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).

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THALIFABORAMINE, A DIMERIC APORPHINOID ALKALOID FROM *THALICTRUM FABERI*

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

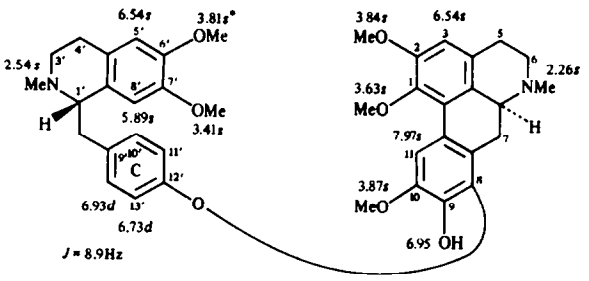
Abstract—A new dimeric aporphinoid alkaloid thalifaboramine was isolated from the roots of *Thalictrum faberi*. The structure of the compound was established by spectral analysis.

INTRODUCTION

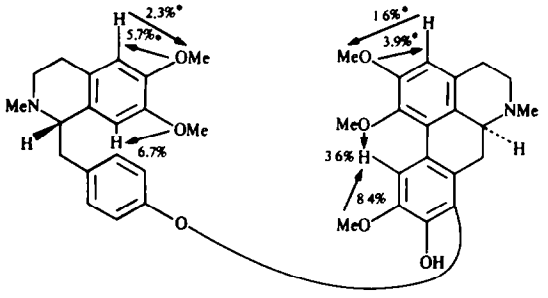
Thalictrum faberi Ulbr., a plant native to China, is used in Chinese folk medicine as an antiphlogistic, antibacterial and, recently, in the treatment of stomach cancer. Over 16 new aporphine-benzylisoquinoline dimers were isolated from the plant [1, 2], and the crude base as well as most of the new alkaloids have shown cytotoxicity against P-388 carcinoma cell [J.-L. Yang, unpublished results].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



1



1A

The circular dichroism curve of thalifaboramine (**1**) is very close to that of thalifaberine which corresponds with *O*-methylthalifaboramine [1, 2] and is supportive of the identical absolute configuration for **1**.

Up to now, about 50 aporphine-benzylisoquinoline dimers in the literature were divided into nine groups [4, 5]. Thalifaboramine belongs to the thalifaberine-type dimers according to the same diaryl ether linkage and same absolute configuration. However, thalifaboramine has a C-9 phenolic group and C-3 proton, instead of a C-9 methoxyl and a C-3 oxygenated group of six other thalifaberine-type dimers [2].

EXPERIMENTAL

NMR spectra were run in $CDCl_3$ at 400 MHz with chemical shifts (δ) reported in ppm.

Isolation. The procedure is reported in detail elsewhere [2, 6]. The residue (100 mg) from fractions 71 and 72 of rechromatographic column of fraction 99–106 (see isolation of thalifarapine and faberidine [2]), contained four alkaloids, which were sepd by prep. TLC in toluene–Me_2CO–NH_4OH (60:90:1) using 3 developments. The lowest R_f band, purified by repeated prep. TLC with the same solvent system, gave thalifaboramine as a yellow solid (24 mg), $[\alpha]_D^{14°}$ + 107.4° (*c*, 0.135, MeOH); IR ν_{max} ($CHCl_3$) 3530 cm^{-1} (OH); UV λ_{max} (MeOH), 283, 313 sh nm (log 4.30, 3.98), λ_{max} (MeOH–NaOH), 290, 330 nm (log ε 4.14, 4.14); NMR(400 MHz), the value and NOE enhancement data are shown around structures **1** and **1A**, respectively; MS (EI) *m/z* 652 ($[M]^+$, *ca* 0.1%, for $C_{39}H_{44}O_7N_2$), 446 ($[M-a]^+$, 5%), 206 (**a**, 100%); CD (nm), −3.29 (305), −3.99 (276), +51.72 (243).

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