A STUDY OF THE ALKALOIDS OF PLANTS OF THE GENUS STEPHANIA

II. The Alkaloids of Stephania Glabra*

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The tubers of Stephania glabra (Roxb.) Miers. (synonym St. rotunda Lour.) have yielded the alkaloids rotundine [1], *l*-tetrahydropalmatine, palmatine, gindaricine [2, 3], stepharine [4], an alkaloid with the empirical formula $C_{18}H_{19}O_3N$, and cycleanine [5].

We have continued our study of the alkaloids of Stephania glabra collected in the Democratic Republic of Vietnam in the early season of the year. The dried tubers of this plant contained an average of about 3% of a mixture of bases. The complete identity of the compositions of the alkaloids in tubers collected at different seasons was established by chromatography.

From the mixture of alkaloids we have isolated *l*-tetrahydropalmatine and three previously unreported bases, designated A, C, and D.

Alkaloid A – $C_{19}H_{18}O_2N$, mp 79-81°C (ether), $[\alpha]_D$ – 88° (c 1; ethanol), contains a N · CH_3 group. The IR spectrum has absorption bands at 1620 and 1580 cm^{-1}, and the UV spectrum has λ_{max} 233 and 316 mμ.

In spite of the absence of a labile hydrogen atom on the nitrogen in the alkaloid, an N-acetyl derivative with mp 146°C (acetone) was obtained, which is characteristic for alkaloids belonging to the aporphine group [6].

Alkaloid C – $C_{21}H_{25}O_4N$, mp 182-183°C (acetone), $[\alpha]_D$ +259° (c 1; ethanol) has a labile hydrogen atom and three OCH_3 groups and one CH_3 group. The IR spectrum exhibits absorption bands at 3160 and 1599 cm^{-1} and the UV spectrum has λ_{max} 267 and 304 mμ.

Alkaloid D – $C_{20}H_{25}O_4N$, mp 153-154°C (benzene), $[\alpha]_D$ – 72° (c 1; ethanol), contains two labile hydrogen atoms and two OCH_3 groups and one N · CH_3 group. The IR spectrum has absorption bands at 1697, 1633, 1633, and 1618 cm^{-1} and the UV spectrum has λ_{max} 265 mμ. Catalytic hydrogenation of the alkaloid over platinum gave a substance with mp 155-156°C (benzene-acetone), whose IR spectrum had absorption bands at 1732 and 1609 cm^{-1}.

Alkaloids A, C, and D have not been described in the literature and are apparently new.

Experimental

Isolation and separation of the mixture of alkaloids. 5.15 kg of the dried and comminuted tubers of Stephania was moistened with 10% ammonia solution, and the alkaloids were exhaustively extracted with dichloroethane. The extract was shaken with 10% sulfuric acid. After the solution had been made alkaline with ammonia, the bases were extracted with chloroform. The resinous residue from the distillation of the solvent was dried. This gave 154.25 g of a dry mixture of alkaloids.

On chromatography in a thin nonfixed layer of alumina (activity grade II) in the ether – methanol (99: 1) system, the presence of seven alkaloids in the mixture was established, with four of them predominating Rf 0.08, 0.42, 0.56, 0.77).

154 g of the dry mixture of alkaloids was chromatographed on 1540 g of alumina (activity grade II). The alkaloids were subsequently eluted in four fractions with 1) an 8: 2 mixture of petroleum ether and ether, 2) a 1 : 1 mixture of the same two compounds, 3) ether, and 4) a mixture of ether and methanol 9 : 1.

Alkaloid A. Fraction 1 gave 4.2 g of base A (from ether).

Found, %: C 78.09; 78.05; H 6.32; 6.38; N 4.78; 4.92; N · CH_3 8.85; 7.98; mol. wt. 284 (Rast method). Calculated for $C_{19}H_{18}O_2N$, %: C 78.08; H 6.16; N 4.79; N · CH_3 9.93; mol. wt. 292.

Hydrochloride. Ether saturated with hydrochloric acid was added to a solution of 0.2 g of the base in 2 ml of alcohol until the reaction was weakly acid; the hydrochloride which was deposited, after crystallization from a mixture of alcohol and ether, melted at 252-253°C. Yield 0.15 g.

Found, %: C 69.08; 69.00; H 6.14; 6.17; N 4.31; 4.46; Cl 11, 25. Calculated for $C_{19}H_{18}O_2N \cdot HCl$, %: C 69.40; H 5.78; N 4.26; Cl 10.80.

*The substances in this paper are denoted by letters. The novelty of these substances has not been established, which contradicts the rules of this journal. The paper is printed as an exception (Editorial Board).

N-Acetyl derivative of alkaloid A. A solution of 0.2 g of alkaloid A in 2 ml of pyridine was treated with 1 ml of acetic anhydride and the mixture was heated under reflux for 6 hr, and then the solvent was evaporated off under vacuum. Yield 0.1 g. The IR spectrum had a band at 1634 cm^{-1} (N-acetyl).

Found, %: C 75.39; 75.91; H 5.95; 5.86; N 4.16; 4.19; Calculated for $C_{21}H_{20}O_3N$, %: C 75.44; H 5.98; N 4,16.

Fraction 2 gave 85 g of *l*-tetrahydropalmatine (from ether).

Alkaloid C. The crystallization of fraction 3 from acetone gave 4.3 g of base C.

Found, %: C 70.96, 70.78; H 7.03; 7.00; N 3.94; H_{labile} 0.281; OCH_3 26.18; N · CH_3 9.4; mol. wt. 355 (Rast method). Calculated for $C_{21}H_{25}O_4N$, %: C 70.98; H 7.04; N 3.94; H_{labile} 0.355; OCH_3 26.33; N · CH_3 8.16; mol. wt. 355.

The hydrochloride was obtained as for base A, mp 230-232°C (from alcohol – ether).

Found, %: C 63.76; 63.61; H 6.59; 6.52 N 3.56; 3.53; Cl 9.23; 9.51; Calculated for $C_{21}H_{25}O_4N \cdot HCl$, %: C 64.11; H 6.64; N 3.57; Cl 9.06.

Alkaloid D. The crystallization of fraction 4 from benzene gave 4.9 g of base D.

Found, %: C 69.81; 70.23; H 7.32; 7.17; N 4.07; 4.03; H_{labile} 0.577; OCH_3 18.84; N · CH_3 8.45; mol. wt. 344 (Rast method). Calculated for $C_{20}H_{25}O_4N$, %: C 69.97; H 7.28; N 4.08; H_{labile} 0.583; OCH_3 18.10; N · CH_3 9.31; mol. wt. 343.

The hydrochloride had mp 227-228°C (from alcohol – ether).

Found, %: C 57.66; 57.51; H 7.28; 7.29; N 3.44; Cl 8.81. Calculated for $C_{20}H_{25}O_4N \cdot HCl \cdot 2H_2O$, %: C 57.76; H 7.21; N 3.36; Cl 8.54.

Hydrobromide, mp 229-230°C (from alcohol).

Found, %: C 52.26; 51.93; H 6.52; 6.51. N 3.26; 3.48; Br 19.39. Calculated for $C_{20}H_{25}O_4N \cdot HBr \cdot 2H_2O$, %: C 52. 19; H 6.52; N 3.04, Br 17.33.

Hydrogenation of alkaloid D. A solution of 0.3 g of the alkaloid in 10 ml of alcohol was shaken with a platinum catalyst (from 0.3 g of PtO_2) in an atmosphere of hydrogen. After 4 hr, about 3 moles of hydrogen had been absorbed. The residue from the evaporation of the solvent was crystallized from a mixture of benzene and acetone. This gave 0.15 g of hydrogenation product with mp 155-156°C.

The IR spectra were taken on a UR-10 spectrometer in the form of a suspension in liquid paraffin, and the UV spectra on a SF-4 instrument.

Summary

Four alkaloids have been isolated from the tubers of Stephania glabra (Roxb.) Miers. (synonym St. rotunda Lour.) collected in the Democratic Republic of Vietnam: *l*-tetrahydropalmatine and three previously undescribed bases (A – $C_{19}H_{18}O_2N$, C – $C_{20}H_{25}O_4N$, and D – $C_{21}H_{25}O_4N$).

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