2,5-Dihydrofuryl- γ -lactam Derivatives from *Hemerocallis fulva* L. var. *kwanso* REGEL. II¹⁾

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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-dioxo-8a-aza-*asym*-indacen-7-hydroxy-8-one (2).

Keywords *Hemerocallis fulva* var. *kwanso*; 2,5-dihydrofuryl- γ -lactam; fulvanine E; Ehrlich reaction; ¹H-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 (¹H-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-CH₂-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 (¹³C-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 ¹H-NMR spectrum (CD₃OD) of 2 also showed the proton signal pattern characteristic of 2,5-dihydrofuryl- γ -lactam de-

Chart 1

Fig. 1. NOE of 2

TABLE I. ¹H-NMR Spectral Data for 1, 2 and 3 (in CD₃OD, 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 2.57 dd 13, 7.5	1.71 ddd 14, 7, 4 2.80 ddd 14, 9, 7	1.98 ddd 13, 9, 6 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 4.65 ddt 13, 6.5, 2	4.57 dddd 13, 5, 3, 2 4.71 m	4.53 dddd 13, 4, 4, 2 4.76 dddd 13, 4, 3, 2
6'	4.09 s	4.69 m	4.08 m
CH ₃ O	3.24 s		

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

TABLE II. ¹³C-NMR Spectral Data for 1, 2 and 3 (in CD₃OD, 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 ₃ O	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 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'-CH₂ proton signals showed a shift to low field of about 0.6 ppm compared with 3. The ¹H-NMR spectrum in dimethylsulfoxide (DMSO)-d₆ 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 ¹³C-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-dioxo-8a-aza-*asym*-indasen-7-hydroxy-8-one, 2.

The electron-impact mass spectrum (EI-MS) of 1 showed M⁺ - H₂O peak at m/z 211 and M⁺ - 2 × H₂O at m/z 193. The cleavage of the N-C-2' bond occurred to give a base peak, 3-hydroxymethyl-2,5-dihydrofuryl 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 3 β ,5 α -dihydroxylate from NOE data,¹⁾ but this was not neces-

sarily the same as that existing in nature because of possible epimerization of the asymmetric carbon 5. In fact, 2 was characterized as a 3 β ,5 β -dioxy derivative in which the ¹H-NMR spectrum exhibited considerable differences in the coupling system of -CH-CH₂-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 (CHCl₃-MeOH-H₂O, 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 CHCl₃-MeOH, 10:1, v/v) to yield a crude 2 (18 mg), which was obtained as colorless needles (6 mg) from MeOH. Fraction b (0.85 g) was also chromatographed on silica gel with CHCl₃-MeOH-H₂O (9:1:0.1, v/v) or CHCl₃-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). [α]_D -0.29° (c = 1.4, MeOH). IR (KBr) cm⁻¹: 3350, 2930, 2860, 1700, 1415, 1395, 1080. Circular dichroism (CD) (c = 0.60 × 10⁻³, MeOH) $\Delta\epsilon$ (nm): -4.62 (227, negative maximum). EI-MS m/z : 229 (M⁺), 211 (M⁺ - H₂O), 193 (M⁺ - 2 × H₂O), 99, 82, 69.

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

¹H- and ¹³C-NMR spectra in Table I.

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