

## Four New Dibenzocyclooctadiene Lignans from *Schisandra rubriflora*

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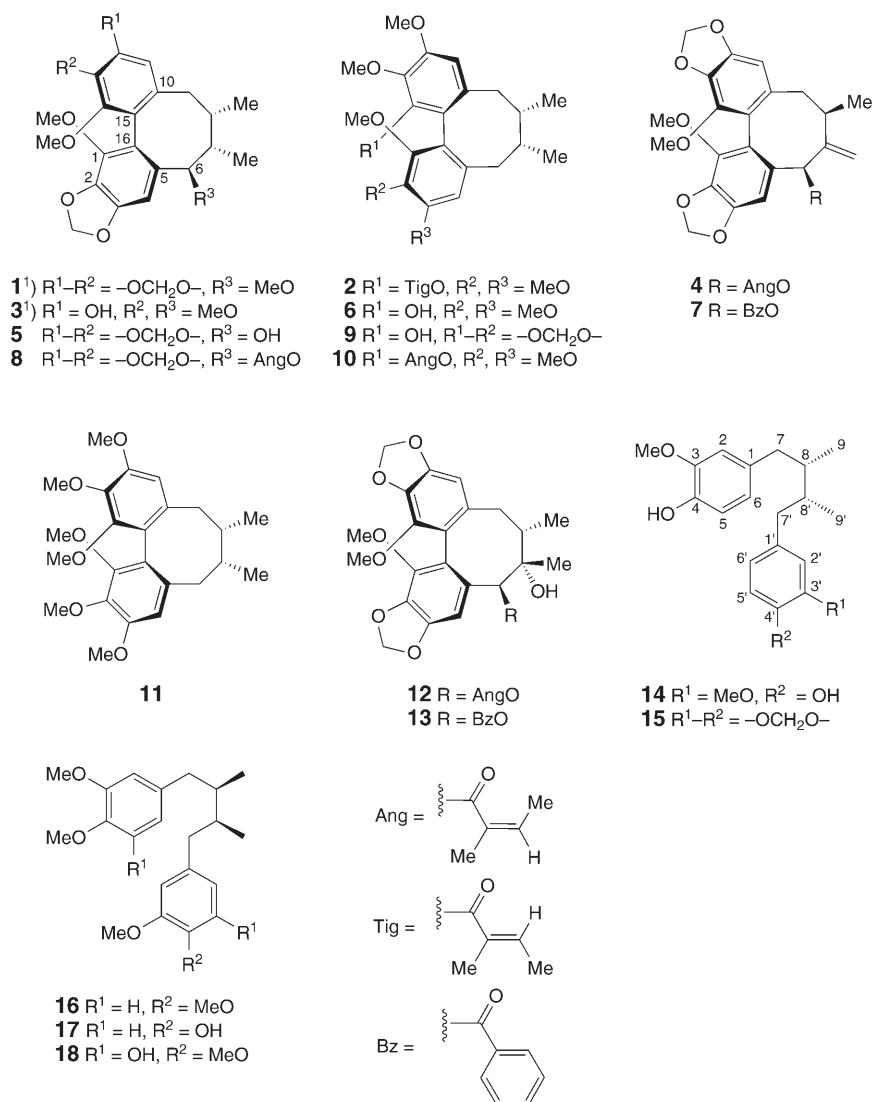
From the aerial parts of *Schisandra rubriflora* (FRANCH) REHD. et WILS., four new dibenzocyclooctadiene lignans, methylgomisin R (**1**), (+)-14-tigloylgomisin K<sub>3</sub> (**2**), 12-demethylwuweilignan I (**3**), schisandrene A (**4**), together with 13 known lignans, were isolated. The structures of four new compounds were elucidated by spectroscopic methods including extensive 1D- and 2D-NMR techniques.

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**Introduction.** – Plants of the economically and medicinally important genus *Schisandra* (Schisandreae), are known to be a rich source of dibenzocyclooctadiene lignans, lanostane and cycloartane triterpenes, which have been found to possess diversified beneficial pharmacological effects [1–6]. Since 2003, the systematical chemical investigation of the genus *Schisandra* conducted by our group led to the discovery of a series of novel nortriterpenoids with a diversity of highly oxygenated structures biogenetically related to cycloartane, and some of them showed promising anti-HIV-1 activities with a low toxicity [7–10]. As a consequence, these discoveries have attracted research programs of natural products and synthetic chemistry [11–13]. As a continuation of our search for more new secondary metabolites with potential bioactivities, four new lignans, methylgomisin R (**1**), (+)-14-tigloylgomisin K<sub>3</sub> (**2**), 12-demethylwuweilignan I (**3**), and schisandrene A (**4**), along with 13 known ones were isolated from the aerial parts of *Schisandra rubriflora*. This article deals with the isolation and structural elucidation of these new compounds.

**Results and Discussion.** – Compounds **1–4** were all dibenzocyclooctadiene lignans based on their UV (214–225 (log  $\epsilon$  > 4), 248–257 (log  $\epsilon$  > 4), 275–294 (log  $\epsilon$  3–4)) and NMR spectra (Tables 1 and 2) [14]. The configurations of the biphenyl groups were determined based on their characteristic circular dichroism (CD) spectra. The CD spectra of **1**, **3** and **4** showed positive Cotton effects around 222–237 nm and a negative Cotton effect around 255 and 259 nm, while **2** showed two positive Cotton effects around 235 and 248 nm, suggesting that **1**, **3** and **4** possessed (aS)-configuration, while **2** possessed an (aR)-configuration [15][16].

Compound **1** was isolated as yellowish amorphous powder. Its molecular formula, C<sub>23</sub>H<sub>26</sub>O<sub>7</sub>, was determined by HR-ESI-MS ( $m/z$  437.1561, [M + Na]<sup>+</sup>), in combination



with  $^1H$ - and  $^{13}C$ -NMR data, indicating 11 degrees of unsaturation. Detailed analysis of the HSQC, HMBC, and ROESY experiments established the structure of **1** as (a*S*)-(5*R*,6*S*,7*S*)-5,6,7,8-tetrahydro-5,13,14-trimethoxy-6,7-dimethyl-1,3-benzodioxolo[5',6':3,4]-cycloocta[1,2-*f*][1,3]benzodioxole.

Analysis of the 1D-NMR data revealed that **1** possessed a biphenyl moiety due to two aromatic H-atoms at  $\delta(H)$  6.47 and 6.38 (2*s*, H–C(4) and H–C(11)<sup>1)</sup>) and twelve aromatic C-atoms. Moreover, two O–CH<sub>2</sub>–O groups at  $\delta(H)$  5.93 and 6.00, and two

<sup>1)</sup> Arbitrary atom numbering.

Table 1.  $^1\text{H-NMR}$  Data of Compounds **1–4**<sup>1</sup>.  $\delta$  in ppm,  $J$  in Hz.

	<b>1</b> <sup>a)</sup> <sup>b)</sup>	<b>2</b> <sup>a)</sup> <sup>c)</sup>	<b>3</b> <sup>a)</sup> <sup>c)</sup>	<b>4</b> <sup>c)</sup> <sup>d)</sup>
H–C(4)	6.47 ( <i>s</i> )	6.49 ( <i>s</i> )	6.48 ( <i>s</i> )	6.77 ( <i>s</i> )
H–C(6) or CH <sub>2</sub> (6)	3.75 ( <i>d</i> , $J = 4.1$ )	2.34 ( <i>dd</i> , $J = 9.7, 13.0$ , $\text{H}_\beta$ ), 2.05 ( <i>d</i> , $J = 13.0$ , $\text{H}_\alpha$ )	3.66 ( <i>d</i> , $J = 10.0$ )	6.34 ( <i>s</i> )
H–C(7) or C(7)	1.60–1.68 ( <i>m</i> )	1.77–1.84 ( <i>m</i> )	1.59–1.69 ( <i>m</i> )	
H–C(8)	1.78–1.85 ( <i>m</i> )	1.85–1.91 ( <i>m</i> )	1.78–1.82 ( <i>m</i> )	2.57–2.60 ( <i>m</i> )
CH <sub>2</sub> (9)	2.29–2.32 ( <i>m</i> , $\text{H}_\beta$ ), 1.97–2.02 ( <i>m</i> , $\text{H}_\alpha$ )	2.58–2.63 ( <i>m</i> )	2.34–2.38 ( <i>m</i> , $\text{H}_\beta$ ), 1.92–1.98 ( <i>m</i> , $\text{H}_\alpha$ )	2.51–2.55 ( <i>m</i> , $\text{H}_\beta$ ), 2.08–2.11 ( <i>m</i> , $\text{H}_\alpha$ )
H–C(11)	6.38 ( <i>s</i> )	6.71 ( <i>s</i> )	6.51 ( <i>s</i> )	6.47 ( <i>s</i> )
Me(17)	0.89 ( <i>d</i> , $J = 6.8$ )	0.79 ( <i>d</i> , $J = 7.1$ )	0.85 ( <i>d</i> , $J = 8.8$ )	1.16 ( <i>d</i> , $J = 6.9$ )
Me(18) or CH <sub>2</sub> (18)	0.86 ( <i>d</i> , $J = 7.1$ )	1.00 ( <i>d</i> , $J = 7.2$ )	0.90 ( <i>d</i> , $J = 8.5$ )	4.94 ( <i>s</i> , $\text{H}_\alpha$ ), 4.63 ( <i>s</i> , $\text{H}_\beta$ )
OCH <sub>2</sub> O	5.93 ( <i>d</i> , $J = 1.33$ )		6.00 ( <i>d</i> , $J = 1.8$ )	5.94 ( <i>s</i> ), 5.91 ( <i>s</i> )
OCH <sub>2</sub> O	6.00 ( <i>d</i> , $J = 1.24$ )			6.03 ( <i>s</i> )
1-MeO	3.89 ( <i>s</i> ) <sup>e)</sup>	3.53 ( <i>s</i> )	3.73 ( <i>s</i> )	3.73 ( <i>s</i> ) <sup>f)</sup>
2-MeO		3.84 ( <i>s</i> )		
3-MeO		3.88 ( <i>s</i> )		
6-MeO	3.03 ( <i>s</i> )		3.02 ( <i>s</i> )	
12-MeO		3.92 ( <i>s</i> )		
13-MeO		3.83 ( <i>s</i> )	3.92 ( <i>s</i> )	
14-MeO	3.80 ( <i>s</i> ) <sup>e)</sup>		3.74 ( <i>s</i> )	3.78 ( <i>s</i> ) <sup>f)</sup>
12-OH			5.70 ( <i>s</i> )	
Ang or Tig		Tig		Ang
H–C( $\beta$ )		6.81 ( <i>dd</i> , $J = 6.4, 12.8$ )		5.97–6.01 ( <i>m</i> )
Me( $\alpha$ )		1.71 <sup>g)</sup>		1.55 ( <i>d</i> , $J = 1.4$ )
Me( $\beta$ )		1.71 <sup>g)</sup>		1.83 ( <i>dd</i> , $J = 1.4, 7.2$ )

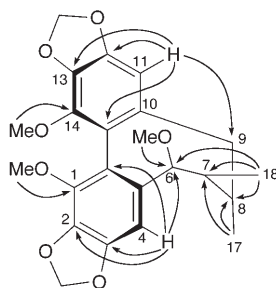
<sup>a)</sup> Measured in  $\text{CDCl}_3$ . <sup>b)</sup> Measured at 500 MHz. <sup>c)</sup> Measured at 400 MHz. <sup>d)</sup> Measured in  $(\text{D}_6)$ acetone. <sup>e)</sup> Assignments may be interchanged. <sup>f)</sup> Assignments may be interchanged. <sup>g)</sup> overlapped.

MeO groups at  $\delta(\text{H})$  3.89, 3.80 (each *s*) were located at the biphenyl rings. In the cyclooctadiene ring, the signal of an oxygenated methine at  $\delta(\text{C})$  90.1 (C(6)) and  $\delta(\text{H})$  3.75 (*d*,  $J = 4.1$ , H–C(6)), and the MeO group at  $\delta(\text{C})$  55.8,  $\delta(\text{H})$  3.03 (*s*) were observed. Further, the HMBC correlation (*Fig. 1*) between the Me group at  $\delta(\text{H})$  0.86 (*d*,  $J = 7.1$ ) and H–C(6) led to the assignment of this Me group as Me(18). Therefore, the other Me group at 0.89 (*d*,  $J = 6.8$ ) was assigned to Me(17) irreproachably. The HMBC correlations from one O–CH<sub>2</sub>–O group ( $\delta(\text{H})$  5.93) to C(12) and C(13), from the other O–CH<sub>2</sub>–O group ( $\delta(\text{H})$  6.00) to C(2) and C(3), and from two MeO groups to C(1) and C(14) indicated the arrangement of the substituents on the biphenyl rings of **1** was the same as that of gomisin R (**5**) [17]. The location of the two MeO groups was further confirmed by the ROESY correlations (*Fig. 2*) observed between H–C(4) and H–C(6), and between H–C(9) and H–C(11). The only difference to gomisin R was the variety of the substitution pattern in the cyclooctadiene ring. The HMBC correlation from the MeO group at  $\delta(\text{H})$  3.03 to H–C(6) revealed that this MeO group was directly attached to C(6). Therefore, **1** was a methyl derivative of gomisin R (**5**).

Table 2.  $^{13}\text{C}$ -NMR Data of Compounds **1–4**<sup>f</sup>.  $\delta$  in ppm.

	<b>1</b> <sup>a)</sup> <sup>b)</sup>	<b>2</b> <sup>a)</sup> <sup>c)</sup>	<b>3</b> <sup>a)</sup> <sup>c)</sup>	<b>4</b> <sup>c)</sup> <sup>d)</sup>
C(1)	141.6 (s)	151.4 (s)	150.7 (s)	142.2 (s)
C(2)	136.6 (s)	140.2 (s)	137.0 (s)	138.0 (s)
C(3)	147.5 (s)	153.1 (s)	147.4 (s)	149.4 (s)
H–C(4)	106.7 (d)	107.7 (d)	107.0 (d)	105.2 (d)
C(5)	132.8 (s)	139.6 (s)	132.7 (s)	134.2 (s)
H–C(6) or CH <sub>2</sub> (6)	90.1 (d)	35.6 (t)	90.4 (d)	79.3 (d)
H–C(7) or C(7)	38.8 (d)	40.8 (d)	38.7 (d)	150.5 (s)
H–C(8)	36.6 (d)	33.9 (d)	36.7 (d)	40.6 (d)
CH <sub>2</sub> (9)	38.1 (t)	39.3 (t)	38.4 (t)	41.1 (t)
C(10)	135.2 (s)	133.8 (s)	137.3 (s)	135.8 (s)
H–C(11)	102.4 (d)	113.2 (d)	109.2 (d)	103.0 (d)
C(12)	148.6 (s)	151.6 (s)	148.7 (s)	149.8 (s)
C(13)	134.4 (s)	140.1 (s)	137.2 (s)	135.1 (s)
C(14)	141.5 (s)	142.8 (s)	141.6 (s)	142.0 (s)
C(15)	121.4 (s)	124.0 (s)	121.5 (s)	122.0 (s)
C(16)	123.1 (s)	121.4 (s)	123.4 (s)	123.4 (s)
Me(17)	17.2 (q)	13.0 (q)	17.0 (q)	20.3 (q)
Me(18) or CH <sub>2</sub> (18)	17.2 (q)	21.5 (q)	18.0 (q)	111.5 (t)
OCH <sub>2</sub> O	100.6 (t)		101.2 (t)	101.5 (t)
OCH <sub>2</sub> O	101.1 (t)			102.3 (t)
1-MeO	59.6 (q) <sup>e)</sup>	60.5 (q)	59.6 (q)	59.6 (q) <sup>f)</sup>
2-MeO		60.8 (q)		
3-MeO		56.0 (q)		
6-MeO	55.8 (q)		55.9 (q)	
12-MeO		56.2 (q)		
13-MeO		60.8 (q)	60.7 (q)	
14-MeO	59.4 (q) <sup>e)</sup>		60.0 (q)	59.3 (q) <sup>f)</sup>
Ang or Tig		Tig		Ang
C=O		165.7 (s)		166.2 (s)
C( $\alpha$ )		128.3 (s)		128.4 (s)
H–C( $\beta$ )		137.6 (d)		139.0 (d)
Me( $\alpha$ )		14.2 (q)		20.2 (q)
Me( $\beta$ )		12.0 (q)		15.7 (q)

<sup>a)</sup> Measured in CDCl<sub>3</sub>. <sup>b)</sup> Measured at 125 MHz. <sup>c)</sup> Measured at 100 MHz. <sup>d)</sup> Measured in (D<sub>6</sub>)acetone. <sup>e)</sup> Assignments may be interchanged. <sup>f)</sup> Assignments may be interchanged.

Fig. 1. Key HMBC correlations of compound **1**

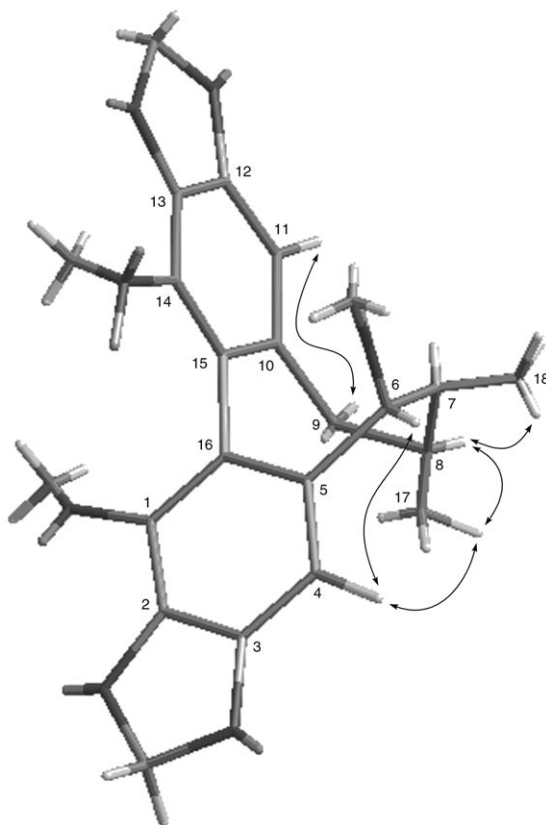


Fig. 2. Key ROESY correlations of compound **1**)

The ROESY spectrum of **1** showed a correlation peak between Me(17) and H–C(4). Furthermore, two Me groups of **1** appeared at  $\delta(\text{C})$  17.2, which differed from those of dibenzocyclooctadiene lignans possessing a twist-boat-chair (TBC) conformation of the cyclooctadiene ring (commonly, the chemical shifts of two Me groups in those possessing a twist-boat (TB) conformation are near; while, the data of those having a TBC conformation have larger difference) [17–19]. The above discussed observations indicated that **1** possessed a TB conformation of the cyclooctadiene ring. A ROESY correlation observed between H–C(4) and H–C(6) indicated that the MeO group was located in  $\beta$ -position [18].

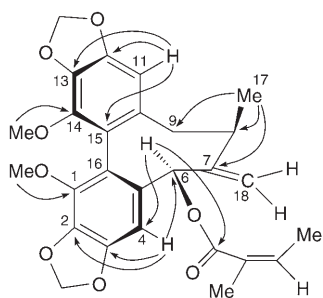
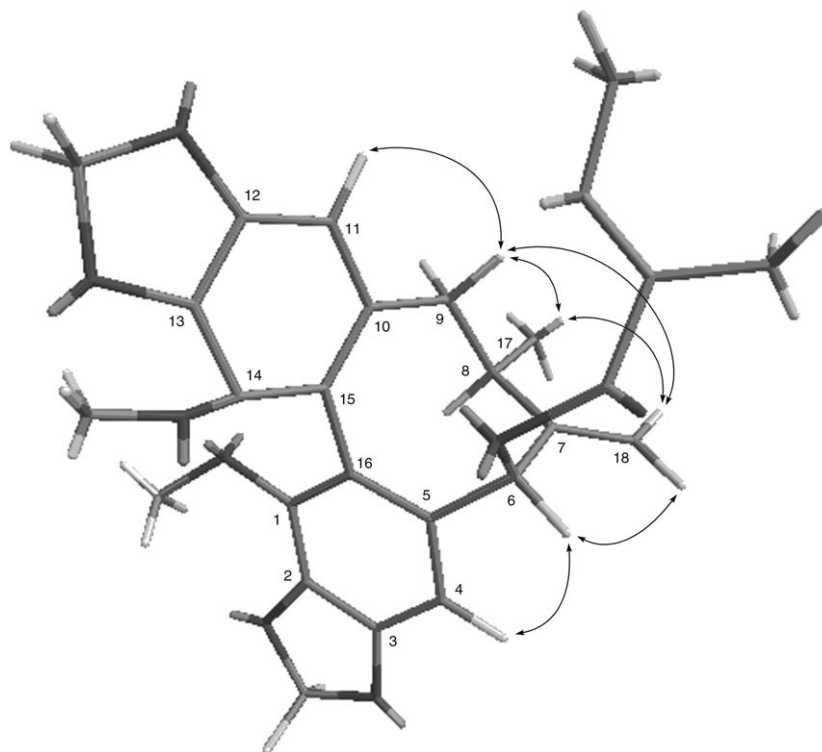
Compound **2** was isolated as yellowish oil and its molecular formula was determined to be  $\text{C}_{28}\text{H}_{36}\text{O}_7$  by means of HR-ESI-MS ( $m/z$  485.2538,  $[M+H]^+$ ) with 11 degrees of unsaturation. The structure of **2** was established from its 1D-NMR, HSQC, HMBC, and ROESY data as (a*R*)-(6*R*,7*S*)-5,6,7,8-tetrahydro-2,3,10,11,12-pentamethoxy-6,7-dimethyldibenzo[*a,c*]cycloocten-1-yl (2*E*)-2-methyl-2-butenoate.

The 1D-NMR spectra revealed that **2** possessed five MeO groups ( $\delta(\text{H})$  3.53, 3.84, 3.83, 3.92, 3.88 (each *s*)) and one tigloyloxy group ( $\delta(\text{C})$  165.7, 128.3, 137.6, 14.2, 12.0) on the aromatic rings, and also two secondary Me groups at  $\delta(\text{H})$  0.79 (*d*,  $J = 7.1$ ), 1.00 (*d*,  $J = 7.2$ ), and two benzylic CH<sub>2</sub> groups ( $\delta(\text{H})$  2.05 (*d*,  $J = 13.0$ , 1 H); 2.34 (*dd*,  $J = 9.7$ , 13.0, 1 H); 2.58–2.63 (*m*, 2 H)) in the cyclooctadiene ring. The MS, with significant peaks at *m/z* 402 ( $[\text{M} - 82]^+$ ), 83 ( $[\text{Me} - \text{CH} = \text{C}(\text{Me})\text{CO}]^+$ ), and 55 ( $[\text{Me} - \text{CH} = \text{C} - \text{Me}]^+$ ), supported the presence of a tigloyloxy group on **2** [20]. HMBC Correlations were observed between five MeO groups and C(1), C(2), C(3), C(12), and C(13)<sup>1</sup>, respectively, which suggested that the tigloyloxy group was placed at C(14). Further, the ROESY correlations between H–C(4) and H <sub>$\alpha$</sub> –C(6), Me(17) and H–C(9), as well as between H–C(9) and H–C(11) indicated a TBC conformation for the cyclooctadiene ring [21]. Thus, the structure of **2** was fully corroborated as the 14-tigloyl derivative of (+)-gomisin K<sub>3</sub> (**6**).

Compound **3**, a colorless oil, had the molecular formula C<sub>23</sub>H<sub>28</sub>O<sub>7</sub> as revealed by its HR-ESI-MS (*m/z* 439.1734,  $[\text{M} + \text{Na}]^+$ ). Detailed comparison of the 1D- and 2D-NMR spectra of **3** with those of **1** revealed that they had the same substitution pattern in the cyclooctadiene ring, but different substituents at the biphenyl rings. Correlations from the O–CH<sub>2</sub>–O group ( $\delta(\text{H})$  6.00) to C(2) and C(3)<sup>1</sup>, from the MeO groups ( $\delta(\text{H})$  3.73, 3.92, 3.74) to C(1), C(13), and C(14), respectively, and from the phenolic OH group ( $\delta(\text{H})$  5.70) to C(11), C(12), and C(13) were observed in the HMBC spectrum, which confirmed that the O–CH<sub>2</sub>–O group, three MeO groups, and the phenolic OH group were attached to C(2), C(3), C(1), C(13), C(14), and C(12), respectively. In addition, the NOE correlations from Me(17) to H–C(4) and the Me shifts ( $\delta(\text{C})$  17.0 and 18.0) of **3** revealed the configuration in the cyclooctadiene ring of **3** was the same as that of **1**. Therefore, the structure of **3** was determined as (a*S*)-(6*R*,7*S*,8*R*)-5,6,7,8-tetrahydro-1,2,8,13-tetramethoxy-6,7-dimethylbenzo[3',4']cycloocta-[1',2':4,5]benzo[1,2-*d*][1,3]dioxol-3-ol.

Compound **4** was obtained as a white amorphous powder. The HR-ESI-MS gave a quasi-molecular ion peak at *m/z* 503.1694 ( $[\text{M} + \text{Na}]^+$ ), corresponding to the molecular formula C<sub>27</sub>H<sub>28</sub>O<sub>8</sub> with 14 degrees of unsaturation. The IR spectrum displayed a band at 1713 cm<sup>-1</sup>, suggesting the presence of an ester CO functionality. Interpretation of the 1D-NMR, HMBC, and ROESY spectral data established the structure of **4** as (a*S*)-(5*R*,7*R*)-5,6,7,8-tetrahydro-13,14-dimethoxy-7-methyl-6-methylene-1,3-benzodioxolo-[5',6':3,4]cycloocta[1,2-*f*][1,3]benzodioxol-5-yl (2*Z*)-2-methylbut-2-enoate.

The <sup>1</sup>H- and <sup>13</sup>C-NMR spectral data of **4** and schisandrene (**7**) were more or less identical concerning the biphenyl group and the cyclooctadiene moiety including their substituents [22]. The only difference was the replacement of a BzO group in schisandrene with an angeloyloxy group ( $\delta(\text{C})$  128.4, 139.0, 20.2, 15.7, and 166.2) in **4**. The presence of the angeloyloxy group was confirmed by the peaks at *m/z* 83 ( $[\text{Me} - \text{CH} = \text{C}(\text{Me})\text{CO}]^+$ ), 55 ( $[\text{Me} - \text{CH} = \text{C} - \text{Me}]^+$ ) and 398 ( $[\text{M} - 82]^+$ ) in the EI-MS [20]. The HMBC correlation (*Fig. 3*) between H–C(6)<sup>1</sup> and the CO group ( $\delta(\text{C})$  166.2) further suggested that the angeloyloxy group was attached to C(6). Strong NOE correlations observed between H–C(4) and H–C(6), H–C(11) and H <sub>$\beta$</sub> –C(9), and H <sub>$\beta$</sub> –C(9) and Me(17) suggested the  $\beta$ -orientations of both the angeloyloxy group and Me(17). In addition, the ROESY correlations (*Fig. 4*) between H–C(4) and H <sub>$\alpha$</sub> –C(6), H <sub>$\alpha$</sub> –C(6) and H <sub>$\alpha$</sub> –C(18), H <sub>$\beta$</sub> –C(18) and Me(17), H <sub>$\beta$</sub> –C(18) and H <sub>$\beta$</sub> –C(9), Me(17)

Fig. 3. Key HMBC correlations of compound **4**)Fig. 4. Key ROESY correlations of compound **4**)

and  $H_{\beta}$ -C(9), as well as  $H_{\beta}$ -C(9) and H-C(11) were observed, which was consistent only with a cyclooctadiene lignan with a TBC conformation having (6*S*)- and (8*R*)-configuration [21][22].

The known compounds were determined to be gomisin R (**5**) [17], angeloylgomisin R (**8**) [18], (+)-gomisin K<sub>3</sub> (**6**) [23], (*R*)-(+)-gomisin M<sub>1</sub> (**9**) [24], (+)-angeloylgomisin K<sub>3</sub> (**10**) [25], dimethylgomisin J (**11**) [19], interiotherin B (**12**) [18], schisantherin D (**13**) [18], *meso*-dihydroguaiaretic acid (**14**) [26], *erythro*-1-(4-hydroxy-3-methoxyphenyl)-4-[3,4-methylenedioxyphenyl]-2,3-dimethylbutane (**15**) [26], *meso*-dimethyl-

dihydroguaiaretic acid (**16**) [27], *meso*-monomethyldihydroguaiaretic acid (**17**) [27], and pregomisin (**18**) [28] by comparison of their spectral data with literature values.

The anti-HIV activities and cytotoxicities of **1**, **2** and **4**<sup>2)</sup> were tested by microtiter syncytium formation infectivity assay, using the method previously described, with AZT as a positive control [29][30]. The results are listed in Table 3. Three compounds all showed weak anti-HIV-1 activity. According to the structure – activity relationship concluded by *Chen et al.*, the aromatic OH groups are important for the anti-HIV activity of dibenzocyclooctadiene lignans [31]. Therefore, maybe the absence of aromatic OH groups in these compounds resulted in the weak anti-HIV-1 activity.

Table 3. In vitro Anti-HIV-1 Activities of Compounds **1**, **2**, and **4**

Compound	CC <sub>50</sub> [µg/ml]	EC <sub>50</sub> [µg/ml]	TI [CC <sub>50</sub> /EC <sub>50</sub> ]
<b>1</b>	68.93	16.42	4.52–3.91
<b>2</b>	27.02	17.88	1.28–1.79
<b>4</b>	141.91	52.86	8.50– > 2.09
AZT <sup>a)</sup>	> 1.00 [mg/ml]	4.00	> 250000

<sup>a)</sup> Positive control

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### Experimental Part

*General.* Column chromatography (CC) and TLC: SiO<sub>2</sub> (200–300 mesh) from *Qingdao Marine Chemical Factory*, Qingdao, P. R. China. Optical rotations: *Jasco DIP-370* digital polarimeter. UV Spectra: *UV-210A* spectrophotometer;  $\lambda_{\max}$  (log  $\epsilon$ ) in nm. CD Spectra: *JASCO J-815* spectropolarimeter;  $\lambda_{\max}$  in nm, ellipticity in mdeg. IR Spectra: *Bio-Rad FTS-135* spectrophotometer; KBr pellets; in cm<sup>-1</sup>. 1D- and 2D-NMR spectra: *Bruker AM-400* and *DRX-500* instruments; TMS as an internal standard. EI-MS: *VG Auto-Spec-3000* spectrometer; in *m/z* (rel.%). HR-ESI-MS: *API Qstar Pulsar* instrument.

*Plant Material.* The aerial parts of *Schisandra rubriflora* were collected in the Dacunqiao Mountain, Yunnan Province, P. R. China, in June 2004, and identified by Prof. *Hong Wang*, Kunming Institute of Botany. A voucher specimen (03-0033) has been deposited in the Herbarium of the Kunming Institute of Botany, Chinese Academy of Sciences.

*Extraction and Isolation.* The air-dried and powdered aerial parts (9 kg) of *Schisandra rubriflora* were extracted with 95% aq. EtOH (4 times) at r.t. to yield the extract, which was dissolved in H<sub>2</sub>O and then extracted successively with petroleum ether and AcOEt. The AcOEt extract (195 g) was decolorized with *MCI-gel CHP-20P* column (90% MeOH/H<sub>2</sub>O) and then subjected to SiO<sub>2</sub> CC, eluting with CHCl<sub>3</sub>/MeOH (gradient 1:0, 9:1, 8:2, 7:3, 6:4, 5:5, and 0:1) to afford fractions A–C. Compounds **1**–**3** (20 mg, 9 mg, and 3 mg, resp.) were obtained from *Fr. B* by repeated SiO<sub>2</sub> CC, and reverse phase CC. *Fr. A* was repeatedly separated by SiO<sub>2</sub> CC, and then purified on semipreparative HPLC (*Agilent-1100* HPLC system, *Zorbax SB-C-18* (*Agilent*), 9.4 mm × 25 cm, 75 % MeOH/H<sub>2</sub>O) to give **4** (3 mg).

<sup>2)</sup> The lack of sufficient material prevented us from testing compound **3** for its anti-HIV-1 activity.



*Methylgomisin R* (= (aS)-(5R,6S,7S)-5,6,7,8-Tetrahydro-5,13,14-trimethoxy-6,7-dimethyl-1,3-benzodioxolo[5',6':3,4]cycloocta[1,2-f][1,3]benzodioxole; **1**). Yellowish amorphous powder.  $[\alpha]_D^{27} = +36.4$  ( $c = 0.82$ ,  $\text{CHCl}_3$ ). UV (MeOH): 215 (4.65), 257 (sh), 282 (3.58). CD ( $c = 0.04$ , MeOH): 234 (+50.52), 257 (–50.33). IR (KBr): 2956, 2925, 2877, 2855, 1477, 1269, 1207, 1084, 1072, 1048.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR: *Tables 1* and *2*. EI-MS: 415 (20,  $[M+H]^+$ ), 414 (83,  $M^+$ ), 383 (27), 382 (100), 327 (25), 297 (29). HR-ESI-MS (pos.): 437.1561 ( $[M+Na]^+$ ,  $\text{C}_{23}\text{H}_{26}\text{NaO}_7^+$ ; calc. 437.1576).

(+)-14-Tigloylgomisin *K*<sub>3</sub> (= (aR)-(6R,7S)-5,6,7,8-Tetrahydro-2,3,10,11,12-pentamethoxy-6,7-dimethyl-dibenzof[a,c]cycloocten-1-yl (2E)-2-Methyl-2-butenolate; **2**). Yellowish oil.  $[\alpha]_D^{27} = +71.7$  ( $c = 0.33$ ,  $\text{CHCl}_3$ ). CD ( $c = 0.05$ , MeOH): 235 (+108.26), 248 (+97.03).  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR: *Tables 1* and *2*. EI-MS: 485 (15,  $[M+H]^+$ ), 484 (51,  $M^+$ ), 403 (25), 402 (100), 83 (97), 55 (24). HR-ESI-MS (pos.): 485.2538 ( $[M+H]^+$ ,  $\text{C}_{28}\text{H}_{37}\text{O}_7^+$ ; calc. 485.2539).

12-Demethylwuweilignan *I* (= (aS)-(6S,7S,8R)-5,6,7,8-Tetrahydro-1,2,8,13-tetramethoxy-6,7-dimethylbenzof[3',4']cycloocta[1',2'-f][1,3]benzodioxol-3-yl (2Z)-2-Methylbut-2-enoate; **3**). Colorless oil.  $[\alpha]_D^{25} = +8.3$  ( $c = 0.10$ ,  $\text{CHCl}_3$ ). CD ( $c = 0.04$ , MeOH): 222 (+19.28), 255 (–38.64). IR (KBr): 3441, 2955, 2929, 2872, 1478, 1467, 1074.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR: *Tables 1* and *2*. EI-MS: 417 (23,  $[M+H]^+$ ), 416 (95,  $M^+$ ), 385 (29), 384 (100), 329 (17), 315 (11), 299 (16), 297 (20), 165 (10), 164 (12). HR-ESI-MS (pos.): 439.1734 ( $[M+Na]^+$ ,  $\text{C}_{23}\text{H}_{28}\text{NaO}_7^+$ ; calc. 439.1732).

*Schisandrene A* (= (aS)-(5R,7R)-5,6,7,8-Tetrahydro-13,14-dimethoxy-7-methyl-6-methylene-1,3-benzodioxolo[5',6':3,4]cycloocta[1,2-f][1,3]benzodioxol-5-yl (2Z)-2-Methylbut-2-enoate; **4**). White amorphous powder.  $[\alpha]_D^{25} = +67.8$  ( $c = 0.12$ , acetone). UV (MeOH): 219 (4.69), 267 (sh), 282 (3.53). CD ( $c = 0.05$ , MeOH): 237 (+57.22), 259 (–39.74). IR (KBr): 3097, 2955, 2922, 2884, 2852, 1713, 1477, 1364, 1271, 1254, 1210, 1153, 1135, 1091, 1053, 984, 939, 899, 832.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR: *Tables 1* and *2*. EI-MS: 481 (28,  $[M+H]^+$ ), 480 (100,  $M^+$ ), 398 (7), 397 (29), 381 (21), 380 (61), 365 (41), 349 (88), 335 (29), 326 (34), 319 (50), 83 (60), 55 (42). HR-ESI-MS (pos.): 503.1694 ( $[M+Na]^+$ ,  $\text{C}_{27}\text{H}_{28}\text{NaO}_8^+$ ; calc. 503.1681).

## REFERENCES

- [1] W.-Z. Song, P.-G. Xiao, *Chin. Trad. Herbal Drugs* **1982**, *13*, 40.
- [2] R.-T. Li, W. Xiang, S.-H. Li, Z.-W. Lin, H.-D. Sun, *J. Nat. Prod.* **2004**, *67*, 94.
- [3] J.-X. Pu, W.-L. Xiao, Y. Lu, R.-T. Li, H.-M. Li, L. Zhang, S.-X. Huang, X. Li, Q.-S. Zhao, Q.-T. Zheng, H.-D. Sun, *Org. Lett.* **2005**, *7*, 5079.
- [4] W.-L. Xiao, L.-M. Yang, N.-B. Gong, L. Wu, R.-R. Wang, J.-X. Pu, X.-L. Li, S.-X. Huang, Y.-T. Zheng, R.-T. Li, Y. Lu, Q.-T. Zheng, H.-D. Sun, *Org. Lett.* **2006**, *8*, 991.
- [5] Y.-G. Chen, Y.-Y. Xie, K.-F. Cheng, K.-K. Cheung, G.-W. Qin, *Phytochemistry* **2001**, *58*, 1277.
- [6] L. Opletal, H. Sovová, M. Bártilová, *J. Chromatogr., B* **2004**, *812*, 357.
- [7] R.-T. Li, Q.-S. Zhao, S.-H. Li, Q.-B. Han, H.-D. Sun, Y. Lu, L.-L. Zhang, Q.-T. Zheng, *Org. Lett.* **2003**, *5*, 1023.
- [8] R.-T. Li, W.-L. Xiao, Y.-H. Shen, Q.-S. Zhao, H.-D. Sun, *Chem.–Eur. J.* **2005**, *11*, 2989.
- [9] W.-L. Xiao, H.-J. Zhu, Y.-H. Shen, R.-T. Li, S.-H. Li, H.-D. Sun, Y.-T. Zheng, R.-R. Wang, Y. Lu, C. Wang, Q.-T. Zheng, *Org. Lett.* **2005**, *7*, 2145.
- [10] S.-X. Huang, R.-T. Li, J.-P. Liu, Y. Lu, Y. Chang, C. Lei, W.-L. Xiao, L.-B. Yang, Q.-T. Zheng, H.-D. Sun, *Org. Lett.* **2007**, *9*, 2079.
- [11] Y. Tang, Y. Zhang, M. Dai, T. Luo, L. Deng, J. Chen, Z. Yang, *Org. Lett.* **2005**, *7*, 885.
- [12] Y.-D. Zhang, Y.-F. Tang, T.-P. Luo, J. Shen, J.-H. Chen, Z. Yang, *Org. Lett.* **2006**, *8*, 107.
- [13] Y.-C. Shen, Y.-C. Lin, M. Y. Chiang, S. F. Yeh, Y.-B. Cheng, C.-C. Liao, *Org. Lett.* **2005**, *7*, 3307.
- [14] R.-T. Li, Ph.D. Thesis, Kunming Institute of Botany, Chinese Academy of Sciences, 2004.
- [15] Y. Ikeya, H. Taguchi, I. Yosioka, H. Kobayashi, *Chem. Pharm. Bull.* **1979**, *27*, 1383.
- [16] H.-R. Li, Y.-L. Feng, Z.-G. Yang, J. Wang, A. Daikonya, S. Kitanaka, L.-Z. Xu, S.-L. Yang, *Chem. Pharm. Bull.* **2006**, *54*, 1022.
- [17] Y. Ikeya, H. Taguchi, I. Yosioka, *Chem. Pharm. Bull.* **1982**, *30*, 3207.
- [18] D.-F. Chen, S.-X. Zhang, K. Chen, B.-N. Zhou, P. Wang, L. M. Cosentino, K.-H. Lee, *J. Nat. Prod.* **1996**, *59*, 1066.

- [19] Y. Ikeya, H. Taguchi, H. Sasaki, K. Nakajima, I. Yosioka, *Chem. Pharm. Bull.* **1980**, 28, 2414.
- [20] H.-B. Zhai, P.-Z. Cong, *Acta Pharm. Sin.* **1990**, 25, 110.
- [21] M. Chen, Z. Liao, D. Chen, *Helv. Chim. Acta* **2004**, 87, 1368.
- [22] Y.-W. Choi, S. Takamatsu, S. I. Khan, P. V. Srinivas, D. Ferreira, J. Zhao, I. A. Khan, *J. Nat. Prod.* **2006**, 69, 356.
- [23] Y. Ikeya, H. Taguchi, I. Yosioka, *Chem. Pharm. Bull.* **1980**, 28, 2422.
- [24] R. Tan, L.-N. Li, Q. Fang, *Planta Med.* **1984**, 414.
- [25] C. Lei, S.-X. Huang, J.-J. Chen, J.-X. Pu, L.-B. Yang, Y. Zhao, J.-P. Liu, X.-M. Gao, W.-L. Xiao, H.-D. Sun, *Chem. Pharm. Bull.* **2007**, 55, 1281.
- [26] N. Nakatani, K. Ikeda, H. Kikuzaki, M. Kido, Y. Yamaguchi, *Phytochemistry* **1988**, 27, 3127.
- [27] M. Miyazawa, H. Kasahara, H. Kameoka, *Phytochemistry* **1997**, 46, 1173.
- [28] Y. Ikeya, H. Taguchi, I. Yosioka, *Chem. Pharm. Bull.* **1978**, 26, 682.
- [29] Y.-J. Zhang, J.-H. Wang, W.-H. Lee, Q. Wang, H. Liu, Y.-T. Zheng, Y. Zhang, *Biochem. Biophys. Res. Commun.* **2003**, 309, 598.
- [30] J.-H. Wang, H.-L. Nie, S.-C. Tam, H. Huang, Y.-T. Zheng, *FEBS Lett.* **2002**, 531, 295.
- [31] M. Chen, N. Kilgore, K.-H. Lee, D.-F. Chen, *J. Nat. Prod.* **2006**, 69, 1697.

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