NEW ALKALOIDS OF *DELPHINIUM*

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The application of the methods of polybuffer separation [1, 2] to various species of *Delphinium* (larkspur) has enabled us to obtain from them six alkaloids not previously reported in the literature which we have called *delfrenine*, *delflexine*, *delpyrine*, and bases A, B, and C. Of these, delfrenine has been studied in most detail.

Delfrenine $C_{27}H_{31}O_6N$ was found in *D. freynii* conrath. It contains no methoxy or methylenedioxy groups, it is unsaturated, and on catalytic hydrogenation (Adams) is converted into a substance with the composition $C_{27}H_{41}O_6N$. The alkaloid delfrenine is an ester. Benzoic acid has been obtained from the products of its alkaline saponification. The nitrogen-containing hydrolysis product is apparently an amino acid, since on methylation with diazomethane it gives a methyl ester $C_{21}H_{31}O_6N$.

The IR spectrum of the alkaloid contains the band of a hydroxy group (3460 cm^{-1}), and there are five bands in the 1600–1700 cm^{-1} region:* 1588 cm^{-1} (w), 1608 (s), 1685 (s), 1710 (s), and 1730 cm^{-1}. The IR spectrum of the hydrogenated substance has four bands in the same region: 1626 cm^{-1} (w), 1667 (s), 1709 (s), and 1733 cm^{-1} (s). The 1558 cm^{-1} band is apparently due to the conjugated bonds of the benzene nucleus [3].

Delflexine $C_{24}H_{39}O_6N$ was isolated from *D. fleuosum* M.B.

Delpyrine is a noncrystalline alkaloid $C_{49}H_{82}O_{17}N_2$ which was first isolated from *D. pyramidatum* Albov. It gives a depression of the melting point in admixture with lycoctonine although their R_f values are similar (0.36 and 0.38, respectively). A comparison of the IR spectra of delpyrine and lycoctonine also showed the complete lack of identity of these substances. Delpyrine contains two hydroxy groups. It forms a single crystalline salt the reineckate, and its hydrochloride has $[\alpha]_D$ +22° (alcohol).

In contrast to lycoctonine, delpyrine is saponified by caustic potash or soda in alcohol. The saponification of delpyrine is saponified by caustic potash or soda in alcohol. The saponification of delpyrine gives an acid and an amorphous base $C_{46}H_{74}O_5N_2$ giving no crystalline salts. Delpyrine is also present in some other species of larkspur.

New crystalline alkaloids have also been found in *D. semibarbatum* Bienert: base A, $C_{15}H_{23}O_4N$ with mp 157–158°C and base B, $C_{20}H_{25}O_7N$ with mp 153–154°C. A crystalline base C, $C_{45}H_{72}O_{14}N_2$ with mp 192.5–193°C, has been isolated from *D. iliense* Huth.

Experimental

The new alkaloids of larkspur are retained by 0.5 M phosphate buffer solution at the following pH values: delpyrine base A, 6; bases B and C, 4.5. Delfrenine and delflexine are not retained by phosphate buffer solutions.

Delfrenine. This has mp 246–247°C [from ethanol–acetone (9 : 1)], R_f 0.78 [the R_f value was determined by paper chromatography in the butanol–5% acetic acid (1 : 1) system].

UV spectrum: λ_{max} 281, 274, 236 mμ (log ε 2.94, 3.02, 3.66, respectively).

Found, %: C 69.94; H 6.63, N 3.39; mol. wt. 467.5. Calculated for $C_{27}H_{31}O_6N$, %: C 69.65; H 6.71; N 3.79; mol. wt. 465.

Delfrenine is readily soluble in chloroform, sparingly soluble in ether and alcohol and insoluble in aqueous solutions of alkalies.

Saponification of delfrenine. A solution of 0.19 g of the alkaloid and 0.8 g of caustic soda in 5 ml of methanol was boiled for 2 hr and the solvent was distilled off. The residue was dissolved in 1 ml of water, acidified with 10% hydrochloric acid, and extracted (4 × 35 ml) with ether. The solvent was distilled off and the residue was recrystallized from 0.5 ml of n-hexane. This gave 0.05 g (70% of theory) of a substance (needles) with mp 122.5–123.5°C. It gave no depression of the melting point in admixture with benzoic acid. After the removal of the benzoic acid, the aqueous solution was neutralized, brought to pH 4.5 (to methyl red) and evaporated to dryness. The residue was treated with 5 ml of ethanol. The substance obtained was recrystallized from 0.5 ml of water and was washed with 0.5 ml of acetone. The aqueous solution contained chloride ions and had an acid reaction to methyl red, mp 250–251°C. IR spectrum: ν_{max} 1629, 1742 cm^{-1}.

Found, %: Cl 8.61. Calculated for $C_{20}H_{27}O_5N \cdot HCL$, %: Cl 8.81.

Methylation of the saponification products of delfrenine. A solution of 0.11 g of the substance in 1 ml of methanol was treated with 5 ml of diazomethane in ether. After evaporation, a noncrystallizing substance was obtained which was dissolved in 1 ml of absolute ethanol and treated with 1 ml of an alcoholic solution of hydrogen chloride. The noncrystalline hydrochloride was precipitated with ether. After drying, the substance had mp 272.5–273°C.

Found, %: OCH_3 6.05. Calculated for $C_{21}H_{29}O_5N \cdot HCL$, %: OCH_3 7.55.

Catalytic hydrogenation of delfrenine. A solution of 0.4 g of the alkaloid in 10 ml of 0.1 N hydrochloric acid was shaken for 40 hr with a previously reduced platinum catalyst (0.01 g) in an atmosphere of hydrogen at room temperature and under a slight excess pressure. The catalyst was filtered off and washed with water (2 ml). The aqueous solution was made alkaline with 25% ammonia solution in the presence of ether and extracted with 50 ml of ether. This gave 0.32 g (79%) of hydrogenation product, mp 107–108°C. UV spectrum: λ_{max} 236 mμ (log ε 3.66).

Found, %: C 68.28; H 8.63; N 2.80. Calculated for $C_{27}H_{41}O_6N$, %: C 68.21; H 8.61; N 2.94.

Delpyrine. The noncrystalline alkaloid had, after trituration with dry ether, mp 76°C, $[\alpha]_D$ +58° (alcohol), R_f 0.68.

Found, %: C 61.92; H 8.93; N 2.84; 2.91; OH 3.16. Calculated for $C_{49}H_{80}O_{15}N_2 \cdot 2OH$, %: C 61.62; H 8.45; N 2.89; OH 3.15.

Reinecke's derivative. A hot saturated aqueous solution of Reinecke's salt was added to a solution of 1 g of delpyrine in alcohol. The precipitate was triturated and filtered off. After drying its mp was 179–180°C.

Saponification of delpyrine. A solution of 1 g of delpyrine in 50 ml of 50% aqueous ethanol was treated with 5 g of caustic soda and boiled for 6 hr. The alcohol was distilled off from the solution and the residue was extracted with chloroform. This gave 0.8 g of an amorphous base; $[\alpha]_D$ +46.6° (alcohol).

Found, %: C 61.65; H 8.20; N 3.14; 3.15. Calculated for $C_{46}H_{74}O_{15}N_2$, %: C 61.97; H 8.28; N 3.13.

Delflexine. After recrystallization from acetone, colorless needles with mp 191–192°C, R_f 0.67, were formed.

Found, %: C 65.23; H 8.53; N 3.19. Calculated for $C_{24}H_{39}O_6N$, %: C 65.90; H 8.47; N 3.20.

Base A. Crystals from alcohol–acetone (1:3), mp 157–158°C, R_f 0.60.

Found, %: C 64.18; 64.51; H 7.90; 8.06; N 4.79; 4.91. Calculated for $C_{15}H_{23}O_4N$, %: C 64.06; H 8.19; N 4.98.

Base B. After recrystallization from acetone, colorless prisms with mp 153–154°C, R_f 0.40, were obtained.

Found, %: C 61.30; 61.60; H 6.85; 6.90; N 3.60; 3.72. Calculated for $C_{20}H_{25}O_7N$, %: C 61.36; H 6.39; N 3.58.

Base C. Colorless crystals from acetone–ether (1:2), mp 192.5–193°C, R_f 0.24.

Found, %: C 62.31; 62.61; H 8.27; 8.52, N 3.21; 3.33; Calculated for $C_{45}H_{72}O_{14}N_2$, %: C 62.50; H 8.21; N 3.24.

Summary

What are apparently new alkaloids have been isolated from five species of Delphinium: delfrenine from *D. freynii* Conrath, delflexine from *D. flexuosum* M. B;, delpyrine from *D. pyramidatum* Albov., bases A and B from *D. semibarbatum* Bienert, and base C from *D. iliense* Huth.

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