Rivulobirin E and Rivulotririn C from *Pleurospermum rivulorum*

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Two new condensed furanocoumarins, the dimer rivulobirin E and the trimer rivulotririn C (1 and 2) were isolated from the underground part of *Pleurospermum rivulorum* (Umbelliferae) and their structures established by spectral means.

Key words *Pleurospermum rivulorum*; rivulobirin E; rivulotririn C; Umbelliferae

In the course of our studies on the chemical constituents of Umbelliferae species we reported the isolation of new bi-coumarins, rivulobirins A—D, and spirotricoumarins, rivulotririns A and B.[1—3] In the present study, we isolated two new condensed furanocoumarins, rivulobirin E (**1**) and rivulotririn C (**2**) from the same coumarin fraction by repeated

Table 1. ^{1}H and ^{13}C NMR Data for Rivurobirin E (**1**) in $CDCl_3$

	^{1}H	^{13}C
2 (2′)		160.21
3 (3′)	6.33 d (9.6)	114.67
4 (4′)	7.74 br d (9.6)	144.15
4a (4′a)		116.37
5 (5′)	7.34 br s	113.06
6 (6′)		126.04
7 (7′)		147.49
8 (8′)		131.52[a)]
8a (8′a)		142.90
9 (9′)	7.68 d (2.2)	146.63[b)]
10 (10′)	6.81 d (2.2)	106.69[c)]
11	4.40 dd (10.1, 5.3)	75.27[d)]
	4.55 dd (10.1, 4.2)	
12	4.03 dd (5.3, 4.2)	77.90
13		72.09
14	1.29 s	24.76
15	1.36 s	26.53
13-OH	2.25 s	
2′ (2)		160.33
3′ (3)	6.31 d (9.6)	114.43
4′ (4)	7.70 br s (9.6)	144.25
4′a (4a)		116.28
5′ (5)	7.29 br s	113.33
6′ (6)		125.90
7′ (7)		147.96
8′ (8)		131.60[a)]
8′a (8)		143.26
9′ (9)	7.67 d (2.2)	146.70[b)]
10′ (10)	6.77 d (2.2)	106.65[c)]
11′	4.55 dd (10.2, 8.6)	75.21[d)]
	4.84 dd (10.2, 2.7)	
12′	4.13 dd (8.6, 2.7)	76.27
13′		78.02
14′	1.44 s	24.18
15′	1.49 s	22.69
12′-OH	3.77 s	

Chemical shifts are in δ values and followed by multiplicities and J values (in Hz). *a—d*) Assignment may be reversed.

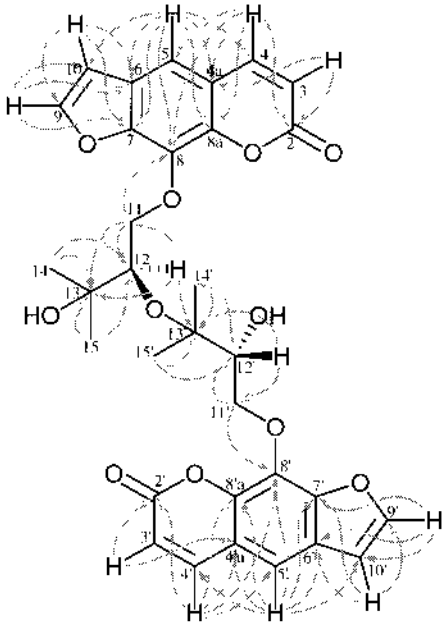

Fig. 1. HMBC Correlations of **1**

Table 2. ^{1}H NMR Data for Rivulotririn C (**2**) in $CDCl_3$

H	**2**
3	5.77 d (9.6)
4	6.85 d (9.6)
5	7.09 s
9	7.54 d (2.1)
10	6.68 d (2.1)
11	4.60 dd (10.3, 2.7)
	4.31 dd (10.3, 7.3)
12	3.74 ddd (7.3, 4.6, 2.7)
14	1.26 s
15	1.28 s
12-OH	3.55 d (4.6)
13-OH	2.80 s
3′	5.72 d (9.6)
4′	6.85 d (9.6)
5′	7.08 s
9′	7.53 d (2.1)
10′	6.68 d (2.1)
11′	4.61 dd (10.1, 6.2)
	4.43 dd (10.1, 6.2)
12′	4.85 dd (6.2, 6.2)
14′	1.41 s
15′	1.72 s
3″	6.35 d (9.6)
4″	7.73 d (9.6)
5″	7.35 s
9″	7.53 d (2.2)
10″	6.77 d (2.2)
11″	4.77 dd (10.1, 5.9)
	4.51 dd (10.1, 6.6)
12″	4.83 dd (6.6, 5.9)
14″	1.40 s
15″	1.69 s

Chemical shifts are in δ values and followed by multiplicities and J values (in Hz).

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chromatographic separation. This communication deals with the structure elucidation of **1** and **2**.

Rivulobirin E (**1**), a colorless viscous oil, was assigned the molecular formula $C_{32}H_{30}O_{11}$ ($[M+H]^+$ *m/z* 591.1857) by HR-SIMS. The NMR (Table 1) signal pattern of **1** is closely related to those of rivulobirin A except for the presence of signals due to two pairs of the 3-methylbutyl-1,2,3-trioxy group instead of the signals due to a 3-methyl-3-butenyl-1,2-dioxy group and a 3-methylbutyl-1,2,3-trioxy group. Thus **1** was assumed to be a *tert*-O-heraclenyl-heraclenol. The entire structure of **1** was determined by extensive 2D-NMR experiments [^{1}H-^{1}H COSY, HMQC, HMBC (Fig. 1) and NOESY spectra]. The determination of the absolute configuration of C-12′ in **1** was carried out by the modified Mosher's method. Further more, the configuration of the C-12 position was assumed to be *R* based on the fact that C-12′ in **1** and C-12 in furanocoumarins previously isolated from this plant have the same configuration.

Rivulotririn C (**2**), a colorless viscous oil, was assigned the molecular formula $C_{48}H_{44}O_{16}$ ($[M]^+$ *m/z* 876.2629) by HR-EI-MS. The ^{1}H-NMR (Table 2) spectrum of **2** showed the presence of three C-8-substituted linear-type furanocoumarin units and three sets of a 3-methylbutyl-1,2,3-trioxy group. Thus **2** was presumed to be a structure resulting from the condensation of three heraculenol units. However, in ^{13}C-NMR (Table 3) only one lactone carbonyl carbon signal and two orthoester carbon signals were observed, indicating that two of three lactone moieties were replaced by the spiro form in **2**. The entire structure including the relative configuration was determined by the analysis of 2D-NMR experiments

Table 3. ^{13}C NMR Data for Rivulotririn C (**2**) in $CDCl_3$

C	**2**
2	117.36[a)]
3	119.55
4	129.54[e)]
4a	117.10[a)]
5	113.15[c)]
6	122.76[d)]
7	147.34
8	131.75[f)]
8a	141.25[g)]
9	144.91[h)]
10	106.70[b)]
11	75.27
12	75.74
13	71.56
14	26.66
15	25.18
2′	117.54[a)]
3′	119.19
4′	129.88[e)]
4′a	117.23[a)]
5′	113.32[c)]
6′	122.86[d)]
7′	147.51
8′	131.89[f)]
8′a	141.54[g)]
9′	144.94[h)]
10′	106.80[b)]
11′	70.85
12′	81.13
13′	83.26
14′	22.59
15′	27.15
2″	160.10
3″	114.84
4″	144.15
4″a	116.48
5″	113.69
6″	126.01
7″	147.86
8″	131.27
8″a	143.23
9″	146.81
10″	106.70
11″	72.21
12″	80.76
13″	83.15
14″	22.59
15″	27.42

Chemical shifts are in δ values. *a*—*h*) Assignment may by reversed.

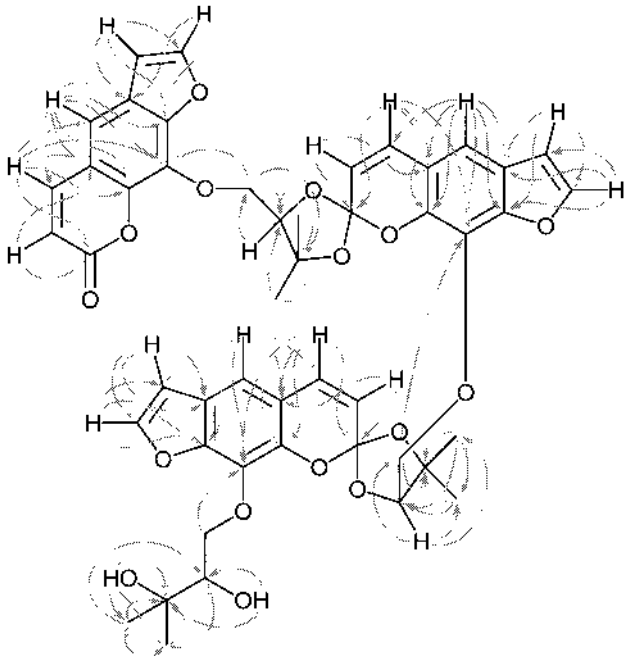

Fig. 2. HMBC Correlations of **2**

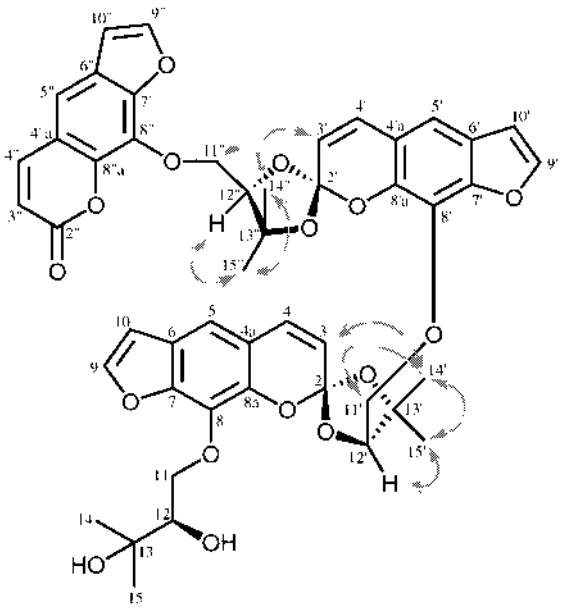

Fig. 3. NOE Correlations of **2**

[^{1}H-^{1}H COSY, HMQC, HMBC (Fig. 2) and NOESY (Fig. 3) spectra]. Compound **2** is the first example of a trifuranocoumarin bearing two orthoester moieties.

Recently, several components have been isolated from grapefruit juice which showed strong inhibitory effects on CYP3A activity and their structure identified them as furanocoumarin derivatives.[4] Thus the furanocoumarin derivatives isolated from Umbelliferous plants including *P. rivulorum* were also tested. As a result, the most linear furanocoumarins examined showed inhibitory effects on CYP3A activity. The dimer derivatives rivulobirin A, C, and D, and the trimer derivative, rivulotririn A showed especially strong inhibitory effects, with an IC_{50} value similar to that of the typical CYP3A inhibitor ketoconazole. Further biological studies on those compounds are now in progress, and the details will be reported elsewhere.

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