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# Biflavonoids. Part 5: Structure and Stereochemistry of the First Bibenzofuranoids☆

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**Abstract**—The rare series of biflavonoids with benzofuranoid constituent units is extended by identification of (2*S*)-2-deoxymaesopsin-(2→7)-(2*R*)-maesopsin, its 2*R*(C):2*S*(F)-enantiomer, (2*R*)-2-deoxymaesopsin-(2→7)-(2*R*)-maesopsin, and its 2*S*(C):2*S*(F)-enantiomer. The collective use of chiral resolution, NMR, X-ray analysis, CD and molecular modeling permit definition of the absolute configuration of all four stereoisomers. © 2000 Elsevier Science Ltd. All rights reserved.

## Introduction

Our initial reports dealing with 2-benzyl-2-hydroxybenzofuranoid-type (maesopsin) **9** constituents from the heartwood of *Berchemia zeyheri* disclosed the existence of several unique natural flavanone[1–3] and isoflavanone-benzofuranoid[4,5] oligomers. A novel approach based on the collective utilization of chemical degradation, $^1$H NMR and CD spectroscopy in conjunction with computational methods permitted the definition of the structures and stereochemistry of these compounds. Continued investigations of the same source has now led to the identification of a further new class of benzofuranoid oligomers comprising two benzofuranoid moieties. These are represented by the diastereomeric pairs of enantiomers, **1/2** and **5/6**, both of which were resolved into their respective enantiomers by means of HPLC using a chiral stationary phase. The foundation established previously[2–5] together with the information obtained from a crystal structure of one of the diastereomers permitted the rationalization of the CD spectra in terms of the absolute configuration for each of the four diastereomers.

## Results and Discussion

Owing to the complexity of the mixture the compounds were identified as their permethylaryl ethers **3**, **4**, **7**, **8** following extensive fractionation via chromatography and confirmation of the absence of natural methoxy groups by $^1$H NMR, methylation with dimethyl sulphate under rigorously dry conditions and separation of the appropriate fractions. The additional chromatographic step offered by derivatization was a prerequisite for sample purity. The four biflavonoids each comprising two maesopsin[6] [2,4,6-trihydroxy-2-(4-hydroxybenzyl)benzofuran-3(2*H*)-one] **9** units were identified as 4,4′,6-tri-*O*-methyl-2-deoxymaesopsin-(2→7)-2,4,4′,6-tetra-*O*-methylmaesopsin **3/4** and their diastereomers **7/8**. To simplify the discussion the numbers **3** and **7** will be used to represent the enantiomeric pairs of the two dimers until the resolution of these into their enantiomers are discussed.

The $^1$H NMR spectra (Table 1) of these diastereomers, conspicuously devoid of signs of dynamic rotational isomerism about the interflavonoid bond, exhibit distinct features associated with the presence of two maesopsin derived moieties. Two AA′BB′ spin systems ($J$=9.0 Hz), an AB spin system ($J$=2.0 Hz) and a residual proton in the region ($\delta$ 5.79–7.21) are reminiscent of the four aromatic B-, E-, A- and D-rings, respectively, the residual proton being indicative of coupling to either 5-C or 7-C of the D-ring. Two methylene groups ($J$=14.0 Hz for both), a shielded methoxy resonance and six aromatic methoxy resonances represent the remainder of the protons. The absence of the second 2-OMe group suggests its replacement by the interflavonoid bond at 2-C(C).

☆ Part 4 is Ref. 4.

*Keywords*: biflavonoids; bibenzofuranoids; maesopsin: *Berchemia zeyheri*; circular dichroism.

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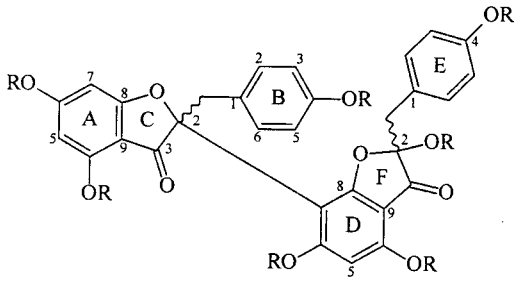
**Table 1.** $^1$H NMR data ($\delta_H$) of the 4,4′,6-tri-*O*-methyl-2-deoxymaesopsin-(2→7)-2,4,4′,6-tetra-*O*-methylmaesopsin **3/4** and 4,4′,6-tri-*O*-methyl-2-deoxymaesopsin-(2→7)-2,4,4′,6-tetra-*O*-methylmaesopsin **7/8**. Splitting patterns and *J* values (Hz) are given in parentheses

| Ring | H | (**3**), $CDCl_3$, 298 K | (**7**), $CDCl_3$, 298 K |
|---|---|---|---|
| A | 7-H | 5.93 (d, *J*=2.0 Hz) | 5.95 (d, *J*=2.0 Hz) |
| | 5-H | 5.79 (d, *J*=2.0 Hz) | 5.79 (d, *J*=2.0 Hz) |
| | 4-OMe | 3.80 (s) | 3.81 (s) |
| | 6-OMe | 3.79 (s) | 3.80 (s) |
| B | 2-H/6-H | 7.13 (d, *J*=9.0 Hz) | 7.13 (d, *J*=9.0 Hz) |
| | 3-H/5-H | 6.63 (d, *J*=9.0 Hz) | 6.63 (d, *J*=9.0 Hz) |
| | 4-OMe | 3.70 (s) | 3.71 (s) |
| C | α-C$H_2$ | 3.60, 4.05 (both d, *J*=14.0 Hz) | 4.18, 3.54 (both d, *J*=14.0 Hz) |
| D | 5-H | 5.88 (s) | 5.87 (s) |
| | 4-OMe/6-OMe | 3.90/3.58 (each s) | 3.90/3.57 (each s) |
| E | 2-H/6-H | 7.20 (d, *J*=9.0 Hz) | 7.21 (d, *J*=9.0 Hz) |
| | 3-H/5-H | 6.77 (d, *J*=9.0 Hz) | 6.78 (d, *J*=9.0 Hz) |
| | 4-OMe | 3.72 (s) | 3.75 (s) |
| F | α-C$H_2$ | 3.16, 3.04 (both d, *J*=14.0 Hz) | 3.17, 3.09 (both d, *J*=14.0 Hz) |
| | 2-OMe | 3.24 (s) | 3.32 (s) |




NOE associations between the residual singlet [5-H(D) (δ 5.88 and 5.87 for **3** and **7**, respectively)] and both 4- and 6-OMe(D) (δ 3.90 and 3.58; δ 3.90 and 3.57 for **3** and **7**, respectively) are indicative of the bonding position as 7-C(D). Similar NOE associations between 5-H(A) (δ 5.79 for both **3** and **7**) and two methoxy resonances [4-OMe(A) (δ 3.80 and 3.81 for **3** and **7**, respectively) and 6-OMe(A) (δ 3.79 and 3.80 for **3** and **7**, respectively)] and between 7-H(A) (δ 5.93 and 5.95 for **3** and **7**, respectively) and one methoxy resonance [6-OMe(A) (δ 3.79 and 3.80 for **3** and **7**, respectively)] only, define the A-ring protons.

**Table 2.** $^{13}$C NMR data ($\delta_C$) of the 4,4′,6-tri-*O*-methyl-2-deoxymaesopsin-(2→7)-2,4,4′,6-tetra-*O*-methylmaesopsins **3/4** and **7/8** at 300 MHz (25°C) in $CDCl_3$ (superscript a, b, c may be interchanged)

| Ring | C | **3** | **7** | Ring | C | **3** | **7** |
|---|---|---|---|---|---|---|---|
| A/C | C-2 | 91.3 | 91.1 | D/F | C-2 | 109.7 | 110.0 |
| | C-3 | 197.5 | 197.7 | | C-3 | 194.4 | 194.3 |
| | C-4 | 158.5[a] | 158.5[a] | | C-4 | 160.1[c] | 160.2[c] |
| | C-5 | 92.2 | 92.2 | | C-5 | 89.4 | 89.5 |
| | C-6 | 169.2 | 169.1 | | C-6 | 169.4[c] | 169.3[c] |
| | C-7 | 88.3 | 88.3 | | C-7 | 103.4 | 103.7 |
| | C-8 | 174.5 | 174.4 | | C-8 | 171.6 | 172.0[c] |
| | C-9 | 106.2 | 106.4 | | C-9 | 105.3 | 105.4 |
| | C-α | 41.6 | 41.4 | | C-α | 40.8 | 40.9 |
| | | | | | OMe | 52.6 | 52.8 |
| B | C-1 | 127.2 | 126.9 | E | C-1 | 125.6 | 125.7 |
| | C-2/C-6 | 132.2[b] | 132.2[b] | | C-2/C-6 | 132.1[b] | 132.1[b] |
| | C-3/C-5 | 113.4 | 113.4 | | C-3/C-5 | 113.9 | 113.9 |
| | C-4 | 158.4[c] | 158.4[a] | | C-4 | 158.9 | 158.9 |
| | OMe | 55.2 | 55.5 | | OMe | 56.3 | 56.6 |
| | | 55.6 | 56.1 | | | 56.6 | 56.7 |
| | | 56.2 | 56.4 | | | 56.7 | |

An HMBC experiment permits differentiation between the A/C- and D/F-ring systems by distinction between the two carbonyl carbons and between the methylene groups. Thus, coupling of 3-C(F) (δ 194.4 and 194.3 for **3** and **7**, respectively) (Table 2) with 5-H(D) ($^4J_{CH}$) as well as with α-C$H_2$(F) (δ 3.04 and 3.16; δ 3.09 and 3.17 for **3** and **7**, respectively) ($^3J_{CH}$) tentatively identifies the resonances of the D/F-moiety. 3-C(C) (δ 197.5 and 197.7 for **3** and **7**, respectively) similarly shows coupling with 7/5-H(A) ($^4J_{CH}$) and with α-C$H_2$(C) (δ 3.60 and 4.05; δ 3.54 and 4.18 for **3** and **7**, respectively) ($^3J_{CH}$). Coupling of α-C$H_2$(C) with 2/6-H(B) (δ 7.13 for both **3** and **7**) and the latter with 3/5-H(B) (δ 6.63 for both **3** and **7**) in a COSY experiment, as well as an NOE association of 4-OMe(B) (δ 3.70 and 3.71 for **3** and **7**, respectively) with 3/5-H(B) concludes the definition of the B-ring system. Similar correlations define the E-ring system. Protonated carbon atoms in the $^{13}$C NMR spectra of **3** and **7** (Table 2) are defined by HMQC spectra of derivatives **3** and **7**. HMBC allows characterization of 2-C(C) (δ 91.3 and 91.1 for **3** and **7**, respectively) by its coupling with α-C$H_2$(C) ($^2J_{CH}$), 2/6-H(B) and 5-H(D) (both $^4J_{CH}$). 4-C(A) (δ 158.5 for both **3**

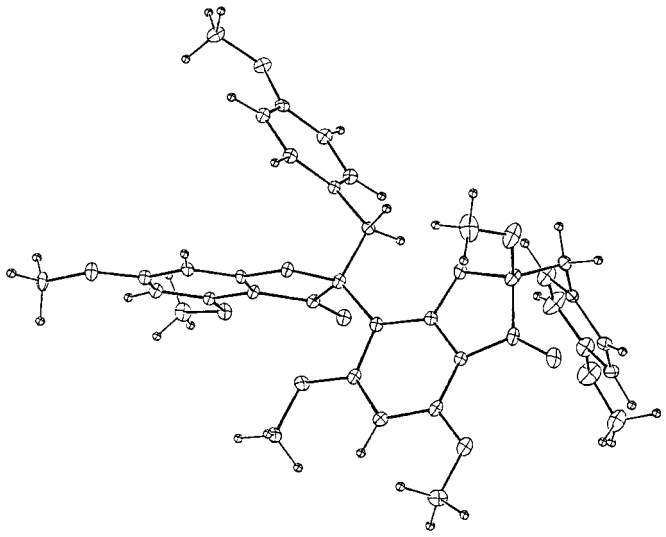


**Figure 1.** The crystal structure of 4,4′,6-tri-*O*-methyl-2-deoxymaesopsin-(2→7)-2,4,4′,6-tetra-*O*-methylmaesopsins **3/4**.

and **7**) is designated by coupling with 5-H(A) and 4-OMe(A) and is distinguished from 6-C(A) ($\delta$ 169.2 and 169.1 for **3** and **7**, respectively) which couples to both 5-H(A) and 7-H(A) as well as 6-OMe(A). Coupling ($^2J_{CH}$) between 7-H(A) and 8-C(A) ($\delta$ 174.5 and 174.4 for **3** and **7**, respectively) defines the latter while 9-C(A) is characterized by coupling ($^3J_{CH}$) with both 7-H(A) and 5-H(A); 1-C(B) ($\delta$ 127.2 and 126.9 for **3** and **7**, respectively) displays distinctive coupling with 3/5-H(B) ($^3J_{CH}$) and α-C$H_2$(C) ($^2J_{CH}$) while 4-C(B) ($\delta$ 158.4 for both diastereomers) shows coupling with 4-OMe(B) ($^3J_{CH}$) and 2/6-H(B) ($^3J_{CH}$). Owing to their close proximity the resonances of 4-C(B) and 4-C(A) may, however, be interchanged.

With few exceptions, similar correlations to those described above allow assignment of the carbon resonances of the DEF-unit. Ambiguous couplings do not facilitate differentiation between 4- and 6-C(D). Thus, both 4- and 6-C(D) ($\delta$ 160.1 and 169.4; $\delta$ 160.2 and 169.3 for **3** and **7**, respectively) couple to 5-H(D) and to either 4-OMe(D) or 6-OMe(D). 7-C(D) ($\delta$ 103.4 and 103.7 for **3** and **7**, respectively) and 9-C(D) ($\delta$ 105.3 and 105.4 for **3** and **7**, respectively) likewise both show coupling with 5-H(D) ($^3J_{CH}$ in both cases), but coupling of 7-C(D) with α-C$H_2$(C) ($^3J_{CH}$) allows distinction between the two carbons. The resonances allocated to 8-C(D) ($\delta$ 171.6 and 172.0 for **3** and **7**, respectively) show no correlations in the HMBC spectra of either epimers and are assigned by a process of elimination.

The EI mass spectral data of compounds **3** and **7** are essentially identical and exhibit a molecular ion $M^+$, *m/z* 656 (1.9 and 2.9% for **3** and **7**, respectively). The base peak, *m/z* 535 (100, 100%), originates from the loss of a 4-methoxybenzyl radical, *m/z* 121 (54.3, 19.6%). Subsequent cleavage of the interflavonoid bond yields a deoxymaesopsin radical, *m/z* 313 (3.3, 5.8%). These fragmentation patterns are consistent with the structures **3** and **7**.

The proposed structure for **3** is unequivocally confirmed by X-ray diffraction analysis (Fig. 1) of crystals obtained from ethanol/water (9:1 v/v). The biflavonoid crystallized in an orthorhombic system exhibiting a $P_{bca}$ point group. The two constituent units are arranged almost perpendicular to each other [dihedral angle O–1(C)–C-2(C)–C-7(D)–C-6(D)=45.86°] and the B- and E-ring systems are folded over the A- and D-rings, respectively, the angle adopted by 2-C(C)–α-$CH_2$–1-C(B) being 118.91° for the ABC-unit and 108.06° for the DEF-unit.

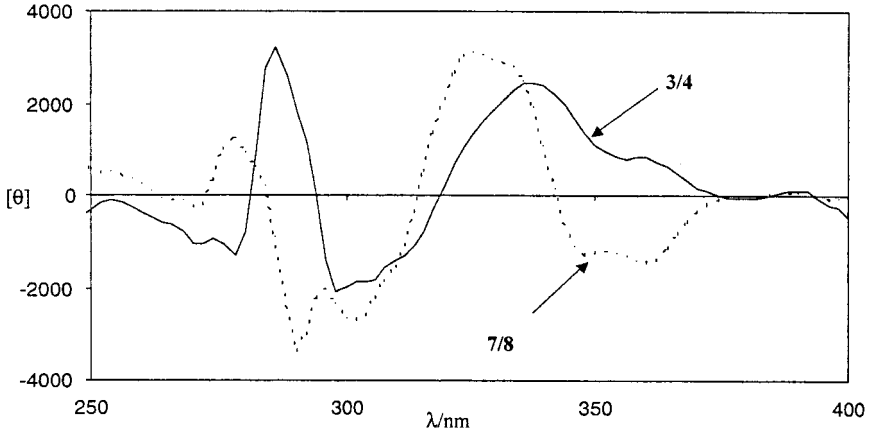



**Figure 2.** CD spectra of the biflavonoid diastereomers **3/4** and **7/8**.

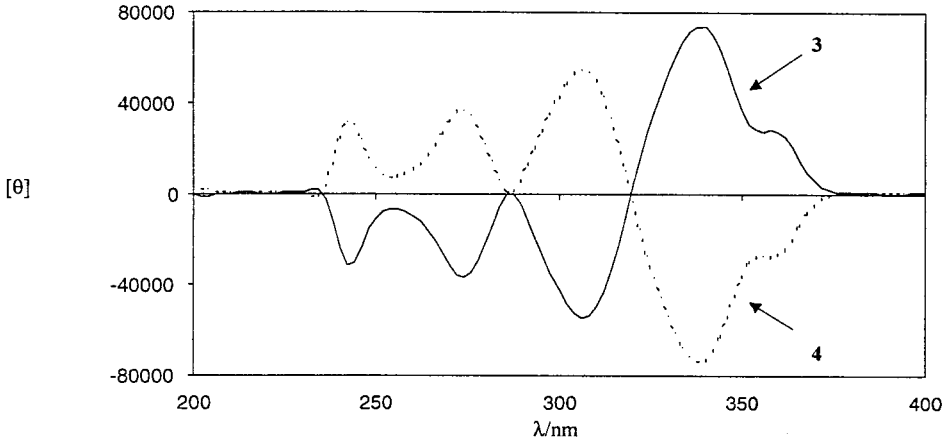



**Figure 3.** CD spectra of the biflavonoid enantiomers **3** and **4**.

While the symmetrical nature of the point group and orientation of the crystal prevent the direct assignment of the stereochemistry from the X-ray data, it limits the possible absolute configuration to 2*R*(C):2*S*(F) or 2*S*(C):2*R*(F). The CD curve (Fig. 2) of **3** clearly indicates an abundance of one of the enantiomers, but contributes little towards differentiation between the two possibilities, especially when it is compared with the CD curve of its diastereomer **7**. It is furthermore unclear to what extent the combined effects of the constituent units of the dimer and the ratio between the enantiomers contribute to the observed Cotton effects.

Contrary to our experience with the collective application of chemical degradation and CD spectroscopy in the determination of the absolute configuration of analogous oligmers,[2–5] attempts at the degradation of these dimers were unsuccessful. The methyl ether derivatives **3** and **7** are stable under both acidic and basic reaction conditions, including those of reductive cleavage with $Na(CN)BH_3$[7] which previously proved highly successful.[2,3]

$^1$H NMR analysis of **3** and **7**, using tris(3-heptafluoropropylhydroxymethylene-d-camphorato) europium(III) [Eu $(hfc)_3$] as chiral shift reagent, revealed that both compounds are enantiomeric mixtures. Thus, addition of ca 1 mg of the shift reagent to compound **3** results in the resolution of 4/6-OMe(D) ($\delta$ 3.90) into two peaks ($\delta$ 3.95 and 3.97) indicating the presence of the two enantiomers in a ratio of ca 45:55. Upon addition of a further portion of the shift reagent, the majority of the signals in the $^1$H NMR spectrum exhibit a resolution of about 0.5 ppm. Compound **7** behaves similarly. Consequently the enantiomers of both dimers become accessible via resolution of the enantiomeric mixtures by means of HPLC using a Chiralcel OD column. Thus, the enantiomeric pair **3/4** is resolved to give derivatives **3** and **4** while the pair **7/8** gives **7** and **8**, all in high enantiomeric purity (>99%).

The CD curves of enantiomers **3** and **4** (Fig. 3) each exhibit five Cotton effects in the 230–380 nm regions. While it is impossible to associate the respective effects with specific chromophores, the Cotton effects for the n→π* transition in the 330–365 nm region have been linked to the absolute configuration of the constituent 2,4,6-trihydroxy-2-(4-hydroxybenzyl)benzofuran-3(2*H*)-one (maesopsin) **9** units, positive and negative Cotton effects indicating 2*R* and 2*S* configurations,[2,3] respectively. Since the sign of the Cotton effect, the conformation of the enone ring[8] system and the absolute configuration are interdependent, the combined influence of the configuration/conformation of both the C- and F-rings on the Cotton effect in the 330–365 nm region must be considered in order to differentiate between the

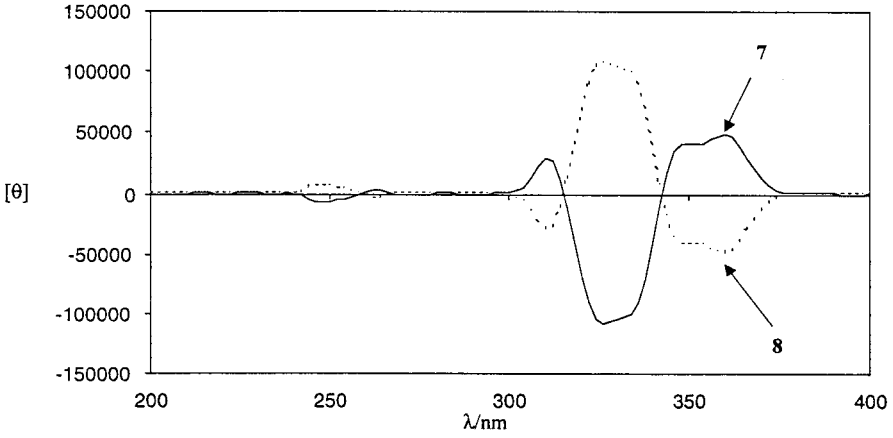


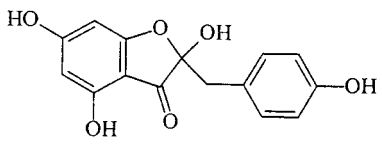

**Figure 4.** CD spectra of the biflavonoid enantiomers **7** and **8**.

2*R*(C):2*S*(F) and 2*S*(C):2*R*(F) absolute configurations indicated for the enantiomers **3** and **4** from the X-ray crystal structure.

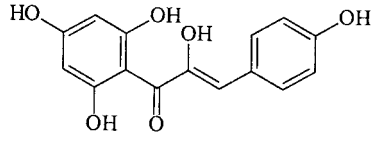
The potential energy surface (PES) of the enantiomer with 2*S*(C):2*R*(F) absolute configuration was explored by means of a global search routine[9] (GMMX 1.0) in order to determine the total aggregate of conformers significantly populated at ambient temperature within a 3 kcal $mol^{-1}$ energy window of the minimum. The results indicate conformers (Boltzmann population 98.21%) with a β-*O*-1-envelope conformation for the F-ring of this enantiomer, consistent with a positive Cotton effect for the $n\rightarrow\pi^*$ transition in its CD curve.[8] While this result corresponds with that previously obtained for a 2*R*-maesopsin derivative,[2,3] the result for the C-ring indicates a mixture of α-*O*-1- and β-*O*-1-envelope conformers with the former (Boltzmann population 64.38%) dominating. Effectively this amounts to a 28.76% excess of the α-*O*-1-envelope conformer for the C-ring and its contribution to the observed Cotton effect, compared to that of the F-ring, would therefore be insignificant. The positive Cotton effect displayed for the $n\rightarrow\pi^*$ transition in the CD curve of **3**, therefore, indicates a 2*R*(F) absolute configuration for this enantiomer and thus a 2*S*(C):2*R*(F) absolute stereochemistry from the X-ray data. The stereochemistry of its enantiomer **4** is then 2*R*(C):2*S*(F).

Similar treatment of the 2*S*(C):2*S*(F) enantiomer indicates conformers (Boltzmann population, 99.11%) with an α-*O*-1 envelope conformation for the F-ring and again a mixture of conformers (Boltzmann population 56.30% for the β-*O*-1 conformer and 43.70% for the α-*O*-1 conformer) for the C-ring. Again the contribution by the latter is negligible and, therefore, the negative Cotton effect observed for the $n\rightarrow\pi^*$ transition in the CD curve of **8** (Fig. 4) indicates a 2*S*(F) absolute configuration and thus a 2*S*(C):2*S*(F) configuration for compound **8**. Its enantiomer **7** then exhibits 2*R*(C):2*R*(F) stereochemistry as reflected by the positive Cotton effect in the 350–370 nm region.

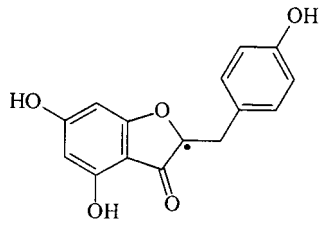
While the biosynthetic origin of these compounds is still unclear, it is feasible that they may be generated by attack of the 7-position of the phloroglucinol-type ring of either maesopsin **9** or the α-hydroxychalcone **10** on a quinomethane radical[10] **12**. Subsequent α-cyclization, as opposed to β-cyclization in the case of the zeyherin dimers,[1,3] will then lead to biflavonoids **3/4** and **7/8**. Although a benzofuranonyl radical **11** or carbocation may also be considered as possible electrophiles, no evidence exists to support this route.



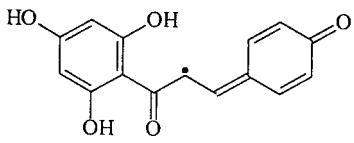

**9**




**10**




**11**




**12**

We have thus amply demonstrated how particularly circular dichroism and molecular modeling may be utilized to establish the absolute configuration of the new class of biflavonoids comprising benzofuranoid constituent units.

## Experimental

$^1$H NMR Spectra were recorded on a Bruker ADVANCE DPX 300 spectrometer for solutions in $CDCl_3$ with $Me_4Si$ as internal standard. Enantiomeric excess (ee) was determined by the addition of the chiral shift reagent, Eu(hfc)$_3$. Mass spectra were obtained with a Kratos MS-80 instrument and CD data in MeOH on a JASCO J-710. High performance liquid chromatography (HPLC) was performed on a Waters chromatograph equipped with a Waters 600 pump and controller and a Waters 486 detector. A Chiralcel OD (4.6×250 mm, 10 μl) stainless steel column was used at room temperature. TLC was performed on precoated Merck plastic sheets (silica gel 60 $PF_{254}$, 0.25 mm) and the plates were sprayed with $H_2SO_4$–HCHO (40:1, v/v) after development. Preparative plates (PLC), 20×20 cm, Kieselgel $PF_{254}$ (1.0 mm) were air-dried and used without prior activation. Separations on Sephadex LH-20 were in EtOH at a flow rate of ca 0.5 ml $min^{-1}$ (30 min fractions). Flash column chromatography (FCC) was carried out in a glass column (5 cm diameter) charged with Merck Kieselgel 60 (230–400 mesh) at a flow rate of 3 ml $min^{-1}$ (30 ml fractions) under $N_2$ pressure. Water-soluble phenolics were freeze-dried with a Virtis Freezemobile 12 SL. Evaporations were carried out under reduced pressure at ca 40°C in a rotary evaporator.

### Methylations

$Me_2CO$ was dried over anhydrous $K_2CO_3$ (oven-dried, 24 h, 200°C) for 24 h. The solvent was filtered, distilled over molecular sieves (3 Å) and stored under $N_2$. Phenolic material was dissolved in dry $Me_2CO$, dry $K_2CO_3$ (8 equiv.) added and $Me_2SO_4$ (3–10 equiv.) introduced dropwise over 30 min under $N_2$. The reaction mixture was refluxed for 8 h, filtered and the $Me_2CO$ removed under reduced pressure. Excess $Me_2SO_4$ was destroyed by

treatment with dilute $NH_4OH$ and the product obtained by extraction with EtOAc.

The extraction of the heartwood of *B. zeyheri* with aqueous $Me_2CO$ (8:2, v/v) and fractionation of the extract by means of countercurrent distribution leading to fraction 7–8.6 were fully described in Ref. 11. Column chromatography of fraction 7–8.6 (14.5 g) on Sephadex LH-20 (4×150 cm column, flow rate 30 ml $h^{-1}$) in EtOH gave seven fractions: 7–8.6.1 (1–38, 7.066 g), 7–8.6.2 (39–49, 0.559 g), 7–8.6.3 (50–92, 0.856 g), 7–8.6.4 (93–112, 0.133 g), 7–8.6.5 (113–133, 0.029 g), 7–8.6.6 (134–161, 0.674 g), 7–8.6.7 (162–347, 0.148 g). Methylation of fraction 7–8.6.3 (500 mg) and subsequent FCC in hexane/$Me_2CO$/EtOAc (55:30:15, v/v) resulted in four fractions: 7–8.6.3.1 (1–9, 93.9 mg), 7–8.6.3.2 (10–23, 130.7 mg), 7–8.6.3.3 (24–30, 131.6 mg), 7–8.6.3.4 (31–40, 212.5 mg).

**4,4′,6-Tri-*O*-methyl-2-deoxymaesopsin-(2→7)-2,4,4′,6-tetra-*O*-methylmaesopsin (3/4).** PLC of fraction 7–8.6.3.2 in hexane/$Me_2CO$/EtOAc (55:30:15, v/v) afforded compounds **3/4** ($R_f$ 0.16, 28 mg) which crystallized from EtOH/$H_2O$ (9:1, v/v) as *yellow cubes*, mp 215.6°C. PLC of fraction 7–8.6.3.3 in benzene/$Me_2CO$ (9:1, v/v) similarly yielded the title compound. ($R_f$ 0.17, 16 mg). (Found: $M^+$, 656.2258, $C_{37}H_{36}O_{11}$ requires *M*, 656.2258); ($\delta_H$) (Table 1); ($\delta_C$) (Table 2); MS *m/z* (%) 656 ($M^+$, 1.9), 535 (100), 371 (23), 313 (3.3), 121(54); CD $[\theta]_{366.6}=8.083\times10^2$, $[\theta]_{337.5}=2.446\times10^3$, $[\theta]_{298.5}=-2.087\times10^3$, $[\theta]_{285.6}=3.268\times10^3$ (Fig. 2); *Crystal data for* **3/4**: $C_{37}H_{36}O_{11}$, *M*=656.2, orthorhombic, space group $P_{bca}$, $a$=6.193(2), $b$=25.8080(5), $c$=27.3020(5) Å, $\alpha=90°$, $\beta=90°$, $\gamma=90°$, $R_1$=0.0570.

Compound **3/4** (2 mg) was dissolved in $CHCl_3$ (2 ml) and resolved by means of HPLC in hexane/EtOH/EtOAc (350:150:0.6, v/v) at a flow rate of 0.1 ml $min^{-1}$ on a Chiralcel OD column to yield the two enantiomers **3** (retention time 4.75 min, 0.83 mg) and **4** (retention time 5.20 min, 0.92 mg).

**(2*S*)-4,4′,6-Tri-*O*-methyl-2-deoxymaesopsin-(2→7)-(2*R*)-2,4,4',6-tetra-*O*-methylmaesopsin (3).** This compound was obtained in high ee (>99%). CD $[\theta]_{358.5}=2.801\times10^4$, $[\theta]_{338.6}=7.383\times10^4$, $[\theta]_{306.3}=-5.415\times10^4$, $[\theta]_{273.7}=-3.627\times10^4$, $[\theta]_{242.8}=-3.232\times10^4$ (Fig. 3).

**(2*R*)-4,4′,6-Tri-*O*-methyl-2-deoxymaesopsin-(2→7)-(2*S*)-2,4,4′,6-tetra-*O*-methylmaesopsin (4).** This compound was obtained in high ee (>99%). CD $[\theta]_{358.5}=-1.774\times10^4$, $[\theta]_{338.4}=-5.038\times10^4$, $[\theta]_{305.8}=3.650\times10^4$, $[\theta]_{274.2}=2.663\times10^4$, $[\theta]_{241.5}=2.378\times10^4$ (Fig. 3).

**4,4′,6-Tri-*O*-methyl-2-deoxymaesopsin-(2→7)-2,4,4′,6-tetra-*O*-methylmaesopsin (7/8).** Fraction D7–8.6.3.4 was purified by PLC in hexane/$Me_2CO$/EtOAc (55:30:15, v/v) to yield compounds **7/8** ($R_f$ 0.10, 33.0 mg) as a *yellow amorphous solid*. (Found: $M^+$, 656.2261, $C_{37}H_{36}O_{11}$ requires *M*, 656.2258); ($\delta_H$) (Table 1), ($\delta_C$) (Table 2); MS *m/z* (%) 656 ($M^+$, 2.9), 535 (100), 371 (22), 313 (5.8), 121(19); CD $[\theta]_{360.1}=-1.470\times10^3$, $[\theta]_{348.7}=-1.287\times10^3$, $[\theta]_{326.2}=3.120\times10^3$, $[\theta]_{301.8}=-2.711\times10^3$, $[\theta]_{290.3}=-3.380\times10^3$, $[\theta]_{277.7}=1.241\times10^3$ (Fig. 2).

Compound **7/8** (2 mg) was dissolved in $CHCl_3$ (2 ml) and resolved by means of HPLC in hexane/EtOH/EtOAc (350:150:0.6, v/v) at a flow rate of 0.1 ml $min^{-1}$ on a Chiralcel OD column to yield the two enantiomers **7** (retention time 4.20 min, 0.87 mg) and **8** (retention time 5.10 min, 0.71 mg).

**(2*R*)-4,4′,6-Tri-*O*-methyl-2-deoxymaesopsin-(2→7)-(2*R*)-2,4,4′,6-tetra-*O*-methylmaesopsin (7).** This compound was obtained in high ee (>99%). CD $[\theta]_{359.8}=2.475\times10^4$, $[\theta]_{349.0}=2.100\times10^4$, $[\theta]_{326.4}=-5.460\times10^4$, $[\theta]_{309.2}=2.288\times10^4$ (Fig. 4).

**(2*S*)-4,4′,6-Tri-*O*-methyl-2-deoxymaesopsin-(2→7)-(2*S*)-2,4,4′,6-tetra-*O*-methylmaesopsin (8).** This compound was obtained in high ee (>99%). CD $[\theta]_{359.8}=-4.918\times10^4$, $[\theta]_{349.2}=-4.179\times10^4$, $[\theta]_{326.1}=1.082\times10^5$, $[\theta]_{310.6}=-3.008\times10^4$ (Fig. 4).

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