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Two Tetrahydroquinoline Alkaloids from *Glycyrrhiza uralensis*

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Abstract□Two alkaloids were isolated from the roots of *Glycyrrhiza uralensis* Fisch. They were identified as 5,6,7,8-tetrahydro-2,4-dimethylquinoline (**1**) and 5,6,7,8-tetrahydro-4-methylquinoline (**2**) by spectral data. The isolation of alkaloid from *Glycyrrhiza* species is reported for the first time.

Keywords□*Glycyrrhiza uralensis* Fisch., tetrahydroquinoline alkaoid, licorice.

Many kinds of the constituents of licorice were isolated and well characterized; for examples, saponins triterpenoids, flavonoids, isoflavonids, coumarin derivatives, and amino acids and their derivatives involving choline and betaine.[1] However, no alkaloid was isolated from licorice untill now, although the presence of several alkaloids in licorice is already known.[2] In the present communication, we report the isolation of two alkaloids from the roots of *Glycyrrhiza uralensis* Fischer et DC.

A crude alkaloidal fraction was prepared from the roots by partitioning their methanol extract between chloroform and ammonia water. Its thin layer chromatogram showed various spots being visualized by Dragendorff's reagent (Fig. 1). Compouds **1** and **2** was obtained by repeated chromatography of the fraction over silica gel column eluting with chloroform/ methanol.

Compound **1** appeared as colorless oil in the room temperature. Its UV spectrum resembling that of pyridine in appearance showed absorption maxima at 270.5 and 275.0 nm and its IR spectrum did absorption bands due to aromatic double bands at 1600 and 1560 cm^{-1}. The molecular formula of **1** was determined as $C_{11}H_{15}N$ (M^+ at m/z 161) by its mass spectrum, and the fragment ions at m/z 160, 146 and 133 were ascribable to the loss of H, CH_3 and $CH_2=CH_2$, respectively. ^{13}C-NMR spectrum of **1** exhibited the signals of two methyl carbons, four methylene carbons and five aromatic carbons. These data indicated that **1** belonged to 5,6,7,8-tetrahydrodimethylquinoline. ^1H-NMR spectrum of **1** also revealed the presence of two methyl groups at δ 2.15 (3H, s) and 2.43 (3H, s), four methylenes at δ 1.82 (4H, m), 2.59 (2H, m) and 2.87 (2H, m), and one aromatic proton at δ 6.76 (1H, s). The aromatic proton was assignable to the meta position of pyridine ring because of its chemical shift at quite high field. Therefore, **1** was identified as 5,6,7,8-tetrahydro-2,4-dimethylquinoline, which appeared in a early synthetic shudy.[3, 4]

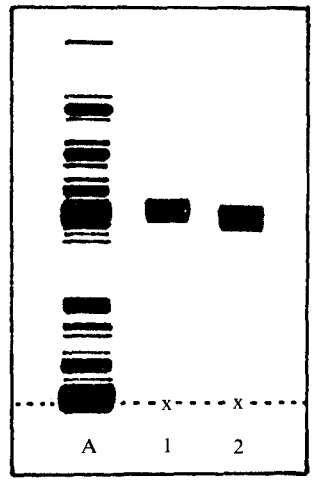

Fig. 1. TLC chromatogram of an alkaloidal fraction and compounds 1 and 2.
A, alkaloidal fraction; 1, compound 1; 2, compound 2. Developing solvent: chloroform/methanol (20:1). Coloring agent: Dragendorff's reagent. Plate: Precoated silica gel (E. Merck, type F254).

Compound **2** was also obtained as colorless oil. Its ^1H-NMR spectrum showed the signals of one methyl group at δ 2.19 (3H, s), and two aromatic

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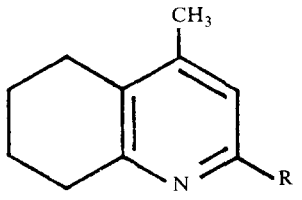

1, R = CH_3
2, R = H

protons at δ 6.87 (1H, d, J = 5Hz) and 8.20 (1H, d, J = 5Hz) together with four methylenes which were susperimposed on those of compound **1**. These data indicated that **2** was 5,6,7,8-tetrahydro-4-methylquinoline.

EXPERIMENTAL

Extraction

Methanol extracts (6kg) were prepared from the roots (24 kg) of *Glycyrrhiza uralensis* after refluxing them with methanol on a boiling water bath. A suspension was made using 12*l* of water, adjusted to pH 10 with *c*-NH_4OH, and then extracted with 20*l* of chloroform to give an emulsion. Passing of the emulsion through a soldium chloride column made to separate chloroform layer from it. The extraction with chloroform and then salting out procedure was repeated more three times. The chloroform layers were combined and fred from the solvent to yield a syrupy residue. A crude alkaloidal fraction (12g) was obtained from the residue by the usual method of acid-base extraction.

Isolation of compounds **1** *and* **2**

The alkaloidal fraction was subjected to column chromatography over silica gel (E. Merck, type 60, no. 7734) using chloroform and then chloroform /methanol (50:1) as eluting solvents to afford fractions A and B, respectively. Compounds **1** and **2** were obtained from Fr. B by repeated chromatography over silica gel (E. Merck, type 60, no. 7729) utilizing two solvent systems of chloroform/ethyl ether (1:1) and then hexane/ethyl acetate (3:1).

Compound **1**

Yield: 60 mg. Colorless oil. Rf: 0.50 ($CHCl_3$ /MeOH = 20:1). UV λ_{max} (ε) in hexane: 270.5 (2180), 275.0 (2160). IR ν_{max} (cm^{-1}): 2930, 2860 (CH), 1600, 1560 (aromatic double bond). MS *m/z* (%): 161 (M^+, 59.9), 160 (M^+-1, 57.4), 146 (M^+-CH_3, 41.7), 133 (M^+-CH_2CH_2, 24.4), 83 (100). ^{1}H-NMR δ ppm in $CDCl_3$:1.82 (4H, m, 6-CH_2 and 7-CH_2), 2.15 (3H, s, 4-CH_3), 2.43 (3H, s, 2-CH_3, 2.59 (2H, m, 5-CH_2), 2.87 (2H, m, 8-CH_2), 6.76 (1H, s, 3-H). ^{13}C-NMR δ ppm in $CDCl_3$: 155.9 (2), 122.0 (3) 145.7 (4), 22.3 (5), 23.9 (6), 23.0 (7), 33.1 (8), 154.0 (9), 127.7 (10), 25.4 (2-CH_3), 18.5 (4-CH_3).

Compound 2

Yield: 30 mg. Colorless oil. Rf: 0.49 ($CHCl_3$ /MeOH = 20:1). ^{1}H-NMR δ ppm in $CDCl_3$:1.82 (4H, m, 6-CH_2 and 7-CH_2), 2.19 (3H, s, 4-CH_3) 2.59 (2H, m, 5-CH_2), 2.87 (2H, m, 8-CH_2)), 6.87 (1H, d, 3-H, J = 5Hz), 8.20 (1H, d, 2-H, J = 5Hz).

Instrumental

A recording spectrophotometer, Gilford type 2600 was used for the measurement of UV spectra. IR spectra were obtained in KBr pellet on a Perkin-Elmer model 283B spectrophotometer. NMR spectra were taken at 25°C using TMS as an internal standard on a Varian model FT 80A spectrometer. EIMS were obtained on a Hewlett-Packard GC/MS spectrometer (Type 5985B).

ACKNOWLEDGEMENT

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