Structures of Furobinordentatin and Furobiclausarin, Two Novel Bicoumarins from *Citrus* Plants[1)]

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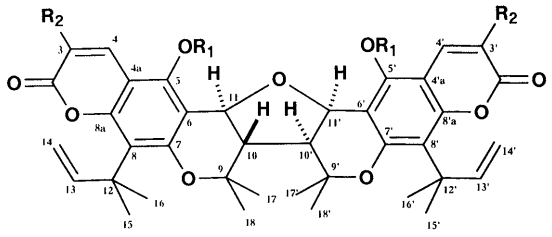
Two novel bicoumarins named furobinordentatin (1) and furobiclausarin (3) have been isolated from the roots of *Citrus yuko* and *C. hassaku*, respectively. The structures were elucidated by single crystal X-ray analysis and/or spectroscopic studies as 1 and 3. The structural characteristic of these new bicoumarins is the presence of a tetrahydrofuran ring connecting two nordentatin or clausarin units.

Keywords furobinordentatin; furobiclausarin; bicoumarin; *Citrus yuko*; *Citrus hassaku*; crystal structure

In our continuing phytochemical studies on the constituents of *Citrus* plants (Rutaceae), we have reported the isolation and structure elucidation of many new acridone alkaloids and coumarins. Acridone alkaloid and coumarin dimers (acrimarines-A—-N[2,3)] and neoacrimarines-A—-E[3,4)]) and dimeric coumarins (khelmarins-A, -B,[5)] -C,[6)] bisosthenon,[7)] bisclausarin,[8)] nordenletin,[9)] citrumarins-A—-D,[10)] hassmarin,[11)] bisparasin,[12)] claudimerin-A,[13)] bisnorponcitrin and bishassanidin[6)]) are unique constituents of this genus. Further investigation on the constituents of *C. yuko* and *C. hassaku* has afforded two novel type bicoumarins named furobinordentatin and furobiclausarin. This paper deals with the structure elucidations of these new compounds.



1 : $R_1=R_2=H$
2 : $R_1=Me$, $R_2=H$
3 : $R_1=H$, $R_2=1,1$-dimethylallyl

Chart 1

Furobinordentatin (1) Furobinordentatin (**1**) was isolated from the roots of *C. yuko* HORT. ex TANAKA as colorless cubes, mp 225—227 °C, $[\alpha]_D \pm 0°$ ($CHCl_3$). The high-resolution mass spectrum (HR-MS) showed a molecular ion peak at *m/z* 640.2675, indicating the

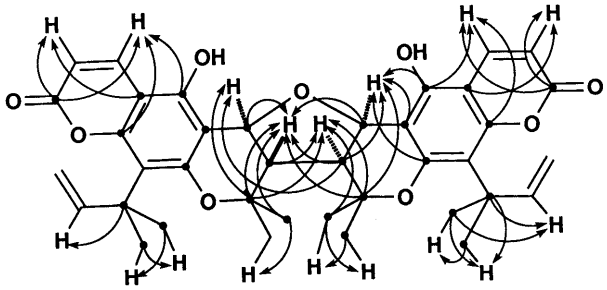


Fig. 1. C–H Long-Range Correlations in the HMBC Spectrum of Furobinordentatin (**1**)

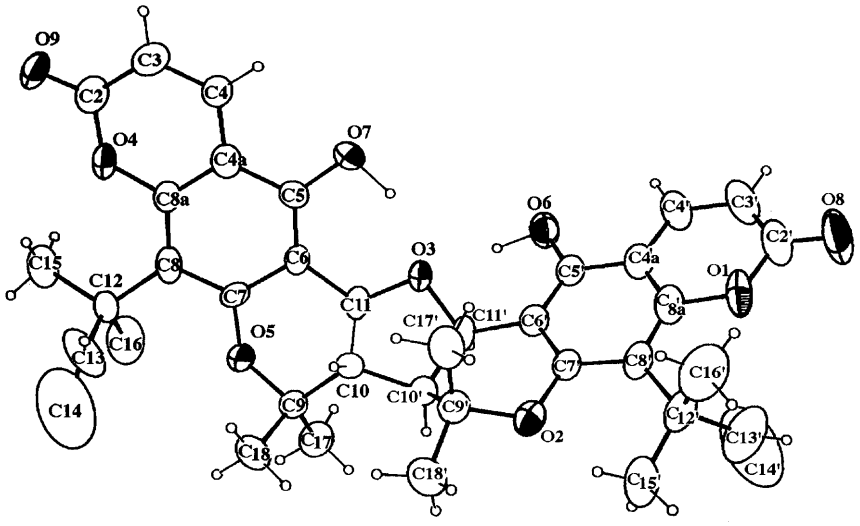


Fig. 2. Perspective View of Furobinordentatin (**1**) with Atomic Numberings

molecular formula $C_{38}H_{40}O_9$. The IR (1720, 1625 cm^{-1}) and UV [213, 228 (sh), 265, 283, 329 nm] absorptions indicated the presence of a coumarin skeleton.[14] The ^{1}H-NMR spectrum showed signals due to two pairs of coumarin H-4 and H-3 [δ 8.19, 6.19, 8.03, 6.12 (each 1H, d, J=9.5 Hz)], and two 1,1-dimethylallyl groups [δ 6.23, 6.22 (each 1H, dd, J=17.6, 11.0 Hz), 4.84, 4.81 (each 1H, d, J=17.6 Hz), 4.82, 4.80 (each 1H, d, J=11.0 Hz), 1.61, 1.58 (each 3H, s), 1.57 (6H, s)]. The remaining four proton signals [δ 4.72 (1H, d, J=11.0 Hz), 1.90 (1H, dd, J=8.1, 11.0 Hz), 2.70 (1H, t, J=8.1 Hz), 5.17 (1H, d, J=8.1 Hz)] in the ^{1}H-NMR spectrum, coupled with the four carbon signals (δ 73.86, 52.08, 45.60, 74.40) in the ^{13}C-NMR spectrum, indicated the presence of the partial structure –(O)–C(11)H–C(10)H–C(10′)H–C(11′)H–(O)–. Further information was obtained from the analysis of the ^{1}H–^{1}H shift correlation spectroscopy (COSY), heteronuclear multiple quantum coherence (HMQC) and heteronuclear multiple-bond connectivity (HMBC) spectra. In the HMBC spectrum (Fig. 1), ^2J and ^3J correlations were observed for H-11′ (δ 5.17)/C-6′ (δ 106.61), C-7′ (δ 155.23), C-9′ (δ 77.87) and C-10′ (δ 45.60), indicating the linear orientation of the pyranocoumarin nucleus. Treatment of **1** with diazomethane afforded the *O*,*O*′-dimethyl ether (**2**). A series of difference nuclear Overhauser effect (NOE) experiments was carried out on **2** in order to determine the orientation of the pyranocoumarin nuclei and the relative stereochemistry of the molecule. Irradiation of the methoxy signal at δ 4.12 (5′-MeO) induced increments of the signals at δ 7.93 (H-4′) and 5.13 (H-11′). When another methoxy signal at δ 3.75 (5-MeO) was irradiated, increments were observed in the signals at δ 7.87 (H-4) and 4.69 (H-11). These results supported the linear orientation of the two pyranocoumarin nuclei. NOEs were also observed between the signals at δ 5.13 (H-11′), 2.41 (H-10′) and 4.69 (H-11) indicating *cis* relationships of these three protons. On the basis of the above results, the structure of furobinordentatin was assigned as **1**, composed of two nordentatin[15] units which are linked to each other with the formation of a tetrahydrofuran ring.

Because this was of the first example of a bicoumarin linked between linear pyranocoumarins by the formation of a tetrahydrofuran ring, a definitive structure was established by X-ray crystallographic analysis. A suitable crystal of furobinordentatin was obtained by slow evaporation of its acetone solution. Crystal data are as follows: triclinic, space group $P\bar{1}$, a=9.768 (1), b=12.706 (1), c=13.847 (3) Å; α=80.79 (1), β=81.87 (1), γ=82.07 (1)°; V=1667 (4) Å^3; Z=2; D_c=1.276 g/cm^3. A molecule of furobinordentatin found in an asymmetric unit is displayed in Fig. 2. The molecule has a dimeric feature of two nordentatin units joined at the central tetrahydrofuran ring. The positional parameters, individual bond lengths and bond angles are listed in Tables I, II and III, respectively. Bond lengths in general accord with expected values. However, a marked conformational and configurational dissymmetry was concentrated in the central rings; two torsion angles, C6′–C11′–C10′–C9′ (22.3°) and C6–C11–C10–C9 (69.1°), indicate *cis* and *trans* arrangements, respectively, of two dihydropyran rings fused on the sides of the tetrahydrofuran ring. The two dihydropyran rings adopt different conformations, (pseudo-)boat for C6′---C9′ and twisted-chair for C6---C9.

TABLE I. Positional Parameters and Their Estimated Standard Deviations

Atom	x	y	z	B (Å^2)
O1	0.9701 (7)	−0.1902 (4)	1.0026 (4)	4.9 (2)
O2	0.7026 (5)	−0.0539 (4)	0.7412 (4)	3.6 (1)
O3	0.9091 (5)	0.1931 (4)	0.6523 (3)	2.8 (1)
O4	0.7786 (5)	0.6887 (4)	0.4494 (3)	3.2 (1)
O5	0.7562 (5)	0.3302 (4)	0.4014 (3)	3.1 (1)
O6	1.1428 (6)	0.0672 (4)	0.7470 (4)	3.9 (1)
O7	0.9049 (6)	0.4042 (4)	0.6961 (4)	3.7 (1)
O8	1.0828 (8)	−0.2533 (6)	1.1302 (5)	7.5 (2)
O9	0.7860 (6)	0.8573 (4)	0.4635 (4)	4.0 (1)
C8′a	0.955 (1)	−0.1255 (6)	0.9131 (6)	3.8 (2)
C2′	1.083 (1)	−0.1971 (7)	1.0527 (6)	5.1 (3)
C3′	1.193 (1)	−0.1347 (8)	1.0056 (7)	5.4 (3)
C4′	1.182 (1)	−0.0688 (7)	0.9195 (6)	4.5 (2)
C4′a	1.0575 (9)	−0.0615 (6)	0.8734 (5)	3.4 (2)
C5′	1.0390 (8)	0.0081 (6)	0.7849 (5)	3.0 (2)
C6′	0.9185 (8)	0.0125 (5)	0.7430 (5)	2.7 (2)
C11′	0.8983 (8)	0.0801 (5)	0.6457 (5)	3.0 (2)
C10′	0.7592 (8)	0.0825 (5)	0.6050 (5)	2.6 (2)
C9′	0.6471 (8)	0.0501 (6)	0.6909 (5)	3.2 (2)
C7′	0.8199 (8)	−0.0557 (5)	0.7857 (5)	2.9 (2)
C8′	0.8340 (9)	−0.1303 (6)	0.8721 (5)	3.6 (2)
C17′	0.6134 (8)	0.1282 (6)	0.7661 (5)	3.8 (2)
C18′	0.5185 (9)	0.0268 (7)	0.6531 (7)	4.9 (2)
C12′	0.726 (1)	−0.2066 (6)	0.9236 (6)	4.3 (2)
C15′	0.602 (1)	−0.2167 (9)	0.8642 (7)	7.4 (3)
C16′	0.661 (1)	−0.1700 (9)	1.0214 (7)	6.9 (3)
C13′	0.793 (1)	−0.3205 (9)	0.9445 (9)	7.0 (4)
C14′	0.883 (3)	−0.367 (2)	0.899 (1)	16.8 (9)
C8a	0.7928 (7)	0.5797 (6)	0.4811 (5)	2.7 (2)
C2	0.7953 (8)	0.7649 (6)	0.5047 (6)	3.3 (2)
C3	0.8247 (8)	0.7288 (6)	0.6022 (6)	3.4 (2)
C4	0.8478 (8)	0.6212 (6)	0.6359 (5)	3.1 (2)
C4a	0.8349 (8)	0.5437 (6)	0.5746 (5)	3.0 (2)
C5	0.8596 (8)	0.4332 (6)	0.6056 (5)	2.8 (2)
C6	0.8399 (7)	0.3630 (5)	0.5459 (5)	2.3 (2)
C11	0.8658 (8)	0.2432 (5)	0.5607 (5)	2.7 (2)
C10	0.7351 (7)	0.1985 (5)	0.5518 (5)	2.6 (2)
C9	0.7072 (8)	0.2245 (6)	0.4440 (5)	3.0 (2)
C7	0.7829 (7)	0.4025 (5)	0.4564 (5)	2.5 (2)
C8	0.7630 (8)	0.5126 (6)	0.4180 (5)	3.0 (2)
C17	0.791 (1)	0.1480 (7)	0.3784 (6)	4.8 (2)
C18	0.5523 (9)	0.2377 (7)	0.4323 (6)	4.7 (2)
C12	0.7076 (8)	0.5473 (6)	0.3165 (5)	3.6 (2)
C15	0.717 (1)	0.6661 (7)	0.2743 (6)	6.0 (3)
C16	0.795 (1)	0.4854 (8)	0.2403 (7)	6.9 (3)
C13	0.554 (1)	0.5312 (9)	0.3319 (8)	7.1 (3)
C14A	0.722 (3)	0.437 (2)	0.178 (1)	9.8 (9)[a]
C14B	0.513 (3)	0.491 (3)	0.255 (2)	14 (1)[a]

a) Occupancy of these atoms is 0.5.

Furobiclausarin (3) Furobiclausarin (**3**) was obtained from *Citrus hassaku* as a yellow oil, $[\alpha]_D \pm 0°$ ($CHCl_3$). The molecular formula $C_{48}H_{56}O_9$ was obtained by HR-MS (M^+, 776.3902). The IR (1705, 1620, 1580 cm^{-1}) and UV (213, 268, 295, 323 nm) spectra showed the presence of coumarin as a nucleus.[14] As shown in Table IV, the signal patterns were similar to those of furobinordentatin (**1**) except for the absence of AB-type signals of coumarin H-4 and H-3 and the appearance of two H-4 singlets at δ 7.96 and 7.78. The additional signals at δ 6.13, 6.08 (each 1H, dd, J=17.6, 11.0 Hz), 5.00, 5.03 (each 1H, d, J=11.0 Hz), 4.99, 5.04 (each 1H, d,

TABLE II. Bond Distances (Å) with Estimated Standard Deviations in Parentheses

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
O1	C2′	1.37 (1)	C4′	C4′a	1.44 (1)	C2	C3	1.41 (1)
O1	C8′a	1.388 (9)	C4′a	C5′	1.41 (1)	C3	C4	1.37 (1)
O2	C7′	1.371 (8)	C5′	C6′	1.37 (1)	C4	C4a	1.43 (1)
O2	C9′	1.464 (8)	C6′	C7′	1.391 (9)	C4a	C5	1.40 (1)
O3	C11	1.418 (7)	C6′	C11′	1.500 (9)	C5	C6	1.358 (9)
O3	C11′	1.472 (8)	C11′	C10′	1.54 (1)	C6	C7	1.420 (9)
O4	C2	1.366 (9)	C10′	C10	1.542 (9)	C6	C11	1.494 (9)
O4	C8a	1.378 (8)	C10′	C9′	1.54 (1)	C11	C10	1.494 (9)
O5	C7	1.356 (8)	C9′	C18′	1.51 (1)	C10	C9	1.531 (9)
O5	C9	1.491 (8)	C9′	C17′	1.52 (1)	C9	C17	1.51 (1)
O6	C5′	1.342 (9)	C7′	C8′	1.413 (9)	C9	C18	1.53 (1)
O7	C5	1.367 (8)	C8′	C12′	1.55 (1)	C7	C8	1.411 (9)
O8	C2′	1.19 (1)	C12′	C13′	1.50 (1)	C8	C12	1.553 (9)
O9	C2	1.219 (8)	C12′	C16	1.53 (1)	C12	C16	1.51 (1)
C8′a	C4′a	1.38 (1)	C12′	C15	1.59 (1)	C12	C13	1.53 (1)
C8′a	C8′	1.39 (1)	C13′	C14	1.15 (2)	C12	C15	1.54 (1)
C2′	C3′	1.44 (1)	C8a	C8	1.40 (1)	C16	C14A	1.45 (3)
C3′	C4′	1.35 (1)	C8a	C4a	1.401 (9)	C13	C14B	1.38 (4)

Numbers in parentheses are estimated standard deviations in the least significant digits.

TABLE III. Bond Angles (°) with Estimated Standard Deviations in Parentheses

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C2′	O1	C8′a	124.2 (7)	C11′	C10′	C10	102.8 (5)	O9	C2	O4	116.1 (7)
C7′	O2	C9′	116.5 (5)	C11′	C10′	C9′	109.2 (6)	O9	C2	C3	126.7 (7)
C11	O3	C11′	100.3 (5)	C10	C10′	C9′	115.7 (6)	O4	C2	C3	117.2 (7)
C2	O4	C8a	124.7 (6)	O2	C9′	C18′	104.0 (6)	C4	C3	C2	120.5 (7)
C7	O5	C9	123.8 (5)	O2	C9′	C17′	108.1 (6)	C3	C4	C4a	120.5 (7)
C4′a	C8′a	O1	118.1 (8)	O2	C9′	C10′	106.3 (6)	C5	C4a	C8a	119.0 (7)
C4′a	C8′a	C8′	125.7 (7)	C18′	C9′	C17′	112.4 (7)	C5	C4a	C4	122.3 (7)
O1	C8′a	C8′	116.2 (8)	C18′	C9′	C10′	111.1 (6)	C8a	C4a	C4	118.7 (6)
O8	C2′	O1	118.0 (1)	C17′	C9′	C10′	114.2 (7)	C6	C5	O7	124.6 (6)
O8	C2′	C3′	126.0 (1)	O2	C7′	C6′	119.2 (7)	C6	C5	C4a	119.8 (6)
O1	C2′	C3′	116.2 (7)	O2	C7′	C8′	116.8 (7)	O7	C5	C4a	115.7 (6)
C4′	C3′	C2′	121.9 (9)	C6′	C7′	C8′	124.0 (7)	C5	C6	C7	119.4 (6)
C3′	C4′	C4′a	118.8 (9)	C8′a	C8′	C7′	112.9 (7)	C5	C6	C11	129.3 (6)
C8′a	C4′a	C5′	118.2 (7)	C8′a	C8′	C12′	121.0 (7)	C7	C6	C11	111.2 (6)
C8′a	C4′a	C4′	120.6 (7)	C7′	C8′	C12′	126.0 (8)	O3	C11	C6	116.7 (6)
C5′	C4′a	C4′	121.3 (8)	C13′	C12′	C16′	108.2 (8)	O3	C11	C10	106.3 (5)
O6	C5′	C6′	124.0 (6)	C13′	C12′	C8′	111.5 (8)	C6	C11	C10	109.2 (6)
O6	C5′	C4′a	116.5 (7)	C13′	C12′	C15′	103.5 (8)	C11	C10	C9	108.1 (6)
C6′	C5′	C4′a	119.5 (7)	C16′	C12′	C8′	109.0 (7)	C11	C10	C10′	102.9 (5)
C5′	C6′	C7′	119.5 (7)	C16′	C12′	C15′	107.4 (8)	C9	C10	C10′	122.6 (6)
C5′	C6′	C11′	121.3 (7)	C8′	C12′	C15′	116.8 (7)	O5	C9	C17	103.4 (6)
C7′	C6′	C11′	118.8 (7)	C14′	C13′	C12′	130.0 (1)	O5	C9	C18	105.5 (5)
O3	C11′	C6′	109.6 (6)	O4	C8a	C8	117.7 (6)	O5	C9	C10	108.8 (5)
O3	C11′	C10′	104.7 (5)	O4	C8a	C4a	117.9 (6)	C17	C9	C18	111.7 (7)
C6′	C11′	C10′	118.0 (6)	C8	C8a	C4a	124.4 (6)	C17	C9	C10	113.7 (6)
C18	C9	C10	112.9 (6)	C8a	C8	C12	127.1 (6)	C13	C12	C15	106.9 (7)
O5	C7	C8	118.3 (6)	C7	C8	C12	119.5 (6)	C13	C12	C8	107.0 (6)
O5	C7	C6	118.0 (6)	C16	C12	C13	114.3 (8)	C15	C12	C8	114.2 (6)
C8	C7	C6	123.4 (6)	C16	C12	C15	104.8 (7)	C14A	C16	C12	117.0 (1)
C8a	C8	C7	113.3 (6)	C16	C12	C8	109.9 (6)	C14B	C13	C12	113.0 (2)

Numbers in parentheses are estimated standard deviations in the least significant digits.

$J=17.6$ Hz), and 1.35, 1.39 (each 6H, s) indicated the presence of two 1,1-dimethylallyl groups at C-3 and C-3′ of both coumarin nuclei. Accordingly, the structure of furobiclausarin was supposed to be **3**, which is composed of two clausarin[16] moieties connected through a tetrahydrofuran ring. The complete structural elucidation of **3** was based on comparisons of chemical shifts and J values of the ^{1}H- and ^{13}C-NMR spectra and detailed ^{1}H–^{1}H, ^{13}C–^{1}H COSY, and HMBC analyses. As shown in Fig. 3, the particularly important ^2J and ^3J correlations from the HMBC study were as follows: (a) H-11′ (δ 5.22) showed correlations with C-5′ (δ 151.75), C-6′ (δ 106.80), C-7′ (δ 154.28), and C-9′ (δ 77.61), (b) H-10′ (δ 2.70) showed correlations with C-9′, C-11′ (δ 74.53), C-9 (δ 83.29), and C-10 (δ 52.34), (c) H-10 (δ 1.84) showed correlations with C-9 (δ 83.29), C-11, C-9′, C-10′,

TABLE IV. ^{1}H- and ^{13}C-NMR Spectral Data of Furobinordentatin (**1**) and Furobiclausarin (**3**)

Carbon	1		3	
	δ_C	δ_H	δ_C	δ_H
2	159.95		158.64	
3	109.50	6.12 (d, 9.5)	127.54	
4	139.43	8.03 (d, 9.5)	132.85	7.78
4a	102.71		102.73	
5	148.59		148.15	
6	107.40		107.50	
7	155.23[a]		153.96	
8	113.88[b]		112.83	
8a	153.45		152.40	
9	83.52		83.29	
17	30.95	1.58	30.99	1.56
18	23.12	1.46	23.18	1.44
10	52.08	1.90 (dd, 11.0, 8.1)	52.34	1.84 (dd, 11.0, 8.1)
11	73.86	4.72 (d, 11.0)	74.21	4.72 (d, 11.0)
12	40.48		40.13	
15	29.52	1.61	29.44	1.53
16	29.64	1.58	29.47	1.55
13	150.12	6.23 (dd, 17.6, 11.0)	149.91[c]	6.20 (dd, 17.6, 11.0)
14	107.97	4.84 (d, 17.6)	107.92	4.82 (d, 17.6)
		4.82 (d, 11.0)		4.78 (d, 11.0)
2′	159.81		158.52	
3′	109.95	6.19 (d, 9.5)	127.93	
4′	139.81	8.19 (d, 9.5)	133.26	7.96
4′a	103.75		103.82	
5′	152.09		151.75	
6′	106.61		106.80	
7′	155.00[a]		154.28	
8′	113.34[b]		113.25	
8′a	153.69		152.69	
9′	77.87		77.61	
17′	27.74	1.43	27.53	1.38
18′	23.27	1.22	23.62	1.18
10′	45.60	2.70 (t, 8.1)	45.89	2.70 (t, 8.1)
11′	74.40	5.17 (d, 8.1)	74.53	5.22 (d, 8.1)
12′	40.48		40.33	
15′	29.24	1.57	29.15	1.54
16′	29.34	1.57	29.24	1.54
13′	149.68	6.22 (dd, 17.6, 11.0)	149.52[c]	6.18 (dd, 17.6, 11.0)
14′	107.54	4.81 (d, 17.6)	107.62	4.82 (d, 17.6)
		4.80 (d, 11.0)		4.78 (d, 11.0)
3 and 3′ DMA			38.87	
			25.69	1.35
			25.64	1.35
			145.48	6.13 (dd, 17.6, 11.0)
			111.83	5.03 (d, 11.0)
				5.04 (d, 17.6)
			39.63	
			25.78 (×2)	1.39 (×2)
			145.48	6.08 (dd, 17.6, 11.0)
			111.83	5.00 (d, 11.0)
				4.99 (d, 17.6)

Spectra were taken in DMSO-d_6. Values are in ppm (δ_H and δ_C). The coupling constants (J values) in parentheses are in Hz. DMA = 1,1-dimethylallyl. *a*—*c*) May be interchanged.

and C-11′. The relative configurations of H-10, H-11, H-11′ and H-10′ were assigned as *trans*, *cis* and *cis* in the same manner as for **1** on the basis of J-values (11.0, 8.1, 8.1 Hz) and NOE experiments (see Experimental). Comparison of these data with those of furobinordentatin (**1**) supported the assignments of relative configurations of H-10, H-11, H-11′ and H-10′, and the structure of furobiclausarin was concluded to be **3**.

Though many bicoumarins[5-13,17] are known, furobinordentatin (**1**) and furobiclausarin (**3**) are the first examples of bicoumarin linked with the formation of a tetrahydrofuran ring between the pyran rings of linear-type pyranocoumarin. The lack of optical rotations of **1** and **3** suggests that they are artifacts or that they are formed in the plant cells without the participation of enzymes.

Experimental

Melting points were measured on a Yanagimoto micromelting point hot-stage apparatus and are uncorrected. Optical rotations were measured on a JASCO DIP-360 polarimeter. ^{1}H- and ^{13}C-NMR spectra were recorded on JEOL GX-270, GX-400 and GSX-500 spectrometers. Chemical shifts are shown on the δ (ppm) scale with tetramethylsilane (TMS) as an internal reference. HMBC spectra were measured at $J = 8$ Hz on the GX-400. Electron impact (EI)- and HR-MS were taken with a JMS-HX-110 spectrometer having a direct inlet system. UV spectra were recorded on a Shimadzu UV-160A spectrometer in EtOH, and IR spectra on a Shimadzu IR-450 spectrometer in $CHCl_3$. The preparative thin-layer chromatography (PTLC) was done on Kieselgel 60 F_{254} (Merck).

Isolation of Furobinordentatin (1) and Furobiclausarin (3) The dried root barks (3.2 kg) of *Citrus yuko* collected at Katsura (Tokushima Prefecture) were extracted with acetone (8 l) (50 h × 2), then with MeOH (8 l) (50 h × 2). The solvents were evaporated under reduced pressure and the residues were combined. A quarter (164.3 g) of the extracts was fractionated by silica gel (1 kg) column chromatography with toluene, CH_2Cl_2, acetone and MeOH. The CH_2Cl_2 eluate (127.6 g) was further submitted to PTLC (silica gel) using acetone–hexane (1 : 1) to afford furobinordentatin (**1**) (9.2 mg).[18] The acetone extract (485 g) of dried roots (3.2 kg) of *Citrus hassaku* collected at Innoshima (Hiroshima Prefecture) was subjected to silica gel (4 kg) column chromatography and eluted with hexane, benzene, CH_2Cl_2, acetone and MeOH. The benzene eluate (205.9 g) was further separated by column chromatography, centrifugal chromatography and PTLC [solvents: isopropyl ether, benzene–AcOEt (9 : 1)] to give furobiclausarin (**3**) (81.8 mg).[18]

Furobinordentatin (1) Colorless cubes, mp 225—227 °C (acetone), $[\alpha]_D$ ±0° (c = 0.14, $CHCl_3$). UV λ_{max} nm: 213, 228 (sh), 265, 283, 329. IR ν_{max} cm^{-1}: 1720, 1625. HR-MS Calcd for $C_{38}H_{40}O_9$: 640.2672. Found: 640.2675. EI-MS m/z (%): 640 (M^+, 31), 328 (10), 313 (base peak, 100), 312 (32). ^{1}H- and ^{13}C-NMR (DMSO-d_6) δ: see Table IV.

***O,O′*-Dimethylfurobinordentatin (2)** Ethereal diazomethane (10 ml) prepared in the usual manner was added to a solution of furobinordentatin (**1**) (35.2 mg) in 10 ml of methanol, and the mixture was allowed to stand overnight at room temperature. The solvent was evaporated, and the residue was subjected to PTLC (benzene–AcOEt (9 : 1)) to give

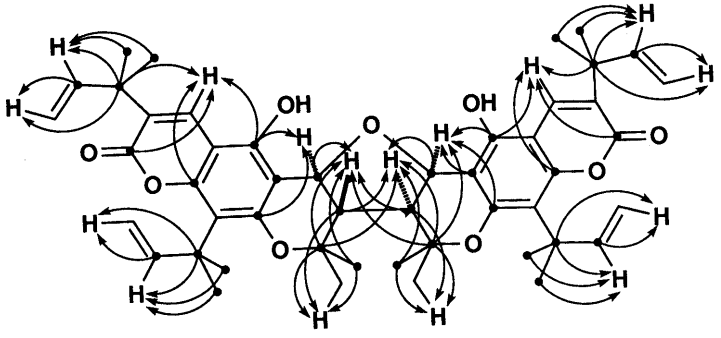


Fig. 3. C–H Long-Range Correlations in the HMBC Spectrum of Furobiclausarin (**3**)

3 (6.1 mg) as a colorless oil, $[\alpha]_D$ ±0° (c=0.61, $CHCl_3$). UV λ_{max} nm: 209, 235 (sh), 255, 264, 325. IR ν_{max} cm^{-1}: 1720, 1585. HR-MS Calcd for $C_{40}H_{44}O_9$: 668.2985. Found: 668.2974. EI-MS m/z (%): 668 (M^+, 15), 382 (32), 381 (base peak, 100). ^{1}H-NMR ($CDCl_3$) δ: 7.93 (1H, d, J=9.8 Hz), 7.87 (1H, d, J=9.8 Hz), 6.31 (1H, dd, J=17.5, 10.7 Hz), 6.28 (1H, dd, J=17.5, 10.7 Hz), 6.25 (1H, d, J=9.8 Hz), 6.19 (1H, d, J=9.8 Hz), 5.13 (1H, d, J=7.7 Hz), 4.92 (1H, d, J=17.5 Hz), 4.91 (1H, d, J=17.5 Hz), 4.87 (1H, d, J=10.7 Hz), 4.86 (1H, d, J=10.7 Hz), 4.69 (1H, d, J=11.1 Hz), 4.12, 3.75 (each 3H, s), 2.41 (1H, t, J=7.8 Hz), 1.99 (1H, dd, J=7.7, 11.1 Hz), 1.67 (6H, s), 1.65, 1.64, 1.51, 1.41, 1.32, 1.26 (each 3H, s). NOE: irradiation at δ 4.12 (5′-MeO) −9.6% and 3.2% enhancement at δ 7.93 (H-4′) and 5.13 (H-11′); irradiation at δ 3.75 (5-MeO) −7.9% and 2.3% enhancement at δ 7.87 (H-4) and 4.69 (H-11); irradiation at δ 5.13 (H-11′) −9.6% and 7.3% enhancement at δ 4.69 (H-11) and 2.41 (H-10′); irradiation at δ 4.69 (H-11) −9.6% enhancement at δ 5.13 (H-11′). ^{13}C-NMR ($CDCl_3$) δ: 160.67 (s), 160.40 (s), 156.21 (s), 155.87 (s), 155.59 (s), 154.40 (s), 153.74 (s), 151.27 (s), 150.34 (d), 149.75 (d), 138.94 (d), 138.90 (d), 120.22 (s), 119.87 (s), 117.07 (s), 114.01 (s), 112.43 (d), 112.04 (d), 108.48 (s), 108.37 (t), 108.04 (s), 107.91 (t), 83.32 (s), 78.20 (s), 74.95 (d), 74.20 (d), 64.51 (q), 63.83 (q), 54.08 (q), 47.07 (q), 41.25 (2×s), 29.91 (q), 29.80 (q), 29.68 (q), 29.52 (q), 29.31 (q), 28.30 (q), 24.06 (q), 23.54 (q).

Furobiclausarin (3) Yellow oil, $[\alpha]_D$ ±0° (c=1.05, $CHCl_3$). UV λ_{max} nm: 213, 268, 295, 323. IR ν_{max} cm^{-1}: 3500, 1705, 1620, 1580. HR-MS Calcd for $C_{48}H_{56}O_9$: 776.3924. Found: 776.3902. EI-MS m/z (%): 776 (M^+, 20), 707 (base peak, 100), 396 (19), 381 (69), 380 (44). ^{1}H- and ^{13}C-NMR (DMSO-d_6) δ: see Table IV. NOE: irradiation at δ 2.70 (H-10′) −3.7% and 7.7% enhancement at δ 4.72 (H-11) and 5.22 (H-10); irradiation at δ 5.22 (H-11′) −18.0% and 8.5% enhancement at δ 4.72 (H-11) and 2.70 (H-10′); irradiation at δ 4.72 (H-11) −10.6% and 1.5% enhancement at δ 5.22 (H-11′) and 2.70 (H-10′).

Crystal Structure Determination and Refinement of Furobinordentatin (1) Rhombic crystals suitable for X-ray analysis were obtained by slow evaporation of an acetone solution of furobinordentatin (**1**). A preliminary examination of a crystal with dimensions of 0.18×0.15×0.09 mm on an Enraf–Nonius CAD4 diffractometer indicated a triclinic unit cell, and the space group $P\bar{1}$ was adopted. A least-squares refinement of the setting angles of 25 reflections, collected in the range of 13°<2θ<23°, led to the unit-cell parameters. Diffraction intensities were measured with graphite-monochromated MoK_α radiation (λ=0.7107 Å). Intensity data were collected to a maximum 2θ=50° by the $\omega-2\theta$ scan technique with the ω scan range (0.75°+0.35° tanθ). The total number of independent reflections measured was 6131, of which 2624 were considered to be observed [$F_O > 3\sigma(F_O)$]. Net intensities were reduced to a set of relative structure factors by the application of the standard Lorenz and polarization factors. No absorption correction was made. The structure was solved by the direct method[19] and refined by least-squares techniques.[20] Most non-hydrogen atoms of the molecule in an asymmetric unit were found in an initial E-map. Subsequent difference Fourier (DF) syntheses revealed all non-hydrogen atomic positions. A 1,1-dimethylallyl group was found to be disordered; two carbon atoms (C14A, C14B) with the occupancy factor of 0.5 were consistent with the results. All non-hydrogen atoms were refined with anisotropic thermal parameters, and the hydrogen atoms bound to carbon were included in calculated positions with isotropic thermal factors as fixed parameters. Final cycles of two-blocked matrix least-squares refinement[20] were carried to convergence at R=0.079 (R_w=0.079).[21] The final difference Fourier was judged to be essentially featureless: the largest residual peak of 0.35 e/Å^3 was found near C15′. The atomic coordinates for non-hydrogen atoms with the isotropic equivalent thermal factors are given in Table I.[22]

Acknowledgement The authors thank Misses K. Suwa and S. Takeyama for measurements of MS and NMR spectra. This work was supported in part by Grants-in-Aid from the Suzuken Memorial Foundation.

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18) Isolation and characterization of other constituents will be reported elsewhere.
19) Programs of the Enraf-Nonius SDP package were used. The package includes modified versions of Main, Hull, Lessinger, Germain, Declerq, and Woolfson's MULTAN 82 and Johnson's ORTEP II.
20) The programs used in the refinement and the e.s.d. calculation were Scheidt and Haller's (Notre Dame) versions of ORFLS and ORFFE originated by W. R. Busing, K. O. Martin and H. A. Levy.
21) The atomic scattering factors were taken from "International Tables for X-ray Crystallography," Vol. IV, Kynoch Press, Birmingham (1974). $R=\sum||F_O|-|F_C||/\sum|F_O|$, $Rw=[\sum w(|F_O|-|F_C|)^2/\sum w(F_O)^2]^{\frac{1}{2}}$ with unit weight.
22) Tables of anisotropic temperature factors for non-hydrogen atoms, the idealized atomic coordinates for hydrogen atoms, the individual bond lengths and angles, and the observed and calculated structure factors are available from one of the authors (K. H.) on request.