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JATROPHAM GLUCOSIDE FROM THE BULBS OF *LILIUM HANSONII*

HIROKO SHIMOMURA, YUTAKA SASHIDA, YOSHIHIRO MIMAKI and YUKO MINEGISHI

Tokyo College of Pharmacy, 1432-1, Horinouchi, Hachioji, Tokyo 192-03, Japan

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Key Word Index—*Lilium hansonii*; Liliaceae; jatropham; jatropham 5-*O*-β-D-glucopyranoside; (±)-5-*O*-methyljatropham; antitumour alkaloid.

Abstract—From the methanolic extract of the fresh bulbs of *Lilium hansonii*, a new glucoside, jatropham 5-*O*-β-D-glucopyranoside, was isolated together with jatropham and (±)-5-*O*-methyljatropham.

Recently, in the course of our studies on the constituents of *Lilium* plants, we focused on *Lilium hansonii* Leichtl. and isolated a new glucoside, jatropham 5-*O*-β-D-glucopyranoside (**2**) together with jatropham (**1**) and (±)-5-*O*-methyljatropham (**3**).

Compound **1** was identified as jatropham by its spectroscopic properties and by comparison with published data [1–4]. The absolute configuration of jatropham at C-5 had not been determined until our examination. We identified it as *R* by comparison of the CD spectrum of **1** with that of (*R*)-dihydromaleimide, showing positive Cotton effects in the $n \rightarrow \pi^*$ region [5].

Compound **2** was suggested to be a glucoside of **1** by its ^{1}H NMR and ^{13}C NMR spectra. Acetylation of **2** with acetic anhydride–pyridine gave a tetraacetate. Enzymatic hydrolysis of **2** with β-glucosidase afforded **1** and D-glucose, and furthermore the ^{1}H NMR spectrum of **2** exhibited a signal of one anomeric proton [δ5.12 (1H, *d*, J = 7.8 Hz)], indicating the presence of a β-glucopyranoside linkage. Compound **2** was therefore confirmed to be jatropham 5-*O*-β-D-glucopyranoside.

Compound **3** was identified as (±)-5-*O*-methyljatropham by its spectral data (IR, MS, ^{1}H NMR and ^{13}C NMR spectra). There has been no report on the isolation of **3**, but it is uncertain whether **3** is a natural product or an artefact because it was obtained as a racemate different from the cases of **1** and **2**.

Jatropham (**1**) is known as an antitumour alkaloid isolated from *Jatropha macrorhiza* (Euphorbiaceae) [1] and it has not been isolated from other natural sources. In this investigation, **1** and its glucoside (**2**) were obtained in good yields. Compound **1** was the first antitumour alkaloid obtained from the *Lilium* plant, and **2** is also expected to show tumour-inhibitory properties.

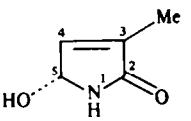
EXPERIMENTAL

Fresh dormant bulbs of *L. hansonii* (4.5 kg), purchased from Heiwaen Co. (Nara Prefecture in Japan), were extracted twice with hot MeOH. The MeOH soln was concentrated to a small vol. under red. pres., and the residue was suspended in H_2O. This suspension was extracted successively with $CHCl_3$ and *n*-BuOH. The *n*-BuOH soluble fraction was repeatedly chromatographed on silica gel and Sephadex LH-20 to afford **1**–**3**.

Compound **1**. 1.6 g, colourless needles ($CHCl_3$–MeOH), mp 119–123°, $[\alpha]_D^{25}$ −76.2° (MeOH; *c* 1.00) (Found: C, 52.93; H, 6.22; N, 12.31. Calc. for $C_5H_7NO_2$: C, 53.09; H, 6.24; N, 12.38%). CD (MeOH; *c* 0.02) nm (θ): 248 (+6544); UV λ_{max}^{MeOH} nm (log ε): 206 (4.30), 240 sh (3.25); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 3250, 1705, 1650; EIMS *m/z*: 113 $[M]^+$, 98, 85, 69, 41; ^{1}H NMR (90 MHz, CD_3OD): δ6.62 (1H, *m*, H-4), 5.43 (1H, *m*, H-5), 1.63 (3H, *m*, Me); ^{13}C NMR (100.6 MHz, CD_3OD) : δ175.3 (C-2), 143.0 (C-4), 136.8 (C-3), 79.8 (C-5), 10.4 (Me).

Compound **2**. 5.0 g, colourless needles ($CHCl_3$–MeOH), mp 178–183°, $[\alpha]_D^{25}$ −15.6° (MeOH; *c* 1.00); IR ν_{max}^{KBr} cm^{-1}: 3400, 1687, 1650; EIMS *m/z*: 276 $[M+1]^+$, 245, 208, 131; ^{1}H NMR (400 MHz, C_5D_5N): δ6.76 (1H, *m*, H-4), 5.89 (1H, *m*, H-5), 5.12 (1H, *d*, J = 7.8 Hz, H-1'), 4.52–3.92 (6H, H-2', 3', 4', 5', 6'), 1.64 (3H, *m*, Me); ^{13}C NMR (100.6 MHz, DMSO-d_6): δ172.2 (C-2), 138.8 (C-4), 135.5 (C-3), 101.8 (C-1'), 84.3 (C-5), 77.2 (C-3'), 76.5 (C-5'), 73.2 (C-2'), 70.0 (C-4'), 61.1 (C-6'), 10.0 (Me).

Acetylation of compound **2**. Compound **2** (62 mg) was acetylated with AC_2O–pyridine for 24 hr at room temp. to give the corresponding tetraacetate, which was purified by silica gel CC to yield colourless needles (EtOH), 69 mg, mp 176–178°; IR ν_{max}^{KBr} cm^{-1}: 3220, 1775, 1712, 1650; EIMS *m/z*: 443 $[M]^+$, 347, 245, 200, 139, 97; ^{1}H NMR (90 MHz, $CDCl_3$): δ7.15 (1H, *br*, NH), 6.55 (1H, *m*, H-4), 5.48 (1H, *m*, H-5), 4.68 (1H, *d*, J = 7.5 Hz, H-1'), 5.23–3.60 (6H, H-2', 3', 4', 5', 6'), 2.08, 2.03, 1.99, 1.93 (each 3H, *s*, OCOMe), 1.85 (3H, *m* Me).



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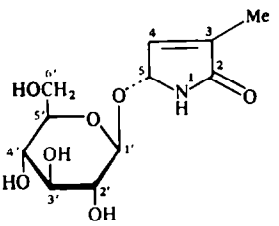

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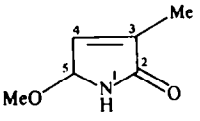

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Enzymatic hydrolysis of compound **2**. A mixture of **2** (100 mg) and β-glucosidase (10 mg) was incubated in HOAc–NaOAc buffer (pH 5) at 37° for 30 hr, and then, after addition of H_2O, it was extracted with *n*-BuOH. The extract was chromatographed on silica gel to give colourless needles ($CHCl_3$–MeOH), 14 mg, mp 107–112°, $[\alpha]_D^{25}$ −76.5°(MeOH *c* 0.16), identical with compound **1** in terms of TLC (R_f 0.40; $CHCl_3$–MeOH, 8:1), IR and ^{1}H NMRspectra. From the H_2O layer, D-glucose was obtained and identified by TLC (R_f 0.36; *n*-BuOH–Me_2CO–H_2O, 4 : 5 : 1).

Compound **3**. 230 mg, colourless syrup, $[\alpha]_D^{25}$ ±0° (MeOH; *c* 0.40); CD: showing no Cotton effect; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3250, 3020, 1705, 1654; EIMS *m/z*: 127 $[M]^+$, 112, 96, 31; ^{1}H NMR (90 MHz, $CDCl_3$): δ7.69 (1H, *br*, NH), 6.54 (1H, *m*, H-4), 5.39 (1H, *m*, H-5), 3.27 (3H, *s*, OMe), 1.63 (3H, *s*, Me); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ173.7 (C-2), 138.7 (C-4), 138.1 (C-3), 84.5 (C-5), 52.7 (OMe), 10.6 (Me).

REFERENCES

1. Wiedhopf, R. M., Trumbull, E. R. and Cole, J. R. (1973) *J. Pharm. Sci.* **62**, 1206.
2. Yakushijin, K., Kozuka, M., Ito, Y., Suzuki, R. and Furukawa, H. (1980) *Heterocycles* **14**, 1073.
3. Yakushijin, K., Suzuki, R., Hattori, R. and Furukawa, H. (1981) *Heterocycles* **16**, 1157.
4. Nagasaka, T., Esumi, S., Ozawa, N., Kosugi, Y. and Hamaguchi, F. (1981) *Heterocycles* **16**, 1987.
5. Masuko, M., Miyamoto, K., Sakurai, K., Iino, M., Takeuchi, Y. and Hashimoto, T. (1983) *Phytochemistry* **22**, 1278.

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THALIFABORAMINE, A DIMERIC APORPHINOID ALKALOID FROM *THALICTRUM FABERI*

LONG-ZE LIN, SHU-FANG LI* and HILDEBERT WAGNER†

Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China; *Shanghai Second Polytechnic University, Shanghai, China; †Institut für Pharmazeutische Biologie der Universität München, West Germany

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Key Word Index—*Thalictrum faberi*; Ranunculaceae; alkaloid; thalifaboramine.

Abstract—A new dimeric aporphinoid alkaloid thalifaboramine was isolated from the roots of *Thalictrum faberi*. The structure of the compound was established by spectral analysis.

INTRODUCTION

Thalictrum faberi Ulbr., a plant native to China, is used in Chinese folk medicine as an antiphlogistic, antibacterial and, recently, in the treatment of stomach cancer. Over 16 new aporphine-benzylisoquinoline dimers were isolated from the plant [1, 2], and the crude base as well as most of the new alkaloids have shown cytotoxicity against P-388 carcinoma cell [J.-L. Yang, unpublished results]. One of them is thalifaboramine, and now, we present its isolation and structural determination in this report.

RESULTS AND DISCUSSION

Extraction and work-up of 10 kg of the dried powdered roots of the plant yielded 24 mg of thalifaboramine (**1**) as a yellow amorphous solid, $C_{39}H_{44}O_7N_2$. The mass spectrum of the compound shows a small $[M]^+$ at *m/z* 652 and a base peak at *m/z* 206 due to facile formation of the dihydroisoquinolinium cation **a** through cleavage of the C-1′ to C-a′ bond, which suggests two OMe groups at the isoquinoline part. The NMR spectrum ($CDCl_3$, FT 400 MHz), outlined around structure **1**, shows a characteristic AA′BB′ quartet (J = 8.9 Hz), typical of the four symmetric protons of the C-ring of the benzylisoquinoline moiety. It follows that the remaining C-12′ site should be the terminus of the diaryl ether bridge in this moiety. The NMR spectrum also shows the presence of two N-Me groups, five OMe groups, four other aromatic protons and one phenolic group (δ6.95, D_2O exchangeable). The UV spectrum shows 17 nm of bathochromic shift with hyperchromism in strong base, suggesting that the phenolic function at the C-3 or C-9 position of the aporphine moiety [3]. In order to assign the NMR signals, an NOE difference study of the alkaloid was undertaken, and the results have been summarized in structure **1A**. There is a significant (3.9 or 5.7%) enhancement of H-3 signal upon irradiation of the C-2 methoxyl, which serves to prove that the phenolic function cannot be at the C-3 position. Similarly, the 8.4% NOE, shown by H-11 upon irradiation of the C-10 methoxyl, proves that the diaryl ether terminal cannot be at C-10. Therefore, the phenolic group must be at the C-9 position.