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ALKALOIDS OF BUXUS BALEARICA. I

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Buxus balearica Wild. (Spanish box tree) is a tall evergreen shrub or small tree with a height of up to 6 m which grows wild in southern Spain and the Balearic Islands. The cultivated variety is found on the Black Sea coast of the Caucasus, in Krasnodar territory, and in the Crimea. Plants of the family Buxaceae are distinguished by a high content of alkaloids. From the leaves of Buxus balearica Wild., French workers have isolated the alkaloids cyclobaleabuxine, baleabuxine, cycloprotobuxine A, cycloprotobuxine C [1, 2], baleabuxidine, buxaline E, buxaminol E, baleabuxoxazine C, N-benzoylbaleabuxidine F, N-isobutyrylbaleabuxidienine F, and N-isobutyrylbaleabuxaline F [3]. All these alkaloids of the family Buxaceae contain a steroid nucleus.

We have studied the alkaloids of the leaves of Buxus balearica Lam. from the Batumi Botanical Garden collected in October 1965. From the total alkaloids (about 10%) isolated by the dichloroethane method, we obtained seven alkaloids: alkaloid A with the composition $C_{30}H_{50}N_2O_2$, which in all probability is baleabuxine [1, 2] and contains an NH group and an NH—C=O grouping (bands at 3400 and 1660 cm^{-1}); alkaloid B with a composition close to $C_{30}H_{50}NO_3$ and constants close to those of N-isobutyrylbaleabuxidienine F [3], containing an NH group (band at 3430 cm^{-1}); alkaloid C—a new, previously undescribed alkaloid with the composition $C_{26}H_{41}NO$, including a C=C—C=O grouping (band at 1669 cm^{-1}) and an $N(CH_3)_2$ group; alkaloid D with the composition $C_{30}H_{50}N_2O_4$, isolated in very small amounts and not investigated in detail; alkaloid E, with the composition $C_{27}H_{50}N_2O_3$ and differing in its constants from the alkaloids of the family Buxaceae isolated up to the present time; alkaloid F, in all probability cyclomicrophylline B [4, 5], with the composition $C_{27}H_{46}N_2O_2$, containing NH and OH groups (bands at 3320 and 3420 cm^{-1}); and alkaloid G with the composition $C_{27}H_{46}N_2O_3$—a new, previously undescribed, alkaloid.

Experimental

The IR spectra of the substances were taken on a UR-10 spectrophotometer (paraffin oil) and the UV spectra on an SF-4 spectrophotometer (methanol). Whatman-2 chromatographic paper and alumina (activity grade II) were used for chromatography, the system for paper chromatography being butanol—acetic acid—water (86 : 40 : 40 ml). All the melting points are uncorrected.

Alkaloids A and B. Five kilograms of the dry comminuted leaves of B. balearica was moistened with 10% ammonia and exhaustively extracted with dichloroethane. The bases were extracted from the dichloroethane solution with 10% sulfuric acid. The acid extract, containing a large amount of resin, was washed with chloroform, into which the sulfates of the alkaloids A and B passed together with the resins. The alkaloids extracted by chloroform from the acid solution were purified from resins by dissolution in water (the resins dissolve with considerable difficulty). The aqueous solution of the sulfates was made alkaline with ammonia and extracted with ether. After drying with sodium sulfate, the extract was evaporated and, in order to separate the amorphous mixture of alkaloids obtained, it was passed through a column containing 200 g of alumina. Elution was carried out with ether [fractions 1–9 (6 g)], ether containing 1% of ethanol [fractions 10–15 (2 g)], and ether containing 2% of ethanol [fractions 16–25 (6.5 g)].

Alkaloid A (baleabuxine) was obtained from fractions 1–4 (0.6 g), mp 236–240° C (from acetone), $[\alpha]_D^{20}$ +120.7° (c 1.1023; chloroform), R_f 0.83, IR spectrum: 3600 cm^{-1} (OH), 3400 cm^{-1} (NH), 1660 cm^{-1} (NH—CO), and 1685 cm^{-1} (C=O). Found, %: C 76.17; H 10.82; N 5.82. Calculated for $C_{30}H_{50}N_2O_2$, %: C 76.52; H 10.71; N 5.95.

Fractions 16–25 yielded 0.36 g of alkaloid B (N-isobutyrylbaleabuxidienine F) with mp 260–262° C (from acetone); $[\alpha]_D^{20}$ −60° (c 1.2; chloroform); R_f 0.84; IR spectrum: 3430 cm^{-1} (NH). Found, %: C 74.29; H 10.40; N 5.79. Calculated for $C_{30}H_{50}N_2O_3$, %: C 74.1; H 10.35; N 5.76.

Alkaloids C, D, E, F, and G. The acid solution, after washing with chloroform and the extraction of alkaloids A, and B, was subjected to fractional precipitation with ammonia and was extracted with ether at pH 6.5, 7.5, 8.0, 9.0, and 10.0.

Alkaloid C was isolated from the fraction extracted at pH 6.5. After drying with sodium sulfate, the extract was evaporated to the consistency of a viscous syrup and was passed through a column of alumina. When the column was eluted with ether, from all the fractions a crystalline base was isolated (2 g). Recrystallization from acetone gave 0.9 g of alkaloid C with mp 180–183° C, $[\alpha]_D^{20}$ +118° (c 0.68; chloroform). UV spectrum: λ_{max} 239 mμ (log ε 4.52). The IR spectrum showed the presence of neither an OH nor an NH group, but had absorption bands in the regions 1669 cm^{-1} (C=C—C=O) and 3075 and 1596 cm^{-1}. Found, %: C 81.57; H 10.68; N 3.65. Calculated for $C_{26}H_{41}NO$, %: C 81.4; H 10.75; N 3.65.

Alkaloid D was isolated from the fraction extracted at pH 7.5. After its concentration, the ethereal solution deposited a crystalline substance. Washing with ethyl acetate and recrystallization from acetone gave 0.2 g of an alkaloid with mp 236–238° C; $[\alpha]_D^{20}$ +76° (c 0.74; chloroform). Found, %: C 71.69; H 9.76; N 5.40. Calculated for $C_{30}H_{50}N_2O_4$, %: C 71.7; H 10.02; N 5.5.

Alkaloid E was isolated from the fraction which precipitated when the pH was brought to 9. This precipitate was not completely soluble in ether. The ether-insoluble residue was filtered off and washed with ethyl acetate. The alkaloid obtained (1 g) was sparingly soluble in ether, acetone, and ethanol. After recrystallization from a mixture of chloroform and methanol (1 : 1), alkaloid E was obtained with mp 287–289° C; $[\alpha]_D^{20}$ +12° [c 0.6; chloroform–methanol (1 : 1)]; R_f 0.45. Found, %: C 71.81; H 10.89; N 6.14. Calculated for $C_{27}H_{50}N_2O_3$, %: C 72.0; H 11.11; N 6.22.

Alkaloid F (cyclomicrophylline B) was extracted with ether at pH 9, and after its concentration, deposited 8.5 g of a crystalline base. Recrystallization from ethanol gave 1.5 g of an alkaloid with mp 246–248° C; $[\alpha]_D^{20}$ −69° (c 0.95; chloroform); R_f 0.41; IR spectrum: 3320 cm^{-1} (NH) and 3410 cm^{-1} (OH). Found, %: C 76.08; H 11.00; N 6.45. Calculated for $C_{27}H_{46}N_2O_2$, %: C 75.3; H 10.75; N 6.5.

Alkaloid G was isolated from the fraction extracted at pH 10. After concentration, the ethereal extracts deposited 4.4 g of a crystalline base. Recrystallization from ethyl acetate gave 0.4 g of an alkaloid with mp 227–230° C; $[\alpha]_D^{20}$ + +114° (c 0.80; chloroform); R_f 0.19; IR spectrum: 1675, 1640 cm^{-1}. Found, %: C 72.01; H 10.33; N 6.33. Calculated for $C_{27}H_{46}N_2O_3$, %: C 72.6; H 10.38; N 6.27.

The spectra were recorded by M. E. Perel'son's group. The elementary composition was determined by E. A. Nikonova's group.

Conclusions

Seven alkaloids have been isolated from the leaves of Buxus balearica Lam: alkaloid A (apparently identical with baleabuxine), $C_{30}H_{50}N_2O_2$; alkaloid B (possibly N-isobutyrylbaleabuxidienine F), $C_{30}H_{50}N_2O_3$; alkaloid C (new), $C_{26}H_{41}NO$, with a $C{=}C{-}C{=}O$ grouping and a $N(CH_3)_2$ group; alkaloid D, $C_{30}H_{50}N_2O_4$; alkaloid E (new), $C_{27}H_{50}N_2O_3$; alkaloid F (possibly identical with cyclomicrophylline B), $C_{27}H_{46}N_2O_2$; and alkaloid G (new), $C_{27}H_{46}N_2O_3$.

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