2,5-Dihydrofuryl-γ-lactam Derivatives from *Hemerocallis fulva* L. var. *kwanso* REGEL. II[1)]

Tomohiro INOUE, Tenji KONISHI, Shiu KIYOSAWA,* and Yasuhiro FUJIWARA

Kyoto Pharmaceutical University, Nakauchi-cho, Misasagi Yamashina-ku, Kyoto 607, Japan. Received July 1, 1993

Two new 2,5-dihydrofuryl-γ-lactam derivatives, fulvanine D and E have been extracted from *Hemerocallis fulva* L. var. *kwanso* REGEL along with fulvanine A, B and C. The structures of fulvanine D and E have been established as 1-(3-hydroxymethyl-2,5-dihydro-2-furyl)azacyclopenta-3-hydroxy-5-methoxy-2-one (1) and 1,2,4,5,5a,6,7,8,-8a,8b-decahydro-1,5-dioxa-8a-aza-*asym*-indacen-7-hydroxy-8-one (2).

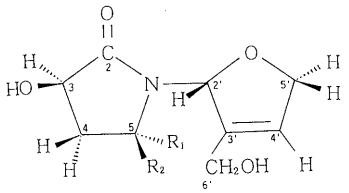
Keywords *Hemerocallis fulva* var. *kwanso*; 2,5-dihydrofuryl-γ-lactam; fulvanine E; Ehrlich reaction; ^{1}H-NMR

The Ehrlich reaction is useful as a reliable means of detecting some natural products. It has been applied to finding the reaction-positive constituents in Dioscoreaceae and Liliaceae for the purposes of chemotaxonomy.[2)] The methanol extract from a fresh aerial part of *Hemerocallis fulva* var. *kwanso*, Liliaceae, was chromatographed to give fulvanine D and E along with fulvanine A, B and C.[1)]

Fulvanine D (**1**), a white powder, gave a positive Ehrlich reaction and exhibited an absorption maximum at 1700 cm^{-1} due to a γ-lactam ring in the infrared (IR) spectrum. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **1** was analogous to that of fulvanine A (**3**), a 2,5-dihydrofuryl-γ-lactam derivative. The proton signals of two methine groups in the low field at δ 6.24 and 6.46 ppm are characteristic of fulvanines having the partial structure of the 2,5-dihydrofuryl ring. The geminal coupled proton signals at δ 1.87 and 2.57 are ascribed to the C-4 methylene of the γ-lactam moiety with the CH–CH$_2$–CH system. One methoxyl proton signal appeared at δ 3.24, and the methine proton signal at C-5 was observed in the upfield about 0.27 ppm from that of **3**, suggesting methylation of 5-OH. The methylation effect was also suggested by the carbon thirteen nuclear magnetic resonance (^{13}C-NMR) spectrum in which the C-4 and C-5 carbons shifted about −4.4 and 7.7 ppm, respectively, compared with the spectrum of **3** (Table II).[3)]

Accordingly, fulvanine D was characterized as 1-(3-hydroxymethyl-2,5-dihydro-2-furyl)azacyclopenta-3-hydroxy-5-methoxy-2-one (**1**).

Fulvanine E (**2**), colorless needles, mp 210—212 °C (dec.) exhibited a bluish purple color with the Ehrlich test and an absorption maximum at 1712 cm^{-1} suggesting a γ-lactam ring like other fulvanines. The ^{1}H-NMR spectrum (CD_3OD) of **2** also showed the proton signal pattern characteristic of 2,5-dihydrofuryl-γ-lactam de-



1 : R_1=OCH_3 R_2=H
3 : R_1=OH R_2=H

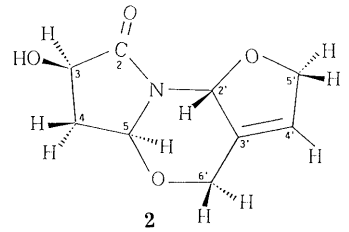


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Chart 1

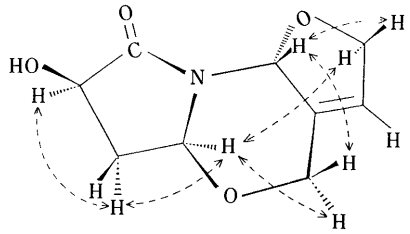

Fig. 1. NOE of **2**

TABLE I. ^{1}H-NMR Spectral Data for **1**, **2** and **3** (in CD_3OD, 300 MHz)

Proton	1	2	3
3	4.51 dd 9, 7.5	4.30 dd 9, 7	4.60 dd 9, 7
4	1.87 ddd 13, 9, 6	1.71 ddd 14, 7, 4	1.98 ddd 13, 9, 6
	2.57 dd 13, 7.5	2.80 ddd 14, 9, 7	2.30 dd 13, 7
5	4.88 d 6	5.07 dd 7, 4	5.15 d 6
2′	6.46 m	6.14 m	6.45 m
4′	6.24 dd 3, 2	6.20 m	6.22 ddd 4, 4, 2
5′	4.52 ddt 13, 3, 2	4.57 dddd 13, 5, 3, 2	4.53 dddd 13, 4, 4, 2
	4.65 ddt 13, 6.5, 2	4.71 m	4.76 dddd 13, 4, 3, 2
6′	4.09 s	4.69 m	4.08 m
CH_3O	3.24 s		

δ in ppm from tetramethylsilane (TMS), and *J* values in Hz.

TABLE II. ^{13}C-NMR Spectral Data for **1**, **2** and **3** (in CD_3OD, 75 MHz)

Carbon	1	2	3
2	178.26	177.06	177.92
3	69.49	68.92	69.50
4	35.84	36.43	40.14
5	86.83	81.70	79.09
2′	88.57	87.80	88.92
3′	137.67	132.53	137.63
4′	129.23	129.09	128.87
5′	75.36	76.71	75.37
6′	58.09	64.28	58.04
CH_3O	54.64		

δ in ppm from TMS.

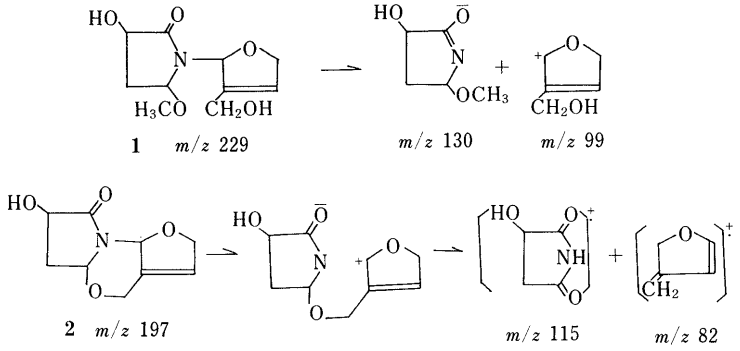

Chart 2

rivative, indicating the unsaturated methine proton signals at δ 6.13 and 6.20 ppm, and two sets of signals of the geminal coupled methylene protons at δ 4.71, 4.57, 2.80 and 1.71 ppm, while some differences were observed in comparison with **3**. The nonequivalent methylene protons at C-4 resonated, respectively, at δ 1.71 and 2.80 indicating a chemical shift difference of about 1 ppm with double double doublet (ddd) split signal; in **3**, the difference in ppm was about 0.3 between the two protons which was characteristic of a coupling system of dd and ddd splits signals. Furthermore, the 6′-CH_2 proton signals showed a shift to low field of about 0.6 ppm compared with **3**. The ^{1}H-NMR spectrum in dimethylsulfoxide (DMSO)-d_6 only exhibited a secondary hydroxyl proton signal at δ 5.75, assigned to the C-3 position by the decoupling experiment. These results suggested an ether linkage formed by dehydration between two hydroxyl functions at C-5 and C-6′. By comparing its ^{13}C-NMR spectrum with that of **3**, C-4 and C-5 showed respective shift differences of about -3.7 and $+2.6$ ppm, and three carbons at C-3′, C-4′ and C-6′ shifted about -5.1, $+0.2$ and 4.2 ppm, respectively, due to a cyclization effect caused by formation of an ether linkage between the C-5 and C-6′ positions.

The stereochemistry of **2** was determined by nuclear Overhauser effect (NOE) data to be as depicted by structure **2**. Therefore, fulvanine E was characterized as 1,2,4,-5,5a,6,7,8,8a,8b-decahydro-1,5-dioxa-8a-aza-*asym*-indasen-7-hydroxy-8-one, **2**.

The electron-impact mass spectrum (EI-MS) of **1** showed $M^+ - H_2O$ peak at *m/z* 211 and $M^+ - 2 \times H_2O$ at *m/z* 193. The cleavage of the N–C-2′ bond occurred to give a base peak, 3-hydroxymethyl-2,5-dihydrofuranyl ion at *m/z* 99. The first step in the EI-MS of 2 was cleavage of the carbon–hetero, C-2′–N bond and facile cleavage of the ether bond at C-6′ gave 3′-exomethylene-2′-hydrofuryl ion as a base peak at *m/z* 82. The peaks in the fragmentations of **1** and **2** arose as shown in Chart 2.

The stereochemistry of **3** was determined as 3β,5α-dihydroxylate from NOE data,[1] but this was not necessarily the same as that existing in nature because of possible epimerization of the asymmetric carbon 5. In fact, **2** was characterized as a 3β,5β-dioxy derivative in which the ^{1}H-NMR spectrum exhibited considerable differences in the coupling system of –CH–CH_2–CH– compared with that of **1** and **3** (Table I, Fig. 1).

It was difficult to know if fulvanine D and E were really natural. No artifacts arising from **3** were formed in the methanol solution by continued heating. The absolute configuration at C-3, C-5 and C-2′ of the fulvanine derivatives are being studied.

Experimental

Extraction of Fulvanine D (1) and E (2) Fraction B (1.35 g)[1] was chromatographed on silica gel ($CHCl_3$–MeOH–H_2O, 8 : 2 : 0.2, v/v) to give three fractions (fr. a, 0.12 g; fr. b, 0.85 g; fr. c, 0.20 g). Fraction a was further subjected to column chromatographies on silica gel (hexane–AcOEt, 1 : 10 and $CHCl_3$–MeOH, 10 : 1, v/v) to yield a crude **2** (18 mg), which was obtained as colorless needless (6 mg) from MeOH. Fraction b (0.85 g) was also chromatographed on silica gel with $CHCl_3$–MeOH–H_2O (9 : 1 : 0.1, v/v) or $CHCl_3$–MeOH (10 : 1 v/v) to give five fractions (fr. d, 50 mg; fr. e, 28 mg; fr. f, 68 mg; fr. g, 20 mg; fr. h, 460 mg). **1** (14 mg) was obtained as an amorphous mass from the MeOH solution of fr. g.

Fulvanine D (1) A white powder (mp 80—83 °C). $[\alpha]_D$ $-0.29°$ (c = 1.4, MeOH). IR (KBr) cm^{-1}: 3350, 2930, 2860, 1700, 1415, 1395, 1080. Circular dichroism (CD) ($c = 0.60 \times 10^{-3}$, MeOH) $\Delta\varepsilon$ (nm): -4.62 (227, negative maximum). EI-MS *m/z*: 229 (M^+), 211 ($M^+ - H_2O$), 193 ($M^+ - 2 \times H_2O$), 99, 82, 69.

Fulvanine E (2) Colorless needles (MeOH), mp 210—212 °C (dec.). $[\alpha]_D$ $+1.35$ (c = 0.2, MeOH). IR (KBr) cm^{-1}: 3350, 2950, 2900, 1712, 1464, 1426, 1384, 1070, 1006. CD ($c = 0.43 \times 10^{-3}$, MeOH) $\Delta\varepsilon$ (nm): 1.54 (227, positive maximum). EI-MS *m/z*: 197 (M^+), 115, 97, 82.

^{1}H- and ^{13}C-NMR spectra in Table I.

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