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SOURCE OF SOME MINOR ALKALOIDS IN *GLAUCIUM FLAVUM*

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Key Word Index—*Glaucium flavum*; Papaveraceae; alkaloids; glaucine; air oxidation; UV irradiation; dihydropontevedrine.

Abstract—Air oxidation of glaucine leads to 7,6′-dehydroglaucine and 1,2,9,10-tetramethoxyoxoaporphine, and UV irradiation gives dihydropontevedrine, pontevedrine, glaucine-*N*-oxide and corunine. These results support the view that glaucine, the main alkaloid in *Glaucium flavum*, may produce all the more oxidized minor alkaloids present in the plant.

INTRODUCTION

The antitussive alkaloid glaucine (**1**) is the main component in the alkaloid mixture of *Glaucium flavum*, a plant widely distributed in southern Europe. Besides **1**, a number of aporphine alkaloids have been isolated as minor components from this mixture. Most of them are the oxidized analogues of **1**. Cataline (**2**), pontevedrine (**5**) and corunine (**9**) were described for *G. flavum* of Spanish origin [1, 2]. In the same plant growing in Bulgaria, 7,6′-dehydroglaucine (**3**), 1,2,9,10-tetramethoxyoxoaporphine (**8**) and 6,6′-dehydronorglaucine (**7**) were found [3, 4]. The above minor alkaloids in *G. flavum* are probably derived from **1** during the processing of the plant material under the influence of air and light. To verify the above suggestion an investigation of the air oxidation and UV light irradiation of **1** was undertaken. In this paper the results are described.

RESULTS AND DISCUSSION

The decomposition of **1** to **8** after 32 hr irradiation with UV light in the presence of air has been described [5]. Photo-oxidation was also used to obtain **8** from **1** and **3** [6]. The direct photo-oxidation of **1** as well as an eosine-sensitized one of **1**, **3** and norglaucine to **8** and **9** is also known [7]. There is no information on the air oxidation of **1**, but it is known that some aporphines which possess a phenolic group on C-1 or C-11, or two phenol groups on C-10 and C-11, undergo such oxidation [12].

The chloroform or ethanol solution of **1** is rather unstable in air. After 1–2 days in the mixture, **3**, **6**, **8** and **9** could be observed by TLC. **3** appears after 20 min when a 1 % ethanol solution of **1** is bubbled with air. **3** and **8** were formed after 2–3 days. When the reaction is carried out in darkness, **3** appears after 5–7 hr.

Irradiation of an ethanol solution of **1** with a mercury lamp for 2 hr in an argon or nitrogen atmosphere generates **3**–**6**, **8** and **9**.

Compound **4** was isolated by preparative TLC as red crystals (mp 248–50°) and exhibited a M^+ peak at m/z 383 in the mass spectrum. There is an absorption band at 1650 cm^{-1} in the IR spectrum for a conjugated carbonyl group and at 1590 cm^{-1} for an aromatic ring. The NMR spectrum shows characteristic peaks for one N-Me group at 3.82 (3 H, *s*), for four OME groups at 4.14 (12 H, *s*) and for five protons in the aromatic region at 7.27, 7.36, 8.21 and 9.15. Some of these peaks are not well resolved which probably arises from tautomerism. **4** gives a positive ferric chloride test. The UV spectrum with λ_{max}^{EtOH} 245, 312, 325 and 470 nm is not affected by acid or base. The colour reaction, UV and IR spectra of **4** are very similar to those of **5** but there are differences in mass and NMR spectra as well as TLC. The above-described spectral data support the structure **4** for the compound which is new and named dihydropontevedrine.

Compound **9** obtained as a photo-product can also be formed from **8** on heating for 32 hr at 150° [8]. We found that **8** forms **9** in 10 % yield when a solution in benzene is boiled. The yield is increased to 45 % when a xylene solution of **8** is boiled for 1.5 hr. Experiments with different concentrations showed that the migration of the O-methyl group to nitrogen is an intermolecular reaction since it is strongly repressed in dilute solutions.

Compound **8** has no *N*-methyl group. The demethylation of tertiary to secondary amines by UV light is well known [9, 10] but the reaction mechanism is not fully understood. The Polonovsky and Meisenheimer procedures for chemical transformation of *N*-oxides of tertiary amines into secondary ones are known. We believe that there are several routes for the demethylation of tertiary amines but *N*-oxides could be intermediates in some of them.

The above experimental data support the assumption that the main alkaloid in *G. flavum*, glaucine, may produce all of the more oxidized minor alkaloids discovered in the alkaloid mixture of the plant. One possible scheme for the formation of these compounds is shown.

EXPERIMENTAL

Mps are uncorr. IR spectra were recorded in $CHCl_3$ or as KBr pellets. NMR spectra were measured at 60 MHz in $CDCl_3$ with TMS as int. standard. Chemical shifts are expressed in δ-units.

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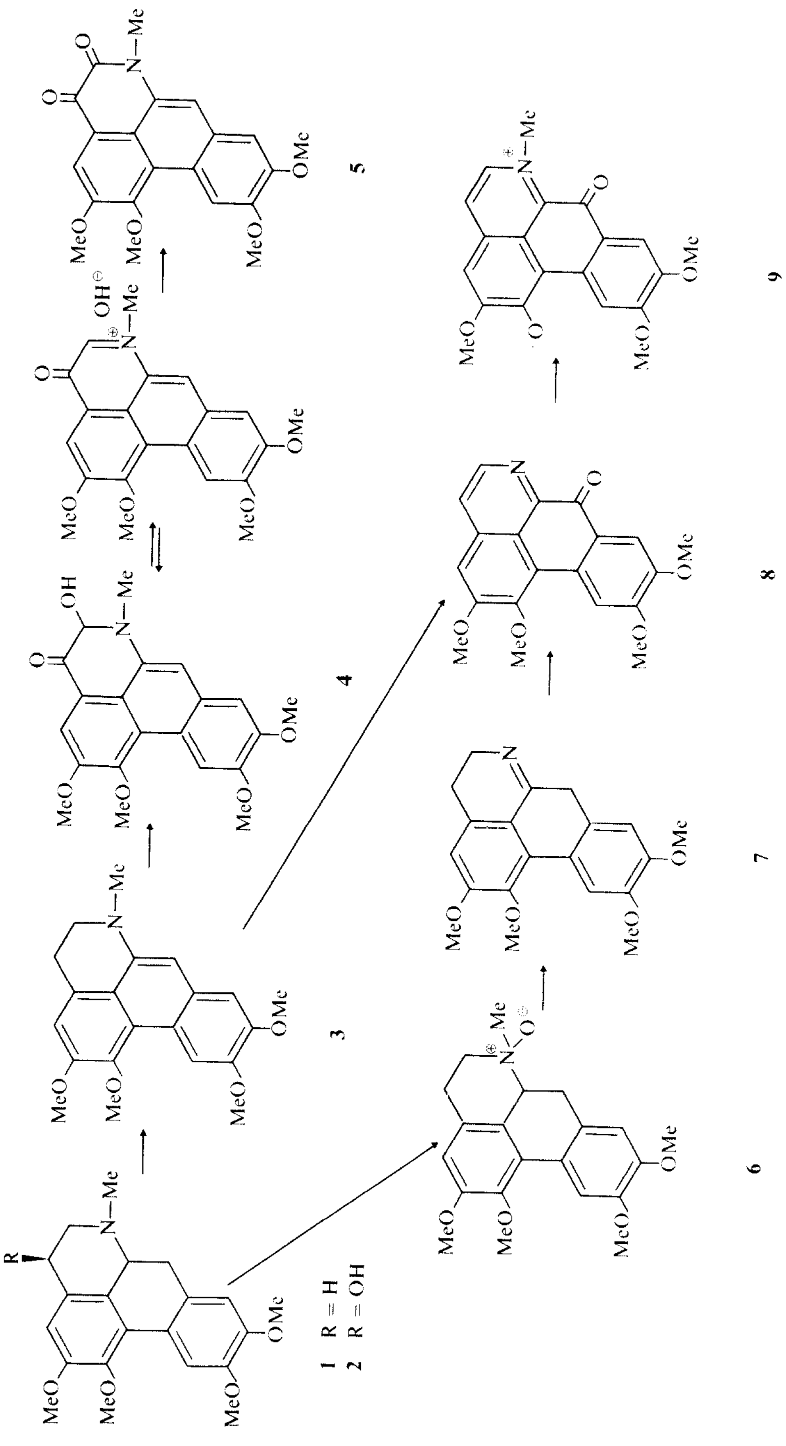
1 R = H
2 R = OH
3
4
5
6
7
8
9

Merck DC-Plasticfolien, Kieselgel 60 and DC-Fertigplaten Kieselgel 60 F_{254} were used for qualitative and quantitative TLC work. $CHCl_3$–MeOH (20:1) was used as eluant.

Air oxidation of **1**. **1** (50 mg) was dissolved in 5 ml EtOH and the soln bubbled 2 days with air. After 20 min, **3** was detected by TLC. Traces of **8** appeared after 1 day. On the second day **8** was also present. A similar experiment in the dark gave **3** after 5–7 hr.

UV irradiation of **1**. **1** (0.5 g) in 50 ml EtOH was irradiated for 2 hr in a nitrogen or argon atmosphere with a TQ-150 Mercury lamp 'Original Hanau' with a Pyrex filter. The main quantity of **1** crystallized after concn of the soln *in vacuo*. From the filtrate the following compounds were isolated and identified by means of prep. TLC. 7,6′-Dehydroglaucine (**3**) appeared as a yellow band, and after elution with Et_2O was isolated as yellow crystals, mp 123–124°. Identification was made by IR, NMR and TLC comparison with an authentic sample. 1,2,9,10-Tetramethoxyoxoaporphine (*O*-methylatheroline) (**8**) was a dark yellow band and after elution with Et_2O was obtained as a crystalline solid mp 223–224° (decomp). It was identified by comparison with an authentic sample (IR, NMR and TLC). Pontevedrine (**5**) was isolated from the dark red TLC band after elution with $CHCl_3$–EtOH (1:1). It was an amorphous compound with similar UV, IR and NMR spectral data as those published in ref. [1, 11]. Corunine (**9**) was isolated from the green part of the prep. TLC plate by elution with $CHCl_3$–EtOH (1:1). The compound crystallized as an amorphous powder, mp 252–254°. The MS M^+ peak at m/z 351, the colour reactions and NMR spectrum are identical to those given in ref. [1]. Dihydropontevedrine (**4**) was isolated from the less polar red band of the prep. TLC plate after elution with $CHCl_3$–EtOH. It was obtained as red crystals, mp 248–250° from EtOH.

Glaucine-*N*-oxide (**6**) was isolated as a colourless, amorphous compound mp 102–103°. Identification was made by comparison of TLC R_f values, IR and NMR spectra with those of the compound obtained after oxidation of **1** with H_2O_2 in HOAc.

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