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Inorganic and Organic Chemistry

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Contents of Number 9/10

Original Communications

Stereochemistry of Two Hydroxybiflavanonols from *Garcinia cola* Nuts

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Biflavanonol, Stereochemistry, Atropisomer, ^{1}H NMR, Circular Dichroism

The absolute configuration of two hydroxybiflavanonols from *Garcinia cola* nuts have been determined by CD and 500 MHz ^{1}H NMR spectroscopy. Additionally the occurrence of atropisomers at room temperature as the consequence of rotational hindrance in the molecules could be demonstrated.

Introduction

In 1971 Jackson *et al.* [1] elucidated the structures of two biflavanonols from *Garcinia buchananii* Baker using UV, IR and ^{1}H NMR spectroscopy. Cotterill and Scheinmann [2] isolated the same compounds from the nuts of *Garcinia cola* Heckel in 1978. Both compounds exhibit antihepatotoxic properties [3]. Very recently [4] we investigated in detail the biochemical mechanism of action of these drugs.

Each of the molecules contains four asymmetric carbon atoms suggesting the possibility of different configurations. The stereochemistry of the molecules, however, has not been investigated up to now. Using 500 MHz ^{1}H NMR spectroscopy at different temperatures and circular dichroism studies we analyzed the absolute configuration of the described biflavanonols and report here the occurrence of both molecules as atropisomers.

Experimental

The *Garcinia* biflavanonols were isolated from defatted *Garcinia cola* nuts by extraction with ethanol followed by elution of the dried and powdered ethanol extract with ethylacetate. Then by column chromatography on Kieselgel 60 (Merck) two major fractions were obtained with a) dichloromethan–methanol (14:9) saturated with water, b) chloroform–methanol–water (64:50:10). This second fraction was further separated into 14 fractions by preparative thin-layer chromatography on Kieselgel 60 F_{254} (Merck) in chloroform–acetone–formic acid (9:2:1). The compounds with R_F values 0.15 and 0.25 represent an octahydroxy- and a heptahydroxybiflavanonol which show decomposition at 217 °C and 200 °C, respectively. If the ethylacetate extract was fractionated by thin-layer chromatography in different solvents avoiding chloroform and acids, the same compounds could be isolated. This indicates that the biflavanonoles are not products of a dimerization reaction during isolation.

The structures were analyzed by UV, MS and NMR spectroscopy.

The NMR spectra were recorded with a Bruker AM-500 spectrometer at different temperatures between 20 °C and 90 °C. The CD spectra were measured in methanol at 25 °C with a Jobin-Yvon Dichrograph Mark IV in 0.2 mM concentrations.

Results and Discussion

After isolation of two biflavanonols from *Garcinia cola* nuts the structures of the purified compounds could be identified by UV, MS and NMR spectroscopy as 2,2′,3,3′-tetrahydro-3′,5,5′,7,7′-pentahydroxy-2,2′-bis(4-hydroxyphenyl)-3,8′-bi-1-4H-benzopyran-4,4′-dion(**I**) and 2′-(3,4-dihydroxyphenyl)-2,2′,3,3′-tetrahydro-3′,5,5′,7,7′-pentahydroxy-2-(4-hydroxyphenyl)-3,8′-bi-4H-1-benzopyran-4,4′-dion(**II**).

The CD spectra (Fig. 1) show a Cotton-Effect at 290 nm (−) and 330 nm (+). By comparing the numerous data of Gaffield [5] for flavonoids with the Cotton-Effect of our compounds it can be deduced that both *Garcinia* biflavanonols have *S*-configura-

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Reprint requests to Prof. Dr. J. Sonnenbichler.

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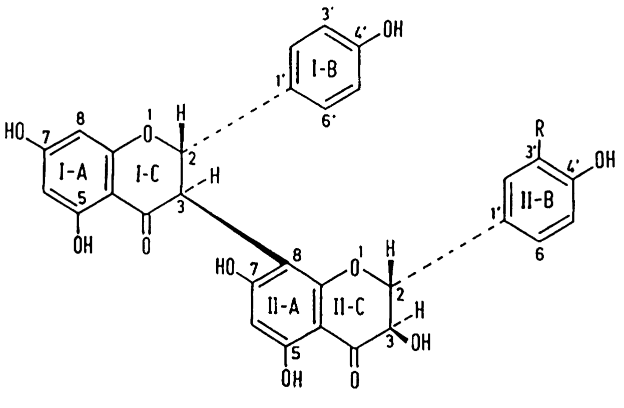

I (R = H): 2,2′,3,3′-Tetrahydro-3′,5,5′,7,7′-pentahydroxy-2,2′-bis(4-hydroxyphenyl)-3,8′-bi-1-4H-benzopyran-4,4′-dion.

II (R = OH): 2′-(3,4-Dihydroxyphenyl)-2,2′,3,3′-tetrahydro-3′,5,5′,7,7′-pentahydroxy-2-(4-hydroxyphenyl)-3,8′-bi-4H-1-benzopyran-4,4′-dion.

tion at carbon **I**-C2 and *R*-configuration at carbon **II**-C2, according to the nomenclature of Cahn-Ingold-Prelog [6].

The NMR data of **I** are listed in Table I. (Because of high analogy, the NMR data of **II** have been omitted in this short communication.) The coupling constants of the protons at **I**-C2 to **I**-C3 (J = 12.1 Hz) as well as **II**-C2 to **II**-C3 (J = 11.6 Hz) respectively manifest *trans*-positions of the hydrogens. Consequently we propose a 2*S*3*R* configuration for the flavanone part and a 2*R*3*R* configuration for the flavanonol part of the molecules, as shown in the formula.

In the NMR spectrum at 20 °C it is remarkable that all resonances for the phenolic and alcoholic protons appear each with half intensity at double positions (Table I). This is also the case for the protons at carbons **I**-A6, **I**-A8, **I**-C2, **I**-C3, **II**-C2 and **II**-C3. This observation indicated a 1:1 mixture of

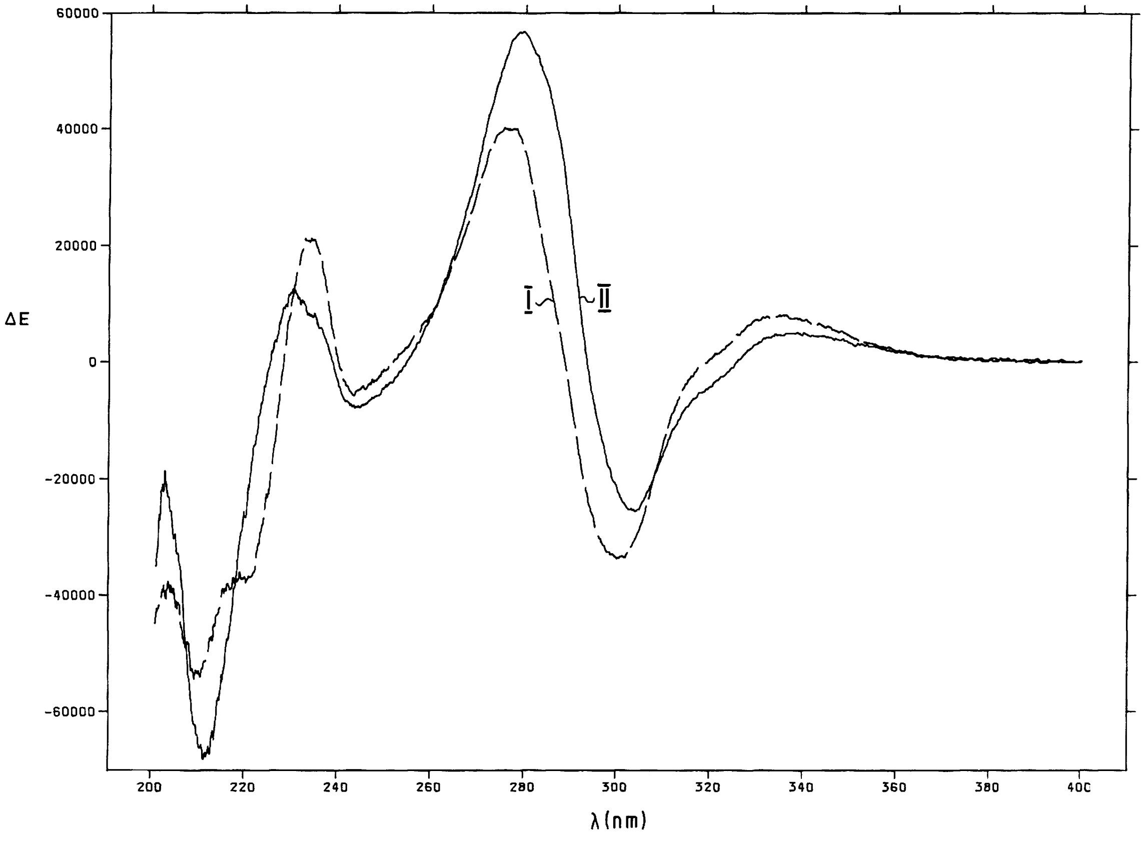

Fig. 1. CD spectra of **I** and **II** at 0.2 mM concentrations in methanol at 25 °C.

Table I. NMR data of **I** at 20 °C in $CDCl_3$.

Protons	ppm-Values	Number	Coupling constant
I-A6	* 5.83/5.78	1	
I-A8	* 5.97/5.87	1	
II-A6	5.91	1	
I-B2′	6.85 or 6.65	1	d (*J* = 8.1 Hz)
I-B3′	7.17	1	d (*J* = 8.1 Hz)
I-B5′	7.17	1	d (*J* = 8.1 Hz)
I-B6′	6.65 or 6.85	1	d (*J* = 8.1 Hz)
II-B2′	6.65 or 6.75	1	d (*J* = 8.1 Hz)
II-B3′	7.10	1	d (*J* = 8.1 Hz)
II-B5′	7.08	1	d (*J* = 8.1 Hz)
II-B6′	6.75 or 6.65	1	d (*J* = 8.1 Hz)
I-C2	* 5.65/5.32	1	d (*J* = 12.1 Hz)
I-C3	* 4.42/4.64	1	d (*J* = 12.1 Hz)
II-C2	* 5.14/4.97	1	d (*J* = 11.6 Hz)
II-C3	* 4.22/3.98	1	dd (*J* = 11.6/6.0 Hz)
Phenolic OH's			
I-A5			
I-A7	* 12.30/12.17;		* 11.86/11.74;
II-A5	* 11.23/10.87;		* 10.75/10.71;
II-A7	* 9.58/ 9.56;		* 9.47/ 9.44
I-B4′			
II-B4′			
Alcoholic OH			
II-C3	* 5.83/ 5.73		d (*J* = 6.0 Hz)

* These protons appear at two different positions with equal intensities of 0.5 H each and coalesce after heating to about 70 °C focussing at intermediate ppm values.

two very similar isomers. However, we did not succeed in separating isomers.

The CD curves of **I** and **II** display *S*-shaped features between 280 nm (+) and 305 nm (−) with a zero value near the UV maximum of the molecules at 293 nm. This indicates a strong excitonic coupling of both parts of the molecule. This behaviour is characteristic for biflavonoids with atropisomers [7]. Presumably this is the case due to hydrogen bonding between the carbonyl group at **I**-C4 and the phenolic hydroxyl at **II**-A7 with the consequence that, at room temperature, the rotation of the 3−8 bond is restricted. This proposal is in good agreement with the observed doubling of the NMR signals (Table I). As was to be expected the described doubled NMR signals disappear with increase in temperature and coalesce at 70 °C to single sharp resonances as a consequence of increased rotations around the 3−8 bond. This behaviour is characteristic for atropisomers and is in good agreement with the rotational barriers visible in space filling models for the established structures of (2*S*,2′*R*,3*R*,3′*R*)-2′-(3,4-dihydroxyphenyl)-2,2′,3,3′-tetrahydro-3′,5,5′,7,7′-pentahydroxy-2-(4-hydroxyphenyl)-3,8′-bi-4H-1-benzopyran-4,4′-dion(**II**) and (2*S*,2′*R*,3*R*,3′*R*)-2,2′3,3′-tetrahydro-3′,5,5′,7,7′-pentahydroxy-2,2′-bis(4-hydroxyphenyl)-3,8′-bi-1-4H-benzopyran-4,4′-dion(**I**).

Because of the differences in shift between the resonances of protons **I**-B2 and **I**-B6, furthermore **II**-B2 and **II**-B6, additionally the bonds between rings **I**-B and **I**-C as well as rings **II**-B and **II**-C respectively must have hindered rotation at room temperature. This again is in good agreement with the atomic situation in space filling models of the molecules.

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