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# BAIYUMINE-A AND -B, TWO ACRIDONE ALKALOIDS FROM *CITRUS GRANDIS*

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**Key Word Index**—*Citrus grandis f. hakunikuyu*; Rutaceae; acridone alkaloids; baiyumine-A; baiyumine-B; NMR.

**Abstract**—Two new acridone alkaloids, baiyumine-A and -B, were isolated from the root bark of *Citrus grandis f. hakunikuyu*. Their structures were elucidated by spectral analysis and chemical transformation.

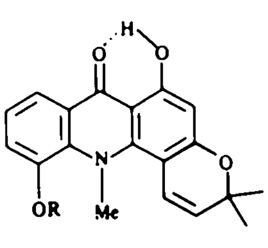
## INTRODUCTION

In a previous paper [1], we reported the isolation of several acridone alkaloids, quinolone alkaloids and coumarins from the root bark of *Citrus grandis f. hakunikuyu* (Chinese name: Baiyu). We now report the isolation and structural elucidation of two new acridone alkaloids, namely, baiyumine-A and -B, obtained from the lower polar fraction of the acetone extract of the same plant.

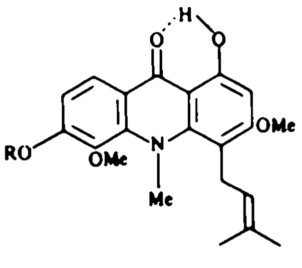
## RESULTS AND DISCUSSION

Baiyumine-A (**1**), was isolated as orange plates, mp 160–161°, $C_{20}H_{19}NO_4$ ($[M]^+$ 337). The UV spectrum of **1** had maximum absorption at 235, 265, 287, 321, 344 and 418 nm characteristic of the 9-acridone nucleus [2–4]. The presence of a chelated phenolic hydroxyl group at the 1-position was indicated by a bathochromic shift of UV bands with aluminium chloride and the $^1$H NMR signal at $\delta$14.25 (1H, *s*, exchangeable with $D_2O$). The $^1$H NMR spectrum of **1** showed an ABC pattern of signals at $\delta$7.10–7.35 (2H, *m*) and 7.96 (1H, *dd*, $J = 2.5$ and 7 Hz) due to H-6, 7 and H-8, respectively. The deshielding of H-8 is reasonable because it lies in the *peri*-position with respect to the 9-carbonyl moiety. The AB type quartets at $\delta$5.54 and 6.65 (each 1H, *d*, $J = 10$ Hz) and a six-proton singlet at $\delta$1.51 revealed the presence of a dimethylpyran system attached to ring C because the lower signal of this AB quartet had a long range coupling ($J = 0.8$ Hz) with the doublet at $\delta$6.25 (H-2). Two sharp singlets at $\delta$3.74 and 4.01 (each 3H) were attributed to *N*-methyl and methoxyl groups. In the $^{13}$C NMR spectrum of baiyumine-A, signals of an *N*-methyl carbon and the olefinic C-1′ of the dimethylpyran ring appeared at $\delta$49.1 and 121.0, respectively. The chemical shift values suggested that the dimethylpyran ring had an angular orientation [5]. Furthermore, treatment of 5-hydroxynoracronycine (**2**) with diazomethane afforded a 5-*O*-methyl derivative which was identical with baiyumine-A by comparisons of $^1$H NMR, IR, TLC and mmp. On the basis of these results, baiyumine-A should be represented by formula **1** which was synthesized by Fraser and Lewis in 1973 [4]. This is the first report of the occurrence of baiyumine-A (**1**) in nature [6].

Baiyumine-B (**3**) was obtained as yellow plates from ether, mp 145–147°. The molecular formula of **3** was established as $C_{22}H_{25}NO_5$ by microanalysis and the $[M]^+$ at $m/z$ 383 in the mass spectrum. The UV and IR spectra (see Experimental) also showed absorptions characteristic of 9-acridones [2–4]. In the $^1$H NMR spectrum of **3** there was a strongly intramolecularly hydrogen bonded proton at $\delta$14.13, which was assigned to the C-1 hydroxyl group of an acridone nucleus. AB-type proton signals at $\delta$6.91 and 8.03 (each 1H, *d*, $J = 8$ Hz) were attributed to mutually *ortho*-located protons on the A ring, and the lower field signal could be assigned to H-8 which was affected by a deshielding of the 9-carbonyl moiety. The presence of three methoxyls, an *N*-methyl and a prenyl group in the molecule was confirmed by NMR and/or mass spectra (methoxyl and *N*-methyl: $\delta_H$ 3.98, 3.89, 3.87 and 3.75; $\delta_C$ 60.1 (*q*), 56.3 (*q*), 55.9 (*q*) and 48.6 (*q*); prenyl: $\delta_H$ 1.70 (3H, *s*), 1.77 (3H, *s*), 3.42 (2H, *d*, $J = 7$ Hz), and 5.24 (1H, *m*); $\delta_C$ 18.0 (*q*), 25.7 (*q*), 26.1 (*t*) and 123.7 (*d*); $m/z$ 328 $[M - CH{=}C(CH_3)_2]^+$ and 315 $[M - CH_2CH{=}C(CH_3)_2 + H]^+$) The chemical shift value of an *N*-methyl carbon and a methylene carbon of **3** appeared at $\delta$48.6 and 26.1, respectively, in the



**1** R = Me
**2** R = H



**3** R = Me
**4** R = H

$^{13}$C NMR spectrum which indicated that both *peri*-positions (C-4 and C-5) of the *N*-methyl group were substituted and the prenyl group was located at C-4 [5]. Thus, a sharp one proton singlet at $\delta$6.33 was assigned to a lone aromatic proton of H-2. The above data suggested the structure of baiyumine-B as formula **3**. In agreement with this proposition, methylation of grandisinine (**4**) with diazomethane furnished a mono-*O*-methyl derivative of **3** which was identical with baiyumine-B by comparisons of $^1$H NMR, IR, TLC and mmp. On the basis of these spectral analysis and chemical transformation, baiyumine-B was assigned structure **3**.

## EXPERIMENTAL

All mps are uncorr. $^1$H and $^{13}$C NMR spectra were recorded in $CDCl_3$; chemical shifts are given in ppm ($\delta$) with TMS as int. ref. MS were measured with a direct inlet system. UV spectra were determined in MeOH and IR spectra in $CHCl_3$.

*Isolation of alkaloids*. Root bark of *C. grandis* Osbeck *f. hakunikuyu* Hayata (6 kg) was macerated in $Me_2CO$ and extracted repeatedly with the same solvent. The $Me_2CO$ extracts were combined and concd under red. press. The crude extract was separated by the method previously described [1]. The $C_6H_6$ fraction was rechromatographed on silica gel and eluted with $C_6H_6$ to provide three fractions. Fraction I was repeatedly chromatographed on prep. TLC plates (silica gel) with $C_6H_6$ to give **1**. Fraction III was also separated by prep. TLC on silica gel in $C_6H_6$ to afford **3**.

*Baiyumine-A* (**1**). Orange plates from $Et_2O$, mp 160–161° (lit. 155–157°) [4] (calculated for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15; found: C, 71.13; H, 5.68; N, 4.13). UV $\lambda_{max}$ nm: 235, 265, 287, 321, 344, 418. UV $\lambda_{max}$ (+ NaOMe) nm: 235, 268, 287, 320, 344, 418. UV $\lambda_{max}$ (+ $AlCl_3$) nm: 216, 260, 290 (sh), 302, 335 (sh), 360, 470. IR $\nu_{max}$ cm$^{-1}$: 1625, 1590, 1555. MS $m/z$ (%): 337 ([M]$^+$, 41), 322 (100), 306 (22), 292 (3), 278 (12), 261 (5), 256 (8). $^{13}$C NMR: $\delta$181.9 (*s*), 164.5 (*s*), 161.4 (*s*), 150.6 (*s*), 147.8 (*s*), 138.1 (*s*), 125.0 (*s*), 123.8 (*d*), 123.1 (*d*), 121.0 (*d*) 117.7 (*d*), 115.4 (*d*) 107.3 (*s*), 102.4 (*s*), 98.2 (*d*), 76.6 (*s*), 56.1 (*q*), 49.1 (*q*), 27.2 (*q*).

*Methylation of 5-hydroxynoracronycine* (**2**). 5-Hydroxynoracronycine (30 mg) was suspended in $Et_2O$ (50 ml), treated with excess $CH_2N_2$ and left overnight. The soln was evaporated to leave an orange crystal, which was recrystallized from $Et_2O$ to give 30 mg of orange plates, mp 160–161°. This derivative was identified as baiyumine-A (**1**) by comparisons of $^1$H NMR, IR, TLC, mmp.

*Baiyumine-B* (**3**). Yellow plates from $Et_2O$, mp 145–147° (calculated for $C_{22}H_{25}NO_5$: C, 68.91; H, 6.57; N, 3.65; found: C, 67.93; H, 6.55; N, 3.67). UV $\lambda_{max}$ nm (log $\varepsilon$): 223 (4.20), 262 (sh, 4.63), 269 (4.65), 335 (4.27), 400 (3.73). UV $\lambda_{max}$ (+ NaOMe) nm: 223, 263 (sh), 270, 336, 400. UV $\lambda_{max}$ (+ $AlCl_3$) nm: 238, 265 (sh), 281, 362, 450. IR $\nu_{max}$ cm$^{-1}$: 1625, 1585, 1560. MS $m/z$ (%): 383 ([M]$^+$, 51), 368 (100), 352 (5), 338 (27), 328 (8), 326 (12), 322 (15), 315 (12), 306 (5), 300 (6), 258 (6), 256 (8), 243 (28). $^{13}$C NMR: $\delta$182.4 (*s*), 164.9 (*s*), 163.2 (*s*), 157.5 (*s*), 150.1 (*s*), 143.6 (*s*), 138.6 (*s*), 131.7 (*s*), 123.7 (*d*), 122.5 (*d*), 118.8 (*s*), 109.3 (*s*), 107.7 (*d*), 106.9 (*s*), 93.8 (*d*), 60.1 (*q*), 56.3 (*q*), 55.9 (*q*), 48.6 (*q*), 26.1 (*t*), 25.7 (*q*), 18.0 (*q*).

*Methylation of grandisinine* (**4**). Treatment of **4** (20 mg) with $CH_2N_2$ in the usual way afforded yellow plates (19 g), mp 145–146°. The product was shown to be identical with baiyumine-B (**3**) by IR, $^1$H NMR, TLC, mmp.

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6. Recently, Dr. Ju-Ichi M., Mukogawa Women's University, Japan has informed me that he obtained **1** from *Citrus natsudaidai* Hayata.