ALKALOIDS OF HAPLOPHYLLUM ROBUSTUM
STRUCTURE OF ROBUSTINE

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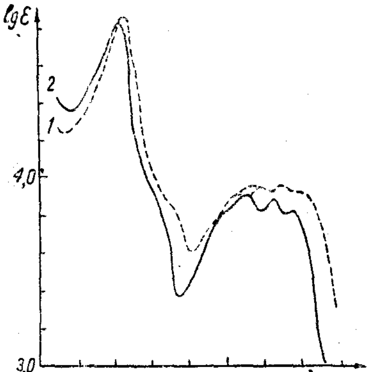
The plant Haplophyllum robustum Bge. (family Rutaceae) was collected in the southern Kyzyl-Kum at the flowering stage (in June). The epigeal part contained 0.04% and the roots 0.34% of total alkaloids. From the mixture of alkaloids of the epigeal part we have isolated haplopine [1], and from the roots skimmianine and a new alkaloid which we have called robustine. Chromatography of the residual mother liquors on alumina gave γ-fagarine and a base with mp 230-231°.

Analysis of the base and its picrate, together with a determination of the molecular weight and the functional groups has established the composition $C_{12}H_9O_3N$ for robustine; developed formula $C_{11}H_5ON(OH)(OCH_3)$.

Robustine is an optically inactive compound readily soluble in acetone and chloroform, less soluble in ethanol, and insoluble in water. Its UV spectrum (Figure) is similar to that of γ-fagarine – an alkaloid with a furanoquinoline structure. The relationship of robustine to this group of alkaloids is also shown by the bands of the IR spectrum at 3130, 1622, 1095, 880, and 810 cm^{-1} and by the characteristic hydrogenolysis reaction of the base [2]. On hydrogenation over a platinum catalyst, robustine absorbs 4 atoms of hydrogen giving tetrahydrorobustine $C_{12}H_{13}O_3N$(II). The IR spectrum of this compound contains no bands of an unsubstituted furan ring, since the latter is opened with the formation of the corresponding 3-alkylquinol-2-one.

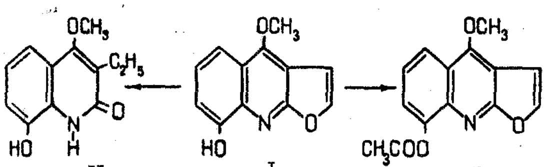
Robustine dissolves in caustic alkalis on gentle heating, giving a green coloration with ferric chloride, and with acetic anhydride forms a monoacetyl derivative $C_{11}H_5ON(CH_3COO)(OCH_3)$(III) saponification of which with alcoholic alkali leads to the initial base. The IR spectrum of acetylrobustine has the band of the carbonyl group of a phenol ester (1758 cm^{-1}). All this shows the phenolic nature of the hydroxyl group of robustine.

The methylation of robustine with diazomethane gives γ-fagarine. Consequently, the mutual location of the hydroxyl and methoxyl groups in the robustine molecule is limited to the 4 and 8 positions. The presence of the hydroxyl group at C_4 and the methoxyl group at C_8 is excluded, since nor-γ-fagarine has this structure [3], and the latter, as a direct comparison has shown, is not identical with robustine.



UV absorption spectrum of robustine (1) and γ-fagarine (2).

Consequently, the methoxyl group in the molecule of robustine occupies position 4 and the hydroxyl group position 8. Thus, robustine has the structure of 4-methoxy-8-hydroxyfuro[2, 3-b]quinoline, i. e., 8-hydroxydictamnine (I):



II I III

EXPERIMENTAL

Extraction of the alkaloids. In a continuous-working apparatus, 7.5 kg of the comminuted roots of H. robustum wetted with 8% ammonia were extracted with chloroform. The chloroform extract was evaporated to give a viscous mass, and this was treated with 10% sulfuric acid. The acid extract was shaken with chloroform, distillation of which gave 24.15 g (0.32%) of total alkaloids. The acid solution was made alkaline with ammonia and was again extracted with chloroform. This fraction gave an additional 1.6 g (0.02%) of a mixture of alkaloids. The over-all yield of total bases was 25.75 g.

Skimmianine. 24.15 g of the total alkaloids from the acid extraction were triturated with acetone. This gave yellowish crystals of skimmianine with mp 175-176° (from methanol). Yield 6.4 g.

Robustine. An alcoholic solution of hydrochloric acid was added to the concentrated acetonic mother liquors until they were acid (to Congo Red). The addition of acetone led to the precipitation of robustine hydrochloride having, after recrystallization from alcohol, mp 199-200°.

The addition of 5% ammonia solution to an aqueous suspension of robustine hydrochloride gave the colorless base with mp 147-148° (from alcohol). Yield 0.8 g.

The chromatography of robustine on paper in the butan-1-ol-hydrochloric acid-water (3:1:4) system gave a single spot, revealed in ultraviolet light and with Dragendorf's reagent, $R_f = 0.85$.

UV spectrum: λ_{max}246, 314, 330, 342 mμ (log ε 4.86, 3.94, 3.94, 3.92, respectively); λ_{min} 280, 324, 335 mμ (log ε 3.62, 3.92, 3.92, respectively).

Found %: C 67.3; 67.2; H 4.44; 4.58; N 6.6; 6.6; OCH_3 14.34; 14.45. $C_{12}H_9O_3N$. Calculated %: C 66.97; H 4.22; N 6.5; OCH_3 14.41.

γ-Fagarine. The acid mother liquor remaining after the separation of robustine hydrochloride was dissolved in chloroform, and the solution was saturated with ammonia and passed through a column containing alumina (1:40), which was then eluted with 0.5-liter portions of ether. The 5th-20th fractions yielded 1.5 g of γ-fagarine with mp 140-141° (from aqueous acetone), and the 25th-34th a base with mp 230-231°.

Robustine pictrate. When an alcoholic solution of the alkaloid and a methanolic solution of picric acid were mixed, yellow crystals of robustine picrate with mp 179-180° (from absolute ethanol) deposited.

Found %: C 49.2; 49.2; H 3.13; 3.25; N 12.81; 12.88. $C_{18}H_{18}O_{10}N_4$. Calculated %: C 49.2; H 3.13; N 12.8.

Tetrahydrorobustine. In a current of hydrogen, 0.15 g of robustine in 30 ml of alcohol was shaken with a platinum catalyst prepared from 0.1 g of platinum oxide. After 1 hr, 40 ml of hydrogen had been absorbed. The catalyst was filtered off with suction and washed with alcohol. Concentration of the alcoholic solution led to the deposition of crystals of tetrahydrorobustine with mp 201-202° (from alcohol).

UV spectrum: λ_{max}256, 286, 330 mμ (log ε 4.48, 3.98, 3.54, respectively); λ_{min}234, 270, 315 mμ (log ε 4.18, 3.90, 3.48, respectively).

Found %: C 65.14; 65.46; H 6.33; 6.32; N 6.29; 6.28. $C_{12}H_{13}O_3N$. Calculated %: C 65.7; H 5.97; n 6.38.

Acetylrobustine. A mixture of 0.2 g of robustine, 4 ml of acetic anhydride, and 2 drops of pyridine was heated for 3 hr. After evaporation, the residue was recrystallized from ethanol. Colorless crystals with mp 174-175° deposited.

Found %: C 65.7; 66.0; H 4.37; 4.56; N 5.55; 5.69. $C_{14}H_{11}O_4N$. Calculated %: C 65.37; H 4.3; N 5.45.

Saponification of acetylrobustine with 20% alcoholic caustic potash gave robustine.

Methylrobustine. A solution of 0.2 g of robustine in a mixture of dry chloroform and absolute methanol (1:1) was mixed with an ethereal solution of diazomethane and the mixture was kept cold for 4 days. When the solution was concentrated, crystals with mp 140-141° (from aqueous acetone) deposited.

UV spectrum of methylrobustine: λ_{max}244, 314, 326, 336 mμ (log ε 4.82, 3.88, 3.84, 3.81, respectively); λ_{min}277, 318, 334 mμ (log ε 3.28, 3.76, 3.74, respectively).

SUMMARY

The following substances have been isolated from Haplophyllum robustum: from the epigeal part haplopine, and from the roots skimmianine, γ-fagarine, a new alkaloid robustine $C_{11}H_5ON(OH)(OCH_3)$, and a base with mp 230-231°.

Robustine has the structure 4-methoxy-8-hydroxyfuro[2,3-b]quinoline.

REFERENCES

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