A STUDY OF THE ALKALOIDS OF Glaucium flavum

THE STRUCTURE OF GLAUVINE

L. D. Yakhontova, V. I. Sheichenko, and O. N. Tolkachev

UDC 547.94

Previously, in a study of the alkaloids of Glaucium flavum (yellow hornpoppy) by chromatography on alumina, glaucine, isocorydine, protopine, and isoboldine were isolated [1]. A stepwise increase in the polarity of the solvents after the elution of the first three alkaloids enabled another three alkaloids to be obtained: a yellow substance with the composition $C_{20}H_{17}NO_5$, identical with the O-methylatheroline (I) isolated from Liriodendron tulipifera [2, 3]; a colorless substance with the composition $C_{19}H_{21}NO_4$ identical with the sinoacutine isolated from Sinomenium acutum [4], the presence of which in the yellow hornpoppy has not previously been recorded; and a green compound with the composition $C_{20}H_{17}NO_5$, which has not been described in the literature and which we have named glauvine (II).

From our subsequent investigations, it can be seen that compound (II) is also formed by heating O-methylatheroline at 150°C for 18-20 h. Acid solutions of glauvine have an orange color which changes to green when the solutions are made alkaline. Glauvine and O-methylatheroline have similar UV spectra in an acid medium (Table 1), which shows the similarity of the chromophoric groupings of their salts.

A difference in the UV spectra of the free alkaloids shows that on passing from (I) to (II) the system of conjugation changes.

The PMR spectra of the salts of (I) and (II) are also similar (Table 2). However, in glauvine the signal of one of the methoxy groups is shifted considerably downfield (4.92 ppm), an analogous shift taking place not only in the salts but also in the bases ($CDCl_3$, 4.85 ppm). The position of this signal showed that one of the methoxy groups in glauvine occupies a position differing from the positions of the methoxy groups in O-methylatheroline. In view of the fact that the mutual locations of the proteins in ring D of (I) and (II) are similar, as follows from the PMR spectra (Fig. 1), it may be assumed that this methoxy group is present in position 7.

When glauvine was heated with dilute hydrochloric acid, one of the methoxy groups was saponified, as is confirmed by the presence of a phenolic shift in the UV spectrum of the hydrolysis product on the addition of a 1% solution of caustic soda ($\Delta\lambda = 12.5$ nm) while (II) gives no such shift.

The reduction of glauvine with zinc in hydrochloric acid formed a colorless substance (III) which, on acetylation with acetic anhydride, was converted into an O,N-diacetyl derivative (IV) [IR spectrum: 1770 cm^{-1} ($OCOCH_3$), 1698 cm^{-1} ($NCOCH_3$)].

TABLE 1. Absorption Maxima of Glauvine and O-Methylatheroline in the UV Region

Compound	Solvent	λ_{max}, (log ε) nm			
		I	II	III	IV
O-Methylatheroline	Ethanol	—	243 (4,52)	273 (4,53)	357 (4,05)
	Ethanol HCl	—	257 (4,54)	288 (4,50)	380 (4,10)
Glauvine	Ethanol	228 (4,44)	258 (4,36)	324 (4,55)	396 (3,78)
	Ethanol HCl	222 (4,35)	256 (4,37)	293 (4,28)	382 (3,91)

All-Union Scientific-Research Institute of Medicinal Plants. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 214-218, March-April, 1972. Original article submitted October 13, 1971.

TABLE 2. Chemical Shifts* of the Protons of Glauvine and of O-Methylatheroline and Their Derivatives

Compound	H_3	H_4	H_5	H_8	H_{11}	C_7-OCH_3	Other OCH_3	NAc	OAc
I†	7,66	8,55	8,78	8,08	9,02	—	4,1—4,4	—	—
II	7,58	8,43	8,61	7,98	8,92	4,92	4,1—4,4	—	—
III	6,78	3,0 — 4,0		6,99	8,23	—	4,0—4,1	—	—
IV	6,87	—	—	6,95	7,56	—	3,8—4,1	2,25	2,48
V	6,93	3,0 — 4,0		7,01	8,18	—	4,06	—	—
VI	6,49	—	—	6,65	7,98	—	3,8—4,1	2,08	—

*Relative to TMS (0 ppm).

† (I-V) were taken in CF_3COOH and (VI) in CCl_4 (HA-100D spectrometer).

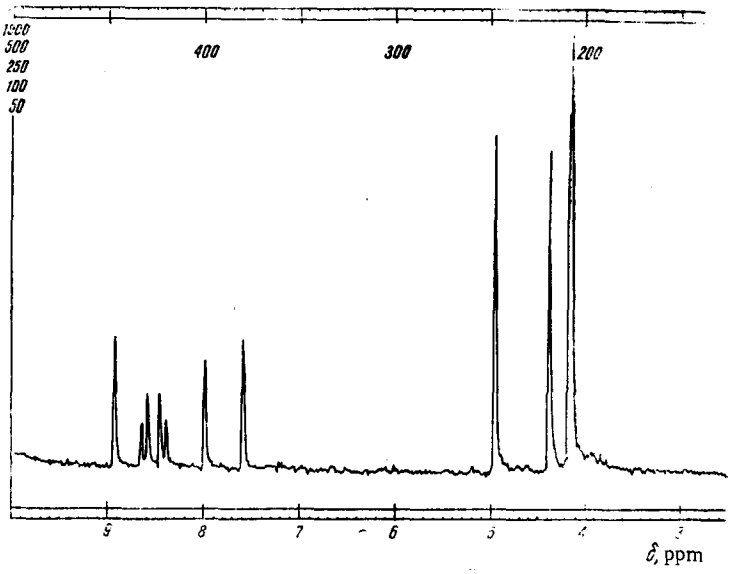
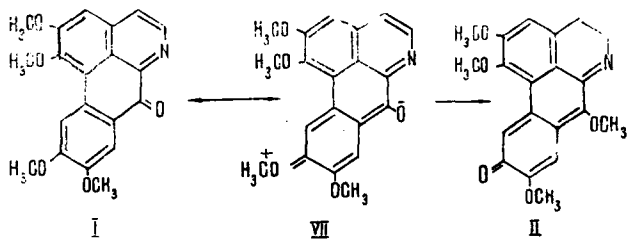


Fig. 1. NMR spectrum of glauvine (II).

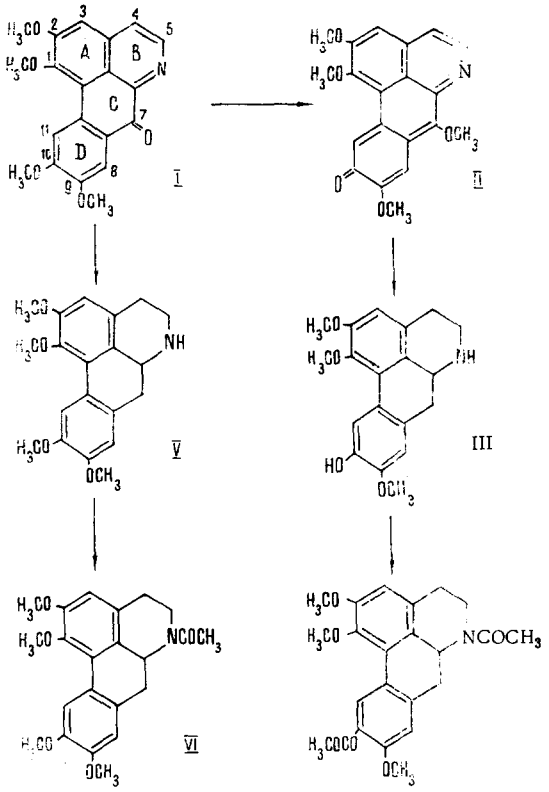
The analogous reduction of O-methylatheroline and subsequent acetylation led to N-acetylnorglaucine (VI), $C_{22}H_{25}NO_5$, mp 177-178°C [IR spectrum: 1630 cm^{-1} ($NCOCH_3$)]. On the basis of the transformations described, it may be assumed that glauvine has a semiquinoid structure of ring D which arises as the result of the enolization of the carbonyl group of (I) with the simultaneous migration of an O-methyl group. This is shown by the NMR spectrum, where the newly formed O-methyl group has a chemical shift differing from those of the other three, while in (I) the signals of all the four O-methyl groups have similar chemical shifts. The O-methyl group mentioned also differs in its chemical properties; in particular, it is readily saponified in an acid medium with the formation of a phenolic hydroxyl.



On passing from (III) to (IV) a considerable shift in the signal of the H_{11} proton is observed (8.23→ 7.56 ppm), while the position of the H_8 signal changes little. It follows from this that in (III) there is a hydroxyl and in (II) a carbonyl group at position 10. Thus, in the production of glauvine from O-methyl-

atheroline a methyl group migrates from the methoxyl at C_{10}. The formation of glauvine from O-methylatheroline, taking into account the fact that it may exist in the resonance form (VII), is expressed by the following scheme:

Scheme



All that has been said above permits the hypothesis to be put forward that glauvine has the structure (II).

EXPERIMENTAL

The analyses of all the compounds corresponded to the calculated figures.

Separation of the Combined Alkaloids. The combined alkaloids (300 g) from a dichloroethane extract of the herbage of yellow hornpoppy (20 kg) were chromatographed on alumina (activity grade II; 1:20). Elution with benzene gave glaucine (158 g); with benzene containing 1% of methanol, protopine (2.5 g); and with benzene containing 5% of methanol, O-methylatheroline (4.5 g) with mp 221-223°C.

Subsequent elution with benzene containing 10% of methanol gave an alkaloid fraction (1.5 g) from which, by recrystallization from ethanol, sinoacutine, $C_{19}H_{21}NO_4$, was isolated, with mp 199-200°C, $[\alpha]_D^{20} - 85°$ (c 2.01; chloroform).

The methiodide, $C_{19}H_{21}NO_4 \cdot CH_3I$, had mp 209-211°C (from acetone). Elution with benzene containing 15% of methanol gave a fraction with a green color (1.3 g), the recrystallization of which from methanol yielded a green substance, $C_{20}H_{17}NO_5$, mp 210-212°C, mol. wt. 351.

Reduction of Glauvine. To a solution of 0.2 g of (II) in 20 ml of 50% acetic acid were added 30 g of zinc dust and 60 ml of 10 N hydrochloric acid. The reaction mixture was heated at 100°C for 12 h, and then 10 g of zinc dust and 30 ml of 10 N hydrochloric acid were added and the mixture was heated for another 8 h. After the end of the reaction, the zinc dust was separated off, the colorless acid solution was made alkaline with ammonia, the base was extracted with chloroform, and the extract was dried and evaporated to dryness. The substance (III) obtained (0.19 g) was dissolved in 30 ml of chloroform and then 3 ml of acetic anhydride was added to the solution and it was boiled for 8 h. This formed 0.18 g of (IV), $C_{23}H_{25}NO_6$, mp 148-150°C (from ethanol).

Reduction of O-Methylatheroline. The reduction of 0.2 g of this compound was performed by the same method as for glauvine. The reduction product – norglaucine (V) – was converted by acetylation with acetic anhydride into the acetate (VI), composition $C_{22}H_{25}NO_5$, with mp 177-178°C (from ethanol).

SUMMARY

From the herb Glaucium flavum have been isolated O-methylatheroline, sinoacutine, and a new alkaloid of the aporphine series, $C_{20}H_{17}NO_5$, which has been called glauvine.

A structural formula has been proposed for glauvine on the basis of chemical reactions and spectral information.

LITERATURE CITED

1. L. D. Yakhontova, in: Medicinal Plants [in Russian], Vol. 15 (1969), p. 348; Khim. Prirodn. Soedin., 285 (1967); 203 (1968).
2. M. P. Cava and K. V. Rao, J. Org. Chem., 33, 2443 (1968).
3. J. Cohen, W. Von Langenthal, and W. J. Taylor, J. Org. Chem., No. 10, 4143 (1961).
4. J.-H. Chu, S. Y. Lo, and Y.-L. Chou, Acta Chim. Sinica, 30, 265 (1965).