detailed review article [24]. The absolute configuration of the stereogenic centres of these flavan derivatives were generally determined either by using the Prelog's atrolactic acid method [25] or by azonolysis [26] prior to the availability of the CD spectroscopy. From the early seventies the CD spectroscopy has been successfully used for this purpose as well [27-31].

The absorption bands of these chromophores are found in two regions: around 280 nm ($^1B_{2u}$ transition) and at about 240 nm ($^1B_{1u}$ transition). In their CD spectra Cotton effects are expected in these two regions. The CD spectra of a series of 3-hydroxyflavans at 25 and -185 °C have been measured by Korver and Wilkins [27]. According to their study, the sign of the Cotton effect due to the $^1B_{2u}$ transition is determined by the chirality of the hetero ring, which in turn is connected with the absolute configuration of the stereogenic centre at position 2 (Fig. 5). Thus, the *2R* absolute configuration gives rise to a negative CD band, while a *2S* absolute

configuration to a positive one [27]. The contribution of the C-3 stereogenic centre to this CD band is small. On the basis of low temperature measurements they managed to evaluate the contribution of the phenyl group at the C-2 atom as well. Therefore, it can be concluded that the CD spectroscopy can be advantageously utilized for the determination of the absolute configuration of the 3-hydroxyflavan derivatives.

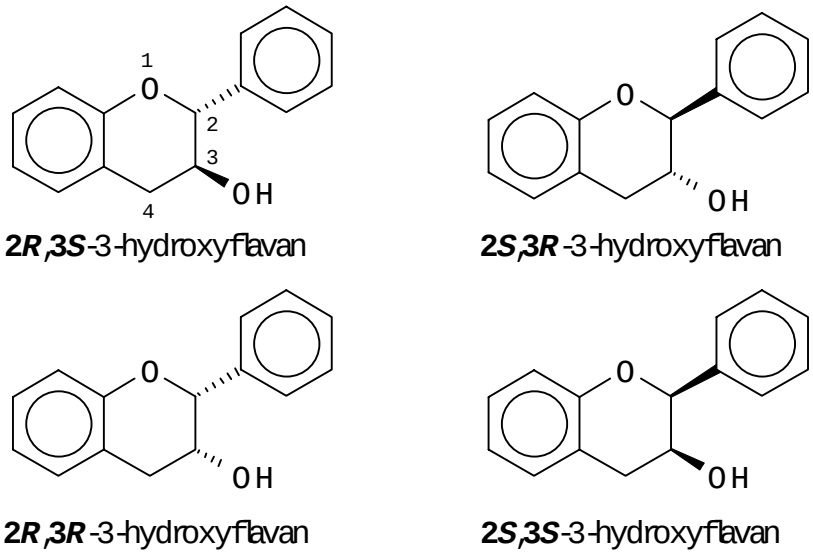


Figure 5

4-Substituted flavans

A series of 4-substituted *cis*- and *trans*-flavan derivatives have been prepared by Bognár et al. [32-36] by the optical resolution and subsequent chemical transformations of 4-amino- and 4-hydroxyflavans. The CD spectra of these compounds have been studied by Snatzke et al. [13]. The absolute configuration of the two stereogenic centres of these compounds result from their conversion into flavanone enantiomers of known absolute configuration [33]. Moreover, the CD spectroscopy could also be utilized for the determination of the conformation of these 4-substituted flavans. The evaluation of the second- and third-sphere contributions revealed a *sofa* conformation for both their *cis*- and *trans*-isomers [13] (Fig. 6). Sofa conformation has also been suggested by Korver and Wilkins [27] in the case of 3-hydroxyflavans. A sector rule for the

estimation of the influence of the 4-substituent has also been proposed by Snatzke et al. [13].

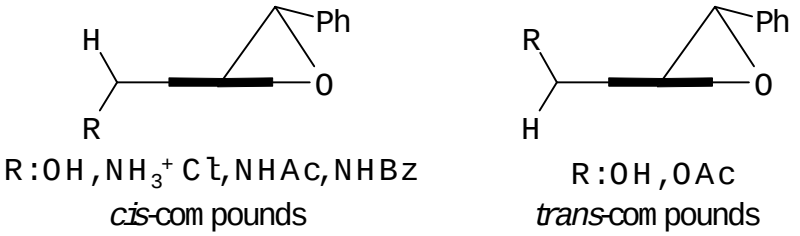
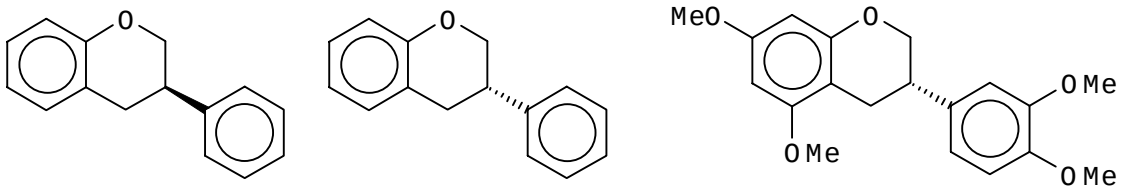


Figure 6

Isoflavans

ORD and CD measurements have been used for the determination of the absolute configuration of naturally occurring isoflavan derivatives [37-41]. Asolute configuration of the (*3S)*-5,7,3',4'-tetramethoxyisoflavan (**4**) (Fig. 7) was established by its chemical correlation with *S*-(-)-methylsuccinic acid [42]. This compound served as a reference for the determination of the absolute configuration of other optically active isoflavans by means of chiroptical methods. The ORD spectra of the *3S*-isoflavans showed a negative Cotton effect in the 260-300 nm region [37]. In the CD spectra of the *3S*-compounds around 280 nm also a negative maximum, while at about 230-240 nm a positive one were measured. The sign was opposite in both regions for the *3R*-enantiomers. On all these bases, it can be concluded that the chiroptical techniques can be beneficially used for the determination of the absolute configuration of optically active isoflavans as well (Fig. 7).



3*R*-isoflavan **3*S*-isoflavan** **4**

Figure 7

Flavone and isoflavone glycosides

Natural flavones and isoflavones are frequently present in their plant sources attached to mono- or oligosaccharides [1-3]. Both the C-glycosides and O-glycosides of these two types of flavonoids have been isolated from a wide variety of plants [1-3]. Owing to their sugar component, all these natural products are optically active compounds making possible the utilization of the chiroptical techniques for their structure elucidation. Herein we provide some characteristic examples for such application of the ORD and CD spectroscopies.

C-Glycosylflavones

The CD spectra of 6- and 8-glycosylflavones (Fig. 8) have been investigated by Gaffield et al. [43,44]. Their studies prove that the sign of the Cotton effect at 250-275 nm depends upon the position of the C-glycosyl residue on the flavone if the sugar belongs to the D-series and the glycosidic linkage is β. In this region all the 6-C-glycosylflavones displayed a positive, and the 8-C-glycosylflavones a negative Cotton effect. On this basis the CD spectroscopy appears to be a sensitive method for the differentiation of the 6- and 8-C-glycosylflavones.

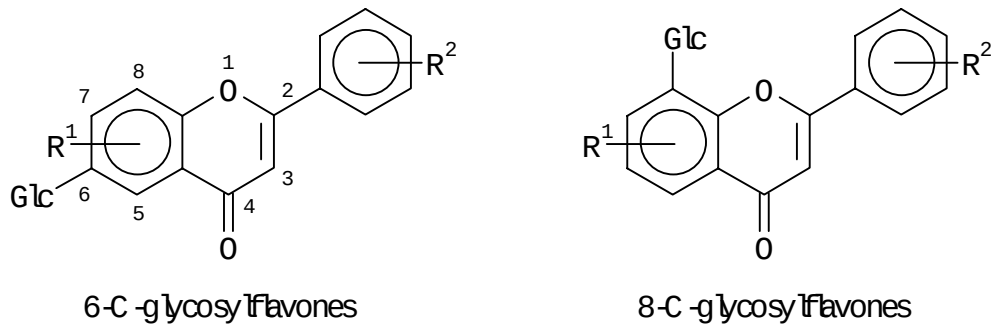


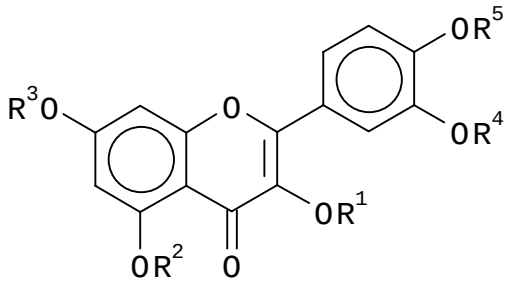
Figure 8

In view of these findings attempts have been made to use the CD for the differentiation of O-glycosylflavones and O-glycosylisoflavones as well. Prior to the discusssion of the chiroptical properties of the O-glycosylflavones and the O-glycosylisoflavones, CD properties of the simple phenyl glycosides should be mentioned.

According to detailed investigations, both $^1B_{2u}$ and $^1B_{1u}$ CD maxima are negative for phenyl β-D-glycosides and positive for the α-anomers [45,46]. This relationship, however, is not necessarily true for glycosides with a more complicated chromophore, e.g. flavone or isoflavone molecules.

O-Glycosylflavones

CD spectra of few O-glycosylflavones are available in the literature [47,48], but the published data do not make possible the establishment of such a relationship between the chiroptical properties and the site of the glycosidic linkage as in the case of C-glycosylflavones [43,44]. To improve these informations, we decided to investigate a systematic series of flavone glycosides, *viz.* the quercetin glucosides, where the aglycone (3,5,7,3',4'-pentahydroxyflavone), the sugar component (D-glucose) and the glycosidic linkage (β) are the same [49] (Fig. 9). Compounds under study (**5**-**12**) were synthesized by Farkas et al. [50-52].



5-12

5: R^1 = Glu, R^2 = R^3 = R^4 = R^5 = H
6: R^1 = R^3 = R^4 = R^5 = H, R^2 = Glu
7: R^1 = R^2 = R^4 = R^5 = H, R^3 = Glu
8: R^1 = R^2 = R^3 = R^4 = H, R^5 = Glu
9: R^1 = R^4 = Glu, R^2 = R^3 = R^5 = H
10: R^1 = R^5 = Glu, R^2 = R^3 = R^4 = H
11: R^1 = R^3 = Glu, R^2 = R^4 = R^5 = H
12: R^1 = R^2 = R^4 = H, R^3 = R^5 = Glu

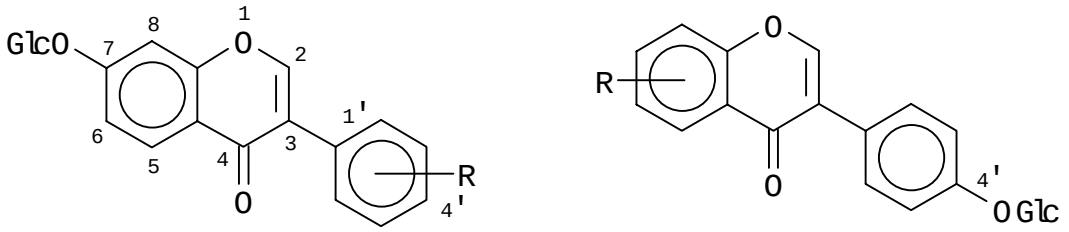
Glu: β-D-glucosyl

Figure 9

A negative CD maximum was observed for all compounds between 340 and 375 nm which seems to belong to the $n \rightarrow \pi^*$ transition. The magnitude of this maximum somewhat alters with the position of the glycosidic linkage. Around 250 nm a characteristic intense positive band was measured for the 3-O-glucoside and a negative one for the 5- and 4'-O-glucosides, respectively. 7-Glucosylquercetin, in which the free rotation of the sugar component is not hindered, exhibited only one negative maximum at 375 nm. The CD spectra of the quercetin diglucosides displayed a superposition of the CD spectra of the corresponding two monoglucosides.

O-Glycosylisoflavones

The sugar component of naturally occurring O-glycosylisoflavones known so far are attached to the aglycone through the hydroxyl group either at C-7 or C-4' of isoflavone by a β-linkage [1-3] (Fig. 10). The position of the glycosidic linkage has been elucidated by means of chemical degradation or by NMR spectroscopy.



negative n→π*-band CD positive n→π*-band CD

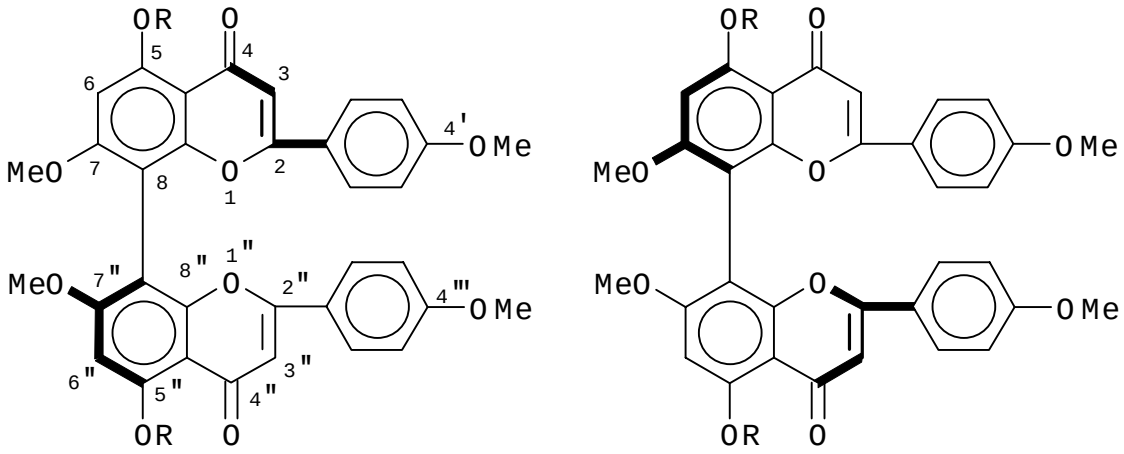
Figure 10

The CD spectra [48,53] of a series of synthetic 7-β-glycosyloxyisoflavones [54-56] and natural 4'-β-glycosyloxyisoflavones have been measured. These measurements revealed that the sign of the CD maximum due to the $n \rightarrow \pi^*$ transition (330-350 nm) is dependent on the site of the glycosidic linkage: it is negative for 7-β-glycosyloxyisoflavones and positive for 4'-β-glycosyloxyisoflavones (Fig. 10). These findings refer only to such isoflavone O-glycosides where a D-sugar is attached to the aglycone by a β-linkage. Therefore, the CD spectroscopy can serve as a simple and

convenient method for the elucidation of the site of the glycosidic linkage of newly isolated natural isoflavone glycosides.

Biflavones

First representatives of the optically active biflavones, the (-)-5,5"-dihydroxy-4',4"',7,7"-tetramethoxy-8,8"-biflavone (Fig. 11 (-)-**13**) was isolated from *Araucaria cunninghamii* and *A. cooki* in 1968 [57]. Later, several other optically active biflavones, *viz.* cupressuflavones [57-59], amentoflavones [60,61] and agathisflavones [62] have also been isolated from various plant sources. Their chirality is due to the atropisomerism of the biflavone moiety. Recently, synthesis of optically pure biflavones has also been achieved [63-65]. However, the first data for the determination of their absolute configuration were published only in 1995 by Lin et al. [63]. X-ray diffraction analysis of the (+)-bis-5,5"-camphonate of (+)-**13** (Fig. 11) revealed an *aR* absolute configuration by correlation with the known configuration of the camphorsulfonate group. This compound served as a reference for the determination of the absolute configuration of other optically active biflavones by CD spectroscopy [63-65]. By means of a combined utilization of the X-ray diffraction analysis and the CD spectroscopy Lin et al. [63] assigned an *aR* configuration to the (+)-biflavones and and *aS* one to their (-)-enantiomers, whereas Harada et al. [59,65] an *aR* configuration to compound (-)-**13** (Fig. 11) on the basis of the same CD data. This contradiction has not hitherto been solved by the reinvestigation of the absolute configuration of the optically active biflavones.



R = H : (+)-**13**
R = Me: (+)-**14**

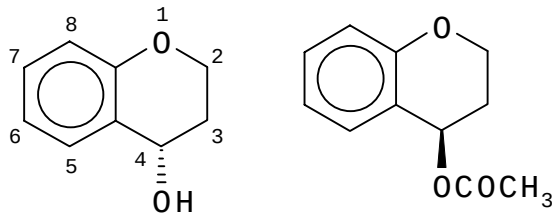
R = H : (-)-**13**
R = Me: (-)-**14**

Figure 11

Other benzopyran derivatives

4-Hydroxychromans

Optically active 4-hydroxychromans have been prepared by kinetic resolution of (±)-chroman-4-ols by microbial lipases using vinyl acetate as acyl donor [66,67]. Under these reaction conditions (+)-chroman-4-ols were converted into their acetates and the (-)-chroman-4-ols remained unchaged materials in high enantiomeric excess (Fig. 12). The absolute configuration of these optically active chroman derivatives has been determined by CD spectroscopy [68] either by using the so-called helicity rule [13,16] or by measuring the exciton-coupled CD spectra of the 4-benzoyloxychromans [68]. These measurements revealed a *4R* configuration to the (+)-4-acetoxychromans and *4S* one to the (-)-4-hydroxychromans (Fig. 12).

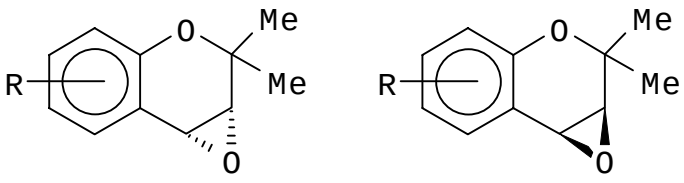


4S ***4R***

Figure 12

2,2-Dimethyl-3,4-epoxychromans

Optically active 2,2-dimethyl-3,4-epoxychromans have been synthesized by several research groups [69-77] by the catalytic enantioselective epoxidation of 2,2-dimethyl-2*H*-chromenes by using Mn(III)salen catalysts. However, no direct determination of their absolute configuration has been published prior to our paper [77] in 1996. Jacobsen et al. [78] described the measurement of the CD spectra of some optically active 2,2-disubstituted 3,4-epoxychromans, but without mentioning the correlation of the CD data with the configuration of their epoxides. In our own study [77], absolute configuration of one optically active 2,2-dimethyl-3,4-epoxychroman was determined by X-ray diffraction analysis which then could be used as reference substance for the CD study of the related epoxides. Thus, the (+)-compounds proved to be the *3R,4R*-enantiomers and the (-)-ones are the *3S,4S*-enantiomers determined by CD measurements (Fig. 13). These CD data [77] may serve as reference for the configurational assignment of related 3,4-epoxychromans by CD spectroscopy or even on the basis of the sign of their specific rotation.



3R,4R ***3S,4S***

Figure 13

3,4-Dihydroxy-2,2-dimethylchromans

All four optically active stereoisomers of the 3,4-dihydroxy-2,2-dimethyl-7-methoxychroman (Fig. 14) were synthesized by Jennings [79]. Absolute configuration of these compounds were determined by the CD measurement of their bis-p-N,N-dimethylaminobenzoate by means of the exciton chirality method [80].

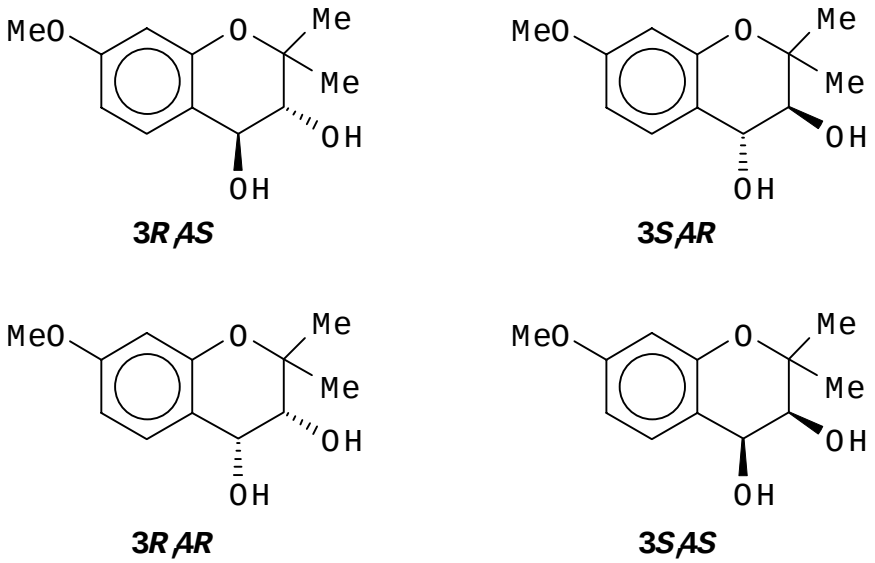


Figure 14

In summary, the present review is aimed to show the utility of the chiroptical spectroscopic methods through the eyes of a synthetic chemist who looks for tools to determine the stereochemistry of optically active flavonoids. Theoretic backgrounds of chiroptical techniques discussed here are, therefore, omitted.

Acknowledgement

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References

1. T. A. Geissman, *The Chemistry of Flavonoid Compounds*, Pergamon Press, Oxford, 1962.
2. J. B. Harborne, T.J. Mabry, J. Mabry, *The Flavonoids*, Chapman and Hall, London, 1975.
3. J.B. Harborne, *The Flavonoids: Advances in Research science 1980*, Chapman and Hall, London, 1988.
4. C. Dejerassi, *Optical Rotatory Dispersion*, McGraw-Hill Book Company, Inc., New York, 1960.
5. G. Snatzke, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry*, Heyden and Son Ltd, London, 1967.
6. W. Moffit, R.B. Woodward, A. Moscowitz, W. Klyne, C. Djerassi, *J. Am. Chem. Soc.* **1961**, *83*, 4013-4018.
7. F. Ciardelli, P. Salvadori, *Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism*, Heyden and Son Ltd, London, 1973.
8. S. Fujise, T. Kubota, *Ber Dtsch. Chem. Ges.* **1934**, *67*, 1905-1908.
9. H. Arakawa, M. Nazaoki, *Liebigs Ann. Chem.* **1960**, *636*,111-117.
10. W. Gaffield, A. C Waiss, Jr., *J. Chem. Soc., Chem. Commun.* **1968**, 29-31.
11. H. Arakawa, Y. Masui, *Bull. Chem. Soc. Jpn.* **1969**, *42*, 1452-1453.
12. W. Gaffield, *Tetrahedron* **1970***26*, 4093-4108.
13. G. Snatzke, F. Snatzke, A.L. Tőkés, M. Rákosi, R. Bognár, *Tetrahedron* 1973, *29*, 909-912.
14. K. Kojima, P. Gombosurengyin, P. Ondognyi, D. Begzsurengyin, O. Zevgeegyin, K. Hatano, Y. Ogihara, *Phytochemistry* **1997**, *44*, 711-714.
15. G. Snatzke, *Tetrahedron* **1965**, *21*, 413-448.
16. S. Antus, E. Baitz-Gács, J. Kajtár, G. Snatzke, A. L. Tőkés, *Liebigs Ann. Chem.* **1994**, 497-502.
17. W. Gaffield, *Chem. Pharm. Bull.* **1996**, *44*, 1102-1103.
18. H. van Rensburg, P.S. van Heerden, B.C.B. Bezuidenhoudt, D. Ferreira, *Tetrahedron* **1997**, *53*, 14141-14152.
19. G.B. Russell, *Aust. J. Chem.* **1997**, *50*, 333-336.
20. C. Galeffi, P. Rasoanaivo, E. Federici, G. Palazzino, M. Nicoletti, B. Rasondratovo, *Phytochemistry* **1997**, *45*, 189-192.
21. L. Farkas, M. Nógrádi, S. Antus, Á. Gottsegen, *Tetrahedron* **1969**, *25*, 1013-1019.
22. A. Lévai, W. Adam, R.T. Fell, R. Gessner, T. Patonay, A. Simon, G. Tóth, *Tetrahedron*, in press.
23. W. Adam, R.T. Fell, A. Lévai, T. Patonay, K. Peters, A. Simon, G. Tóth, *Tetrahedron:Asymmetry* **1998**, *9*, 1121-1124.
24. K. Weinges, W. Bähr, W. Ebert, K. Göritz, H.D. Marx, *Fortschr. Chem. Org. Naturst.* **1969**, *27*, 158-260.
25. A.J. Birch, J.W. Clark-Lewis, A.V. Robertson, *J. Chem. Soc.* **1957**, 3586-3594.
26. E. Hardegger, H. Gempeler, H. Züst, *Helv. Chim. Acta* **1957**, *40*, 1819-1822.
27. O. Korver, C.K. Wilkins, *Tetrahedron* **1971**, *27*, 5459-5465.
28. R.S. Thompson, D. Jacques, E. Haslam, R.J.N. Tanner, *J. Chem. Soc., Perkin Trans. 1* **1972**, 1387-1399.
29. D.W. Engel, M. Hattingh, H.K.L. Hundt, D.G. Roux, *J. Chem. Soc., Chem. Commun.* **1978**, 695-696.
30. M.W. Barrett, W. Klyne, P.M. Scopes, A.C. Fletcher, L.J. Porter, E. Haslam, *J. Chem. Soc., Perkin Trans. 1* **1979**, 2375-2377.
31. H. van Rensburg, P.S. van Heerden, D. Ferreira, *J. Chem. Soc., Perkin Trans. 1* **1997**, 3415-3421.
32. R. Bognár, A. L. Tőkés, M. Rákosi, *Magy. Kém. Foly.* **1970**, *76*, 271-274.
33. M. Rákosi, A.L. Tőkés, R. Bognár, *Tetrahedron Lett.* **1970**, 2305-2308.
34. R. Bognár, J.W. Clark-Lewis, A.L. Tőkés, M. Rákosi, *Aust. J. Chem.* **1970**, *23*, 2015-2025.
35. R. Bognár, A.L. Tőkés, M. Rákosi, *Acta Chim. Acad. Sci. Hung.* **1973**,*79*, 357-363.
36. M. Rákosi, A.L. Tőkés, R. Bognár, *Acta Chim. Acad. Sci. Hung.* **1975**,*87*, 161-164.
37. K. Kurosawa, W.D. Ollis, B.T. Redman, I.O. Sutherland, O.R. Gottlieb, H.M. Alves, *J.Chem. Soc., Chem. Commun.* **1968**, 1265-1266.
38. L. Verbit, J.W. Clark-Lewis, *Tetrahedron* **1968**, *24*, 5519-5527.
39. D.M.X. Donnelly, P.J. Keenan, J.P. Prendergast, *Phytochemistry* **1973**, *12*, 1157-1161.
40. M.D. Woodward, *Phytochemistry* **1980**, *19*, 921-927.

41. S. Yahara, R. Saijo, T. Nohara, R. Kouishi, J. Yamahara, T. Kawasaki, K. Miyahara, *Chem. Pharm. Bull.* **1985**, *33*, 5130-5133.
42. J.W. Clark-Lewis, *Rev. Pure Appl. Chem.* **1962**, *12*, 96-116.
43. W. Gaffield, R.H. Horowitz, *J. Chem. Soc., Chem. Commun.* **1972**, 648-649.
44. W. Gaffield, R.M. Horowitz, B. Gentili, J. Chopin, M.L. Bouillant, *Tetrahedron* **1978**, *34*, 3089-3096.
45. T. Sticzay, C. Peciar, S. Bauer, A.L. Tőkés, A. Lévai, R. Bognár, *Chem. zvesti* **1974**, *28*, 90-94.
46. A. Lévai, A. Lipták, I. Pintér, G. Snatzke, *Acta Chim. Acad. Sci. Hung.* **1975,** *84,* 99-107.
47. W. Voelter, O. Oster, G. Jung, E. Breitmeier, *Chimia* **1971**, *25*, 26-27.
48. T. Sticzay, S. Bistricky, C. Peciar, A. Lévai, R. Bognár, *Chem. zvesti* **1975**, *29*, 538-543.
49. A. Lévai, *Flavonoids and Bioflavonoids Current Research Trends* (Eds. L. Farkas, M. Gábor, F. Kállay), Akadémiai Kiadó, Budapest, 1977, pp. 295-306.
50. L. Farkas, M. Nógrádi, B. Vermes, A. Wolfner, H. Wagner, L. Hörhammer, H. Kramer, *Chem. Ber.* **1969**, *102*, 2583-2587.
51. L. Farkas, B. Vermes, M. Nógrádi, *Chem. Ber.* **1972**, *105*, 3505-3510.
52. L. Farkas, B. Vermes, M. Nógrádi, *Chem. Ber.* **1974**, *107*, 1518-1525.
53. A. Lévai, R. Bognár, C. Peciar, S. Bistricky, T. Sticzay, *Acta Chim. Acad. Sci. Hung.* **1973**, *79*, 365-367.
54. R. Bognár, A. Lévai, *Acta Chim. Acad. Sci. Hung.* **1973**, *77*, 435-442.
55. A. Lévai, R. Bognár, *Acta Chim. Acad. Sci. Hung.* **1973**, *79,* 191-195.
56. A. Lévai, R. Bognár, *Acta Chim. Acad. Sci. Hung.* **1974**, *81*, 93-96.
57. M. Ilyas, J.N. Ushami, S.P. Bhatnager, W. Rahman, A. Pelter, *Tetrahedron Lett.* **1968**, 5515-5517.
58. M. Ilyas, O. Seligmann, H. Wagner, *Z. Natursforsch.* **1977**, *32c,* 206-209.
59. N. Harada, H. Ohno, H. Uda, M. Parveen, N.U. Kahn, B. Achari, P.K. Dutta, *J. Am. Chem. Soc.* **1992**, *114,* 7687-7692.
60. A. Pelter, R. Warren, K.K. Chexal, B.K. Handa, W. Rahman, *Tetrahedron Lett.* **1971**, *27*, 1625-1634.
61. R. Madhav, *Tetrahedron Lett.* **1969**, 2017-2019.
62. N.U. Kahn, M. Ilyas, W. Rahman, T. Mashima, M. Okigawa, N. Kawano, *Tetrahedron* **1972**, *28*, 5689-5694.
63. F. J. Zhang, G.Q. Lin, Q.C. Huang, *J. Org. Chem.* **1995**, *60*, 6427-6430.
64. G.Q. Lin, M. Zhong, *Tetrahedron Lett.* **1997**, *38*, 1087-1090.
65. A.Y. Li, T. Nehira, M. Hagiwara, N. Harada, *J. Org. Chem.* **1997**, *62*, 7222-7227.
66. M. Majerič, M. Gelo-Pujic, V. Sunjič, A. Lévai, P. Sebők, T. Tímár, *Tetrahedron:Asymmetry* **1995**, *6*, 937-944.
67. S. Ramadas, G.L.D. Krupadanam, *Tetrahedron:Asymmetry* **1997**, *8*, 3059-3066.
68. Zs. Majer, M. Hollósi, A. Lévai, M. Majerič, V. Sunjič, *Spectroscopy Lett.* **1995**, *28*, 1181-1190.
69. N.H. Lee, A.R. Muci, E.N. Jacobsen, *Tetrahedron Lett.* **1991**, *32,* 5055-5058.
70. A. Hatayama, N. Hosoya, R, Irie, Y. Ito, T. Katsuki, *Synlett* **1992**, 407-409.
71. N. Hosoya, R. Irie, T. Katsuki, *Synlett* **1993**, 261-263.
72. H. Sasaki, R. Irie, T. Katsuki, *Synlett* **1993**, 300-302.
73. R. Irie, N. Hosoya, T. Katsuki, *Synlett* **1994**, 255-256.
74. N. Hosoya, A. Hatayama, R. Irie, H. Sasaki, T. Katsuki, *Tetrahedron* **1994**, *50*, 4311-4322.
75. P. Pietikäinen, *Tetrahedron Lett.* **1995**, *36*, 319-322.
76. W. Adam, J. Jekő, A. Lévai, Cs. Nemes, T. Patonay, P. Sebők, *Tetrahedron Lett.* **1995**, *36*, 3669-3672.
77. W. Adam, J. Jekő, A. Lévai, Zs. Majer, Cs. Nemes, T. Patonay, L. Párkányi, P. Sebők, *Tetrahedron:Asymmetry* **1996**, *7*, 2437-2446.
78. S.L. Vander Velde, E.N. Jacobsen, *J. Org. Chem.* **1995**, *60*, 5380-5381.
79. R.C. Jennings, *Tetrahedron Lett.* **1982**, *23*, 2693-2696.
80. N. Harada, K. Nakanishi, *Accounts Chem. Res.* **1972**, *5*, 257-263.

Povzetek. Kirooptične spektroskopske metode, še posebej optična rotacijska disperzija (ORD) in cirkularni dihroizem (CD), so odigrale pomembno vlogo pri določanju strukture različnih naravnih organskih spojin. Namen članka je prikazati uporabo teh metod na na primeru flavonoidov.