Alkaloids of *Glaucium oxylobum* Boiss and Buhse, Population Ab-Ali

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Abstract □ *Glaucium oxylobum* Boiss and Buhse, population Ab-Ali, was demonstrated to contain one major alkaloid, glaucine (0.7%), and two minor alkaloids, *O*-methylatheroline and predicentrine, in the aerial parts. The root also contains protopine. Glaucine and *O*-methylatheroline were detected for the first time in this species, and predicentrine was detected for the first time in the *Glaucium* genus.

Keyphrases □ *Glaucium oxylobum*—aerial parts and roots, alkaloids isolated and identified □ Alkaloids—isolated and identified in *Glaucium oxylobum* aerial parts and roots

As part of chemotaxonomic studies of Iranian wild *Papaveraceae* (1–4), the alkaloids of *Glaucium oxylobum* Boiss and Buhse[1], population Ab-Ali (a perennial wild plant scattered in Ab-Ali, located on the southern slopes of the Alborz mountains north of Tehran at about 2200 m above sea level), were isolated and identified. The height of the plant is 50–100 cm. The plant blooms from April to September. The four petals are yellow at the edge and orange at the bottom with a brown spot at the base of each petal.

EXPERIMENTAL

Plant Material—The whole aerial parts or roots were collected during May, air dried in the shade, then dried at 60° to a constant weight, and powdered so that all material possesses a mesh size not greater than 0.5 mm. The aerial parts and roots were extracted separately.

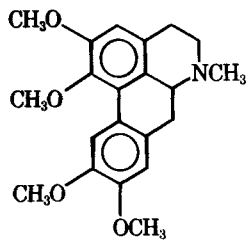
Extraction—Powdered plant material, 200 g, was moistened with 200 ml of 15% NH_4OH, stirred with 600 ml of chloroform at room temperature for 1 hr, and filtered. The extraction was repeated four times. After evaporation of the solvent, the residue was extracted with 100 ml of 5% sulfuric acid. The solution was filtered and extracted with petroleum ether (3 × 20 ml) to remove the colored material. The aqueous layer was made alkaline with 15% NH_4OH and extracted with chloroform (4 × 50 ml). Evaporation of the solvent gave 1.8 g of the crude alkaloids.

RESULTS AND DISCUSSION[2]

Chromatography of the crude alkaloids from the aerial parts [TLC, silica gel, ethyl acetate–methanol–ammonia (85:10:5)] gave glaucine (I, 1.4 g, 0.7%), mp 118–119° [lit. (5) mp 117–118°], mixed melting point with an authentic sample 117–119°. For the hydrobromide, the melting point was 239–241° (ethanol) [lit. (6) mp 241°]. The UV, IR, and NMR data of the separated alkaloid were identical with those reported previously (7, 8).

Glaucine was isolated by Bubeva-Ivanova *et al.* (9) from *Glaucium flavum* and claimed to have antitussive, spasmolytic, antiedematous, and tranquilizer effects but no depressing activity.

O-Methylatheroline (II) was obtained as a minor alkaloid, mp 224° [lit. mp 225–227° (10), 227–229° (11), and 235–236° (12)]. The IR spectrum was identical to the published spectrum for II (12), and the UV and



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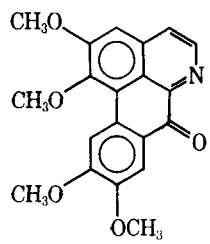
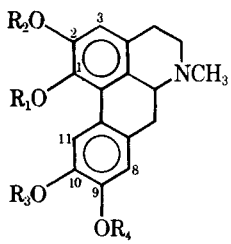


II



III: R_2 = H, R_1 = R_3 = R_4 = CH_3
IV: R_1 = H, R_2 = R_3 = R_4 = CH_3 (thaliporphine)
V: R_3 = H, R_1 = R_2 = R_4 = CH_3
VI: R_4 = H, R_1 = R_2 = R_3 = CH_3 (*N*-methyllaurotetanine)

NMR spectral data were in accord with published data (11, 13). The mass spectrum had major peaks at *m/e* 351, 336, 320, 308, and 234.

Anal.—Calc. for $C_{20}H_{17}NO_5$: C, 68.38; H, 4.84; N, 3.99. Found: C, 68.21; H, 4.93; N, 4.05.

A second minor alkaloid was an oil which could not be crystallized in various solvents. Its hydrochloride salt was a solid, mp 214–217° (methanol–ethyl acetate). As the free base, the UV spectrum showed λ_{max} (ethanol) 301 (log ϵ 4.11) and 280 (4.15) nm and λ_{min} 252 (3.73) nm; UV λ_{max} (ethanol, 2 drops of 10% NaOH): 301 and 280 nm; NMR ($CDCl_3$): δ 2.50 (s, 3H, NCH_3), 3.56 (3H, s, OCH_3), 3.88 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.56 (s, 1H, aromatic), 6.73 (s, 1H, aromatic), and 7.88 (s, 1H, aromatic) ppm. The mass spectrum had peaks at *m/e* 341 (M^+), 340 (M − 1), 326 (M − CH_3), 310 (M − OCH_3), 298 (M − CH_2=NCH_3), 165, 152, and 149.

Anal.—Calc. for $C_{20}H_{23}NO_4$: C, 70.38; H, 6.74; N, 4.11. Found: C, 70.42; H, 6.68; N, 4.02.

The UV spectrum was similar to that of dicentrine and glaucine (7); in addition, its mass spectrum fragmentation pattern was characteristic of aporphine alkaloids (14). The three singlet aromatic protons in the NMR spectrum showed that adjacent aromatic protons did not exist; in addition, the most deshielded aromatic proton must be at C_{11}. The NMR spectrum was in agreement with the four possible structures (III–VI) for this compound.

The UV spectrum in a basic solution did not show a hypsochromic shift given above, indicating that the hydroxyl was not at C-9. In addition, the spectral data for this alkaloid were different from the data for IV–VI (8, 15, 16). The UV, NMR, and IR (chloroform) spectra were identical with the spectra of predicentrine[3], which was synthesized by Charubala *et al.* (17). This alkaloid is, therefore, predicentrine. It was reported to exist also in *Ocotea macropoda*[4].

From the root of the plant, protopine was also isolated, mp 205–207° [lit. (18) mp 207°], mixed melting point with an authentic sample 205–207°. The NMR spectrum was identical with the one reported previously (19).

[1] The plant was identified by Dr. C. R. Gunn, Plant Taxonomy Laboratory, Plant Genetics and Germplasm Institute, Agricultural Research Service, Beltsville, MD 20705. A herbarium sample was deposited in the Herbarium of the College of Pharmacy, Tehran University.

[2] Melting points were taken with a Koffler hot-stage microscope and are uncorrected. UV spectra were recorded on a Varian Techtron 635 instrument. NMR spectra were taken with a Varian T-60A instrument, using tetramethylsilane as the internal standard. Mass spectra were recorded on a CH5 spectrometer at Arya-Mehr Technical University. IR spectra were obtained with a Leitz model III spectrograph.

[3] The spectra of predicentrine was provided by Professor B. R. Pai, Presidency College, Madras, India.

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A literature survey (20, 21) revealed that glaucine and *O*-methylatheroline had not been found previously in *G. oxylobum* and predicentrine had not been detected in the genus *Glaucium*.

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Synthesis of 5,6-Benzo-2-azabicyclo[2.2.2]octane Derivatives as Potential Benzomorphan-Type Analgesic Agents

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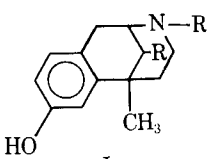
Abstract □ The synthesis of two *N*-substituted 5,6-benzo-2-azabicyclo[2.2.2]octane analogs of benzomorphan-type analgesics *via* benzyne addition to appropriate *N*-substituted *N*-alkyl-2-pyridones is described. Neither derivative possessed observable analgesic activity at the doses tested.

Keyphrases □ 5,6-Benzo-2-azabicyclo[2.2.2]octanes, *N*-substituted—synthesized, analgesic activity evaluated, mice □ Structure–activity relationships—*N*-substituted 5,6-benzo-2-azabicyclo[2.2.2]octanes synthesized, analgesic activity evaluated, mice □ Analgesic activity—*N*-substituted 5,6-benzo-2-azabicyclo[2.2.2]octanes evaluated, mice

The structural features of narcotic analgesics related to morphine have been well documented (1, 2). Studies of structure–analgesic activity requirements within the benzomorphan-type analgesics have also received considerable attention. While the structural features of benzomorphans are generally incorporated in structures such as I, many analogous structures have been demonstrated to possess significant analgesic activity. For example, 2-methyl-6,7-benzomorphan (II) (3), 7-methoxy-2-methyl-B-norbenzomorphan (III) (4), and 5-methano-3-methyl-6-phenyl-1,2,3,4,5,6-hexahydro-3-benzazocine (IV) (5)



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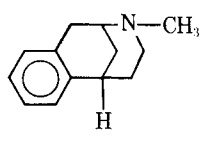

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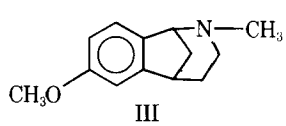
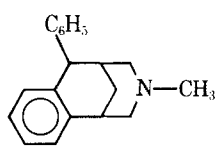


III



IV

possessed analgesic potencies comparable to that of codeine.

Compounds II–IV all lack "quaternary central carbon atoms," a structural feature once thought to be essential for activity (1, 2). Additionally, II and IV lack phenolic functions, and IV contains only a one-carbon separation from the basic nitrogen and the central carbon atom. While the active benzomorphans are characterized by the presence of a basic nitrogen atom 4.1 Å from the center of an