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## Diterpenes from Rhizomes of *Hedychium coronarium*

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Two new labdane-type diterpenes, coronarin E and coronarin F containing borneol in the molecule, were isolated from the rhizomes of the Brazilian medicinal plant, *Hedychium coronarium* (Zingiberaceae).

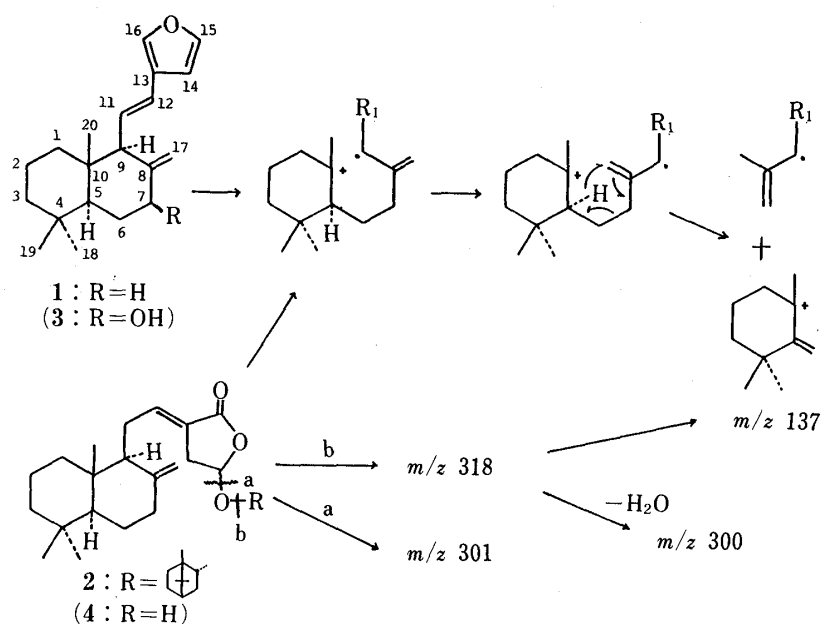
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In our previous paper,<sup>1)</sup> four cytotoxic diterpenes, coronarins A—D, isolated from *Hedychium coronarium* (a Brazilian medicinal plant<sup>2)</sup>), were reported. Further examination of *H. coronarium* led us to isolate two new labdane-type diterpenes, named coronarins E (**1**) and F (**2**). In this paper, we describe their isolation and structural elucidation.

The CHCl<sub>3</sub> extract of the rhizomes of *H. coronarium* was subjected to silica gel column chromatography to give fractions A—H. Repeated chromatography of fractions B and C using silica gel and octadecyl silica (ODS) as a stationary phase resulted in the isolation of two new labdane-type diterpenes, named coronarins E (**1**) and F (**2**).

Coronarin E (**1**), C<sub>20</sub>H<sub>28</sub>O, unstable colorless oil, [ $\alpha$ ]<sub>D</sub> +22.3°, showed similar spectral data to those of coronarin A (**3**). The infrared (IR) and proton nuclear magnetic resonance (<sup>1</sup>H-NMR) spectra showed the presence of an *exo*-methylene (3080, 1645 and 895 cm<sup>-1</sup>;  $\delta$  4.53 (1H, dd, *J*=1.8, 3.7 Hz) and 4.76 (1H, dd, *J*=1.8, 3.7 Hz)), a  $\beta$ -substituted furan ring (1510 and 870 cm<sup>-1</sup>;  $\delta$  6.54 (1H, d, *J*=1.6 Hz), 7.34 (1H, brs) and 7.35 (1H, brs)) and a *trans* ethylenic double bond ( $\delta$  5.98 (1H, dd, *J*=9.8, 15.8 Hz) and 6.19 (1H, d, *J*=15.8 Hz)). The latter two functional groups were revealed to be conjugated in the ultraviolet (UV) spectrum (234 nm,  $\epsilon$ =9100). The mass spectrum (MS) showed the characteristic fragment ion peak (*m/z* 137) of labdane-type diterpenes.<sup>3)</sup> The most noticeable differences in the spectral data in comparison with coronarin A (**3**) were the chemical shift values at C-6 and C-7 in the carbon-13 nuclear magnetic resonance (<sup>13</sup>C-NMR) spectrum and the absence of a hydroxyl band in the IR spectrum. From the above spectral data, the structure of **1** was established to be as shown in Fig. 1.

Coronarin F (**2**), C<sub>30</sub>H<sub>46</sub>O<sub>3</sub>, colorless needles, mp 157—159°C, [ $\alpha$ ]<sub>D</sub> +90.0°, contained *exo*-methylene (3080, 1640 and 890 cm<sup>-1</sup>) and  $\alpha,\beta$ -unsaturated  $\gamma$ -lactonic (1770 and 1680 cm<sup>-1</sup>) bands in the IR spectrum. The <sup>1</sup>H-NMR spectrum also suggested the presence of *exo*-methylene protons ( $\delta$  4.44 (1H, d, *J*=1.1 Hz) and 4.84 (1H, d, *J*=1.3 Hz)), a lactonic methine proton ( $\delta$  5.57 (1H, dd, *J*=2.5, 6.4 Hz)) linked to an oxygen function and an olefinic proton ( $\delta$  6.73 (1H, ddt, *J*=1.9, 2.8, 5.8 Hz)). These <sup>1</sup>H-NMR and IR spectral data were closely similar to those of coronarin D (**4**), except for the presence of one additional proton signal ( $\delta$  3.89 (1H, ddd, *J*=1.8, 3.3, 9.8 Hz)) linked to an oxygen function. The chemical shift values of twenty carbons in the <sup>13</sup>C-NMR spectrum were also similar to those of **4** and the

Fig. 1. Fragmentation of Labdane-Type Diterpenes from *H. coronarium*TABLE I.  $^{13}\text{C}$  Chemical Shifts of Coronarins E (1), F (2), A (3) and D (4), and (–)-Borneol

Carbon No.	1	3	2	4	(–)-Borneol
1	40.8 (t)	40.4 (t)	39.4 (t)	39.2 (t)	
2	19.2 (t)	19.1 (t)	19.4 (t)	19.3 (t)	
3	42.4 (t)	42.0 (t)	42.1 (t)	42.0 (t)	
4	33.6 (s)	33.5 (s)	33.6 (s)	33.5 (s)	
5	54.9 (d)	52.6 (d)	55.4 (d)	55.3 (d)	
6	23.4 (t)	33.2 (t)	24.1 (t)	24.1 (t)	
7	36.8 (t)	73.4 (d)	37.4 (t)	37.8 (t)	
8	150.2 (s)	152.2 (s)	147.9 (s)	148.0 (s)	
9	61.5 (d)	59.8 (d)	56.2 (d)	56.1 (d)	
10	39.2 (s)	39.2 (s)	39.5 (s)	39.4 (s)	
11	121.8 (d)	122.3 (d)	25.5 (t)	25.4 (t)	
12	128.3 (d)	127.0 (d)	142.4 (d)	143.5 (d)	
13	124.6 (s)	124.4 (s)	124.7 (s)	124.5 (s)	
14	107.7 (d)	107.7 (d)	33.2 (t)	33.5 (t)	
15	139.6 (d)	139.8 (d)	102.9 (d)	96.5 (d)	
16	143.3 (d)	143.4 (d)	170.0 (s)	170.6 (s)	
17	108.0 (t)	104.9 (t)	107.7 (t)	107.8 (t)	
18	33.6 (q)	33.5 (q)	33.6 (q)	33.5 (q)	
19	22.0 (q)	21.9 (q)	21.8 (q)	21.7 (q)	
20	15.0 (q)	15.0 (q)	14.4 (q)	14.3 (q)	
1'			49.4 (s)		49.4 (s)
2'			86.6 (d)		77.2 (d)
3'			37.8 (t)		38.9 (t)
4'			45.0 (d)		45.1 (d)
5'			28.0 (t)		28.2 (t)
6'			26.7 (t)		25.9 (t)
7'			47.5 (s)		47.9 (s)
8'			19.7 (q)		20.1 (q)
9'			18.8 (q)		18.6 (q)
10'			13.8 (q)		13.3 (q)

The chemical shifts of 3 and 4 were cited from our previous paper,<sup>1)</sup> and those of (–)-borneol were assigned according to the literature.<sup>4)</sup>

other carbon signals resembled those of (–)-borneol.<sup>4)</sup> As the chemical shifts of C-15 ( $\delta$  102.9) and C-2' ( $\delta$  86.6) linked to an oxygen function were shifted downfield in comparison with those of **4** and borneol, it was concluded that borneol was attached to C-15 of **4**. The fragmentation in the MS also supported the above structure, as can be seen in Fig. 1. The absolute configuration at C-2' remains to be clarified.

These two new diterpenes did not show cytotoxic activity against Chinese hamster V-79 cells.

### Experimental

All melting points were measured with a Yanaco MP-3 apparatus and are uncorrected. <sup>1</sup>H-(400 MHz) and <sup>13</sup>C-NMR (100 MHz) spectra were measured on a Bruker AM400 spectrometer in CDCl<sub>3</sub> with tetramethylsilane as an internal standard. In general, silica gel (Kieselgel 60) for column chromatography (CC) was used in amounts equivalent to 50–100 times the sample amount. For further purification, high-performance liquid chromatography (HPLC) was carried out on a CIG column system (22 mm i.d.  $\times$  30 cm, Kusano Scientific Co., Tokyo) packed with Iatrobeads (60  $\mu$ m spherical silica gel, Iatron Co., Tokyo) or RP-18 (25–45  $\mu$ m). Thin layer chromatography (TLC) was done on 0.25 mm silica gel (60F<sub>254</sub>, Merck) or RP-18 (F<sub>254S</sub>, Merck) plates. Spots were visualized under UV light (254 nm), and further by spraying with 10% H<sub>2</sub>SO<sub>4</sub> and heating the plates.

**Plant Material**—The rhizomes of *Hedychium coronarium* were collected in the Universidade de São Paulo (USP), September 1986, and identified by Prof. Dr. Sylvio Panizza, Departamento de Botanica, USP. A sample was deposited in the Laboratory of Pharmacognosy, Tokyo College of Pharmacy.

**Extraction and Isolation**—The dry rhizomes (3.9 kg) were extracted twice with hot CHCl<sub>3</sub> and concentrated to give a brown oil (123.5 g). A portion of the CHCl<sub>3</sub> extract (80.0 g) was subjected to silica gel CC using a linear hexane–EtOAc gradient system and separated into eight fractions (frs. A–H). Fraction B was subjected to silica gel HPLC with *n*-hexane to give **1** (390 mg). Fraction C was subjected to silica gel and ODS HPLC (eluted with *n*-hexane–EtOAc (15:1) and MeOH, respectively) to give **2** (320 mg).

Coronarín E (**1**), colorless oil,  $[\alpha]_D^{25} + 22.3^\circ$  ( $c = 0.44$ , CHCl<sub>3</sub>). EIMS  $m/z$  (%): 284 ( $M^+$ , 100), 195 (9), 147 (95), 37 (34), 81 (28). HRMS: Calcd. for C<sub>20</sub>H<sub>28</sub>O 284.2139. Found: 284.2143. IR  $\nu_{\max}^{\text{CCl}_4} \text{ cm}^{-1}$ : 3080, 1645, 895 (C=CH<sub>2</sub>), 1510, 870 (furan ring), 2940, 2860, 1460, 1440, 1390, 1370, 1160, 1070, 1025, 970, 595. UV  $\lambda_{\max}^{\text{EtOH}} \text{ nm}$  ( $\epsilon$ ): 234 (9100). <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.84, 0.85, 0.90 (each 3H, s, 18, 19 and 20-CH<sub>3</sub>), 2.40 (1H, d,  $J = 9.8$  Hz, 9-H), 4.53 (1H, dd,  $J = 1.8, 3.7$  Hz, 17-H), 4.76 (1H, dd,  $J = 1.8, 3.7$  Hz, 17-H), 5.98 (1H, dd,  $J = 9.8, 15.8$  Hz, 11-H), 6.19 (1H, d,  $J = 15.8$  Hz, 12-H), 6.54 (1H, d,  $J = 1.6$  Hz, 14-H), 7.34, 7.35 (each 1H, brs, 15 and 16-H).

Coronarín F (**2**), colorless needles, mp 157–159 °C,  $[\alpha]_D^{25} + 90.0^\circ$  ( $c = 0.2$ , CHCl<sub>3</sub>). EIMS  $m/z$  (%): 454 ( $M^+$ , 1), 318 (6), 301 (12), 283 (2), 217 (10), 215 (9), 191 (5), 177 (9), 137 (100). HRMS: Calcd for C<sub>20</sub>H<sub>29</sub>O<sub>2</sub> 301.2165. Found: 301.2144. Calcd for C<sub>20</sub>H<sub>30</sub>O<sub>3</sub> 318.219. Found: 318.2233. IR  $\nu_{\max}^{\text{CCl}_4} \text{ cm}^{-1}$ : 3080, 1640, 890 (C=CH<sub>2</sub>), 1770 (C=O), 1680 (C=C), 2950, 1460, 1390, 1335, 1170, 1160, 1140, 1115, 1050, 1030, 950. UV  $\lambda_{\max}^{\text{EtOH}} \text{ nm}$  ( $\epsilon$ ): 227 (12500). <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.73, 0.82, 0.84, 0.85, 0.86, 0.89 (each 3H, s, 18, 19, 20, 8', 9' and 10'-H), 2.75 (1H, ddd,  $J = 1.9, 2.5, 17.2$  Hz, 14-H), 2.98 (1H, ddd,  $J = 2.8, 6.4, 17.2$  Hz, 14-H), 3.89 (1H, ddd,  $J = 1.8, 3.3, 9.8$  Hz, 2'-H), 4.44 (1H, d,  $J = 1.2$  Hz, 17-H), 4.84 (1H, d,  $J = 1.2$  Hz, 17-H), 5.57 (1H, dd,  $J = 2.5, 6.4$  Hz, 15-H), 6.73 (1H, ddt,  $J = 1.9, 2.8, 5.8$  Hz, 12-H).

### References and Notes

- 1) H. Itokawa, H. Morita, I. Katou, K. Takeya, A. J. Cavaleiro, R. C. B. de Oliveira, M. Ishige, and M. Motidome, *Planta Medica*, in press.
- 2) M. Pio Correa, "Dicionário das Plantas Uteis do Brasil," Vol. IV, Imprensa Nacional, Rio de Janeiro, 1969, p. 674.
- 3) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-day, Inc., San Francisco, 1964.
- 4) F. Bohlmann and R. Zeisberg, *Org. Mag. Res.*, 7, 426 (1975).