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STEREOCHEMISTRY OF TWO TETRASTILBENES FROM *CAREX* SPECIES

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Key Word Index– *Carex* species; Cyperaceae; oligostilbene; stereochemistry.

Abstract—The stereochemistry of two tetrastilbenes, miyabenols A and B, was determined by NOE measurements. Their biogenetic relationship with other oligostilbenes and the absolute configuration are also presented.

INTRODUCTION

In the course of our chemical investigations of phenolic constituents of *Carex* species, several characteristic oligostilbenes, di-, tri- and tetramers of resveratrol (3,5,4′-trihydroxystilbene), have been isolated [1–5]. Among the isolated oligostilbenes, there has been no information about the stereochemistry of miyabenols A (**1**) and B (**2**), which were first isolated as constituents of *C. fedia* var. *miyabei* [1], whereas other stilbenoids are well-characterized including their stereochemistry. Here, we report determination of the stereochemistry of the compounds **1** and **2** by extensive analyses of NOE results and a chemical transformation reaction.

RESULTS AND DISCUSSION

Complete assignments of the ^{1}H and ^{13}C signals of **1** and **2** were unambiguously achieved by means of HH COSY, HMQC and HMBC spectra, and are shown in Tables 1 and 2, although tentative assignments have been made [1]. The relative configuration of **2** was established from NOESY measurements. The presence of NOEs of H-7a/H-10(14)a and H-8a/H-2(6)a indicates a *trans*-2,3-diaryl-2,3-dihydrobenzofuran system for ring A3. In the similar manner, NOEs of H-8b/H-2(6)b, H-7c/H-14c, H-8c/H-2(6)c, H-7d/H-14d and H-8d/H-2(6)d support the *trans*-diaryl substitution on rings B3, C3 and D3. Furthermore, in the central nine-membered ring, NOEs of H-8b/H-8d and H-8c/H-8d were clearly detected, although no NOE cross-peak appeared between H-8b and H-8c. These results suggest the relative stereochemistry around the central ring to be that shown in Fig. 1. This relative configuration is also supported by the presence of NOEs of H-8b/H-7c and H-8b/H-14d. It was difficult to determine the stereochemical relationship between ring A3 and the other dihydrofuran rings, B3, C3 and D3, since no significant NOEs were observed on H-7a or H-8a to the protons around the central nine-membered ring, except only NOE between H-8a and H-12c. The signals of H-10(14)a and H-12c appeared at the higher field, however, indicating that rings A2 and C2 are shielded from each other as shown in Fig. 1. The vicinity of the two rings is also accounted for by the NOE of H-8a/H-12c. The complete relative stereochemistry of **2** was thus established.

On the other hand, miyabenol A (**1**) is a linear-type resveratrol oligomer like the dimer, (−)-ε-viniferin (**3**) and the trimer, miyabenol C (**4**) [1, 3, 5]. The structural flexibility due to its 'linear' structure discouraged the determination of the stereochemistry since sufficient NOEs were not available under the usual conditions. Then, we measured the NOE spectra, NOESY and NOEDS, using dimethyl sulphoxide-d_6 as a solvent in order to suppress molecular motion and several negative NOEs appeared in this relatively viscous solution. The presence of NOEs of H-7a/H-10(14)a, H-8a/H-2(6)a, H-7b/H-14b, H-8b/H-2(6)b, H-7c/H-14c and H-8c/H-2(6)c indicates an all *trans*-configuration on each dihydrofuran ring, A3, B3 and C3. Three diaryl methine protons, H-8a, H-8b and H-8c are located in the vicinity each other from NOEs of H-8a/H-8b, H-8a/H-8c and H-8b/H-8c. Inter-unit NOEs of H-10(14)a with H-2(6)d, H-8b and H-8c, and H-2(6)d with H-2(6)b, suggest the spatial vicinity of ring A2 with D1, B3 and C3, and of ring D1 with B1. A molecular model study suggested the molecular conformation of **1** as shown in Fig. 2. This conformation is also supported by the up-field shifts of H-10(14)a, H-14c and H-2(6)c, which are caused by the shielding effect from rings C1, A1 and A2, respectively, compared to the corresponding protons of the other *Carex* oligostilbenes [5]. The relative stereochemistry of rings A3, B3 and C3 shown in Fig. 2 is the same as that of **2**. In order to

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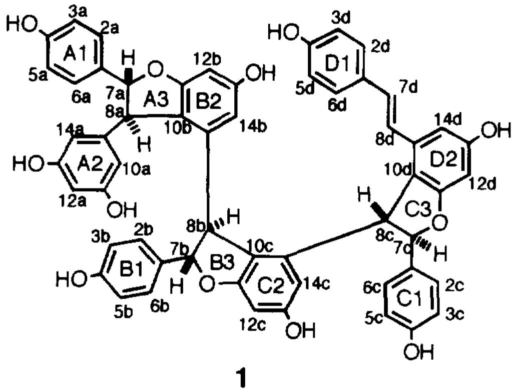

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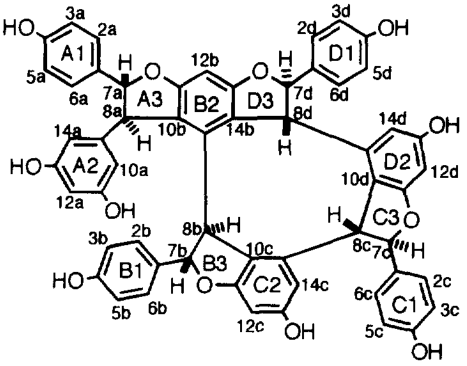


2

Table 1. ^{1}H NMR spectral data of compounds **1** and **2** (500 MHz, acetone-d_6)

H	**1**	**2**
2(6)a	6.81 *d* (8.5)	7.04 *d* (8.6)
3(5)a	6.63 *d* (8.5)	6.78 *d* (8.6)
7a	5.11 *d* (5.7)	5.21 *br s*
8a	4.12 *d* (5.7)	4.54 *br s*
10(14)a	5.90 *d* (2.1)	5.99 *d* (2.0)
12a	6.09 *t* (2.1)	6.18 *t* (2.0)
2(6)b	6.58 *d* (8.5)	6.81 *d* (8.6)
3(5)b	6.42 *d* (8.5)	6.63 *d* (8.6)
7b	5.08 *d* (1.9)	5.83 *br s*
8b	4.68 *d* (1.9)	4.49 *br s*
12b	6.31 *d* (2.0)	6.42 *s*
14b	5.97 *d* (2.0)	—
2(6)c	6.61 *d* (8.5)	7.01 *d* (8.5)
3(5)c	6.64 *d* (8.5)	6.76 *d* (8.5)
7c	5.11 *d* (1.6)	5.21 *d* (7.2)
8c	4.31 *d* (1.6)	4.59 *d* (7.2)
12c	6.18 *d* (2.1)	5.86 *d* (2.1)
14c	6.05 *d* (2.1)	6.03 *d* (2.1)
2(6)d	7.00 *d* (8.6)	7.21 *d* (8.6)
3(5)d	6.71 *d* (8.6)	6.78 *d* (8.6)
7d	6.87 *d* (16.2)	5.94 *d* (7.2)
8d	6.63 *d* (16.2)	4.91 *d* (7.2)
12d	6.34 *d* (1.9)	6.20 *d* (1.9)
14d	6.67 *d* (1.9)	6.51 *d* (1.9)

confirm the stereochemistry of **1**, an oxidative phenolic coupling of **1** to **2** was carried out. Oxidation of **1** with vanadium oxytrichloride [6] gave two products. Both products showed a $[M]^+$ at *m/z* 904 in the FD-mass spectrum. The physicochemical properties of the major product coincided well with those of **2**. The minor product seems to be a stereoisomer of **2** since no olefinic protons appeared in the NMR spectrum. Hence, the stereochemistry of **1** was deduced in comparison with that of **2**.

The absolute configuration of **1** and **2** was estimated to be (7a*R*, 8a*R*, 7b*S*, 8b*S*, 7c*R*, 8c*R*) and (7a*R*, 8a*R*, 7b*S*, 8b*S*, 7c*R*, 8c*R*, 7d*R*, 8d*R*), respectively, on the basis of their plausible biogenetic route starting from resveratrol (**5**) *via* (−)-ε-viniferin (**3**) and miyabenol C (**4**) (Scheme 1). The stereochemical aspects of the biogenesis of **4** and higher oligostilbenoids have already been discussed [5].

EXPERIMENTAL

^{1}H and ^{13}C NMR: Me_2CO-d_6 using TMS as int. standard except for NOE experiments of **1**: Me_2SO-d_6.

Table 2. ^{13}C NMR spectral data of compounds **1** and **2** (125 MHz, acetone-d_6)

	a		b		c		d	
C	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**
1	132.6	134.0	132.9	132.2	133.4	131.7	129.2	132.1
2(6)	128.3	127.6	127.9	128.0	127.4	128.8	128.9	128.5
3(5)	115.9	116.2	115.7	115.6	116.0	116.0	116.9	116.0
4	157.9	158.3	157.9	157.7	157.9	158.2	158.0	158.4
7	95.1	93.5	92.5	87.5	93.1	94.8	131.6	88.9
8	56.1	57.6	49.9	48.1	51.5	55.9	122.5	51.3
9	147.3	148.1	142.8	139.6	142.9	140.4	136.4	140.1
10	107.0	106.3	119.2	119.6	120.0	117.9	120.9	118.9
11	159.8	159.6	162.9	163.8	162.1	162.2	162.2	161.3
12	102.4	101.8	96.7	93.2	96.7	97.9	97.1	97.1
13	159.8	159.6	160.2	160.4	160.2	159.4	159.5	161.0
14	107.0	106.3	107.8	124.1	107.2	109.6	104.4	104.6

Oxidative conversion of **1** *to* **2**. To a soln of vanadium oxytrichloride (49 mg) in dry Et_2O (22 ml) was added dropwise **1** (100 mg) in dry Et_2O (22 ml) for 5 min under N_2 at − 78°. The soln was stirred for a further 3 hr at this temp. and then warmed to reflux for 2 hr. The reaction

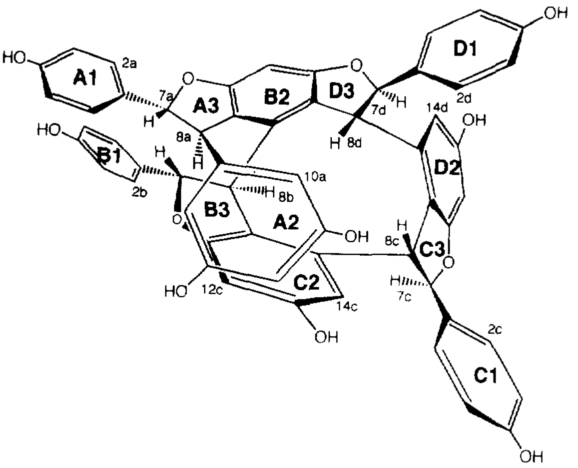


Fig. 1. Stereostructure of miyabenol B (**2**).

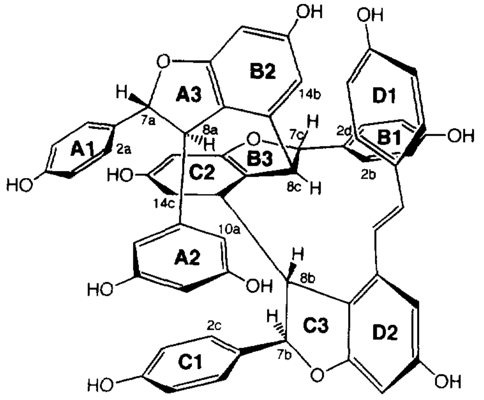
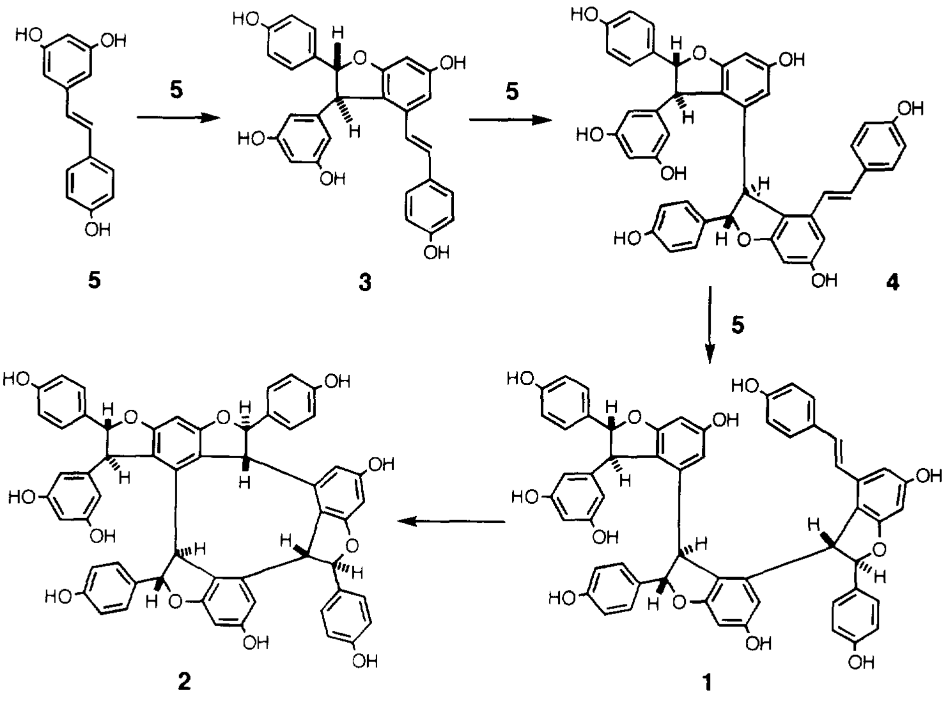


Fig. 2. Stereostructure of miyabenol A (**1**).



Scheme 1. Plausible biogenetic route for miyabenols A (**1**) and B (**2**).

mixt. was washed with H_2O, evapd and purified by silica gel prep. TLC (benzene–$CHCl_3$–MeOH, 8:7:6) to give two products. The less polar major product (27% yield) was obtained as a glassy solid. The physicochemical properties were identical with those of authentic **2**. The minor product (12% yield) showed a $[M]^+$ at *m/z* 904 and was considered to be a stereoisomer of **2**.

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