## STRUCTURE OF PRANGOSINE

Kh. S. Mukhamedova, S. T. Akramov, and S. Yu. Yunusov Khimiya Prirodnykh Soedinenii, Vol. 3, No. 2, pp. 117-121, 1967

As reported previously, an optically inactive alkaloid prangosine has been isolated from the seeds of <u>Prangos</u> <u>pabularia</u> [1]. By repeated elemental analysis, the composition  $C_{14}H_{13}O_3N$  had been established for prangosine, the molecular weight having been confirmed by mass spectrometry.

The base is soluble in 5% methanolic alkali, giving a yellow coloration, and is reprecipitated on acidification. The absorption curve of prangosine in the UV region has maxima at 250, 292, and  $332 \text{ m}\mu$  (log  $\varepsilon$  4.46, 4.02, 3.84), which are characteristic for furocoumarins [2].

The IR spectrum of prangosine has the bands of a lactone carbonyl (1715 cm<sup>-1</sup>) an aromatic ring (1580, 1600 cm<sup>-1</sup>), a primary amino group (3290, 3350 cm<sup>-1</sup>), and deformed  $- CH_3$  vibrations in an isopropyl group (1382, 1365 cm<sup>-1</sup>). Acetone, identified in the form of the 2, 4-dinitrophenylhydrazone, has been isolated from the products of the oxidation of the alkaloid with chromic acid, which confirms the presence of an isopropyl grouping in the molecule of the base. Thus, the formula of prangosine can be analyzed in the following way:

$$C_{10}H_5\left(-C \begin{pmatrix} CH_3 \\ -C \end{pmatrix} (-NH_2)(-C - O - )(-O - ).$$

The action of boiling acetic anhydride on prangosine has given a nitrogen-free substance—hemiprangosine (II) with the composition  $C_{14}H_{10}O_3$ . The IR spectrum of (II) has the absorption bands of a lactone carbonyl (1728 cm<sup>-1</sup>) and an aromatic ring (1638, 1582 cm<sup>-1</sup>). From the features of its UV spectrum, the substance is a furocoumarin. In the re-action mentioned, the nitrogen is split off in the form of ammonia.

When prangosine was methylated by Hess's method, trimethylamine was evolved and two substances were formed: hemiprangosine (II) and a substance with mp  $160^{\circ}-162^{\circ}$  C. The latter contains nitrogen but its IR spectrum lacks the doublet characteristic for an amino group. The molecular weight found by mass spectrometry is 273, which corresponds to a N-dimethyl derivative of prangosine (III). Acetic anhydride converts N-dimethylprangosine into hemiprangosine (II). With methyl iodide, N-dimethylprangosine forms a crystalline methiodide (IV); the first stage of the Hofmann degradation of (IV) liberates trimethylamine, giving a nitrogen-free substance which, by mixed melting point and IR spectrum, is also identical with hemiprangosine (II).

No acetone was detected when hemiprangosine was oxidized with chromic acid.

The catalytic hydrogenation of (II) gave a noncrystalline substance which, on oxidation with chromic acid, yielded acetone.

Thus, the amino group must be attached to a tertiary carbon atom in the following manner:

$$H_2N-C < CH_3 \\ CH_3$$

Only in this way is it possible to explain the formation of hemiprangosine (II) under the action of acetic anhydride, by the methylation of prangosine, and by the Hofmann degradation of N-dimethylprangosine methiodide. From the products of the oxidation of prangosine with concentrated nitric acid a yellow crystalline substance with the composition  $C_6H_3O_8N_3$  was isolated which, by a mixed melting point test and the IR spectrum, was identical with synthetic styphnic acid (V). The formation of the latter is characteristic for coumarins with a hydroxy group in position 7 [3] and also for furocoumarins [4]. These results show the presence of a furan nucleus in the molecule of the alkaloid.

Consequently, prangosine is an isopropylaminofurocoumarin. The position of the furan ring has not yet been demonstrated experimentally. However, the close similarity of the spectra of prangosine and of anhydromarmesin in the 700-900 cm<sup>-1</sup> region where the coplanar C-H deformation vibrations of aromatic rings appear permits the assumption that the alkaloid molecule has a linear structure. This is confirmed by the fact that the UV spectrum of hemiprangosine

(II) differs from that of oroselone [5], which has an angular structure. Since all the trisubstituted natural furocoumarin derivatives have a substituent at C-2, we assume that the isopropylamino group in prangosine occupies the same position.

The transformations of prangosine can be represented in the following way:



We have found no literature information relating to the absorption of trisubstituted furan rings in the region of the C-H stretching vibrations (3100-3150 cm<sup>-1</sup>). But, judging from the IR spectrum of anhydromarmesin, in which the doublet at 3100-3150 cm<sup>-1</sup> characteristic for disubstituted furans is absent, trisubstituted furans do not absorb in this range. This justifies our consideration that the furan ring in prangosine is trisubstituted.

## Experimental

Isolation of prangosine (I). The comminuted seeds of P. pabularia (230 kg) collected in the Bostandyk region of the Tashkent Oblast were steeped in 5% ammonia solution and extracted 12 times with chloroform.

The chloroform solution was concentrated to a volume of 180 l and treated with 10% sulfuric acid. The acid solution was washed with ether and made alkaline with ammonia. The alkaloids were extracted with ether (120 l) and chloroform (70 l). The concentrated ethereal solution deposited crystals of prangosine with mp 131°-132° C (from ace-tone). The yield of prangosine was 30 g, the ethereal fraction of the total alkaloids 36.5 g, and the chloroform fraction 33.5 g. The total alkaloids in the seeds amounted to 0.03% of the weight of raw material. When the seeds were steeped in a 5% solution of sodium carbonate or in diethylamine, the total alkaloids were obtained, and on paper chromato-graphy [isopropyl alcohol-acetic acid-water(5:1:5)] and in a thin layer [gypsum-silica gel(9:1) in the ethyl acetate-water system] these gave  $R_f$  values identical with those of prangosine.

Prangosine (I) forms white crystals with a creamy tinge. Paper chromatography in the butan-1-ol-acetic acid-- water (4:1:5) system gives a single spot with  $R_f$  0.67 revealed in UV light and by Dragendorff's reagent. On a thinlayer chromatogram [Al<sub>2</sub>O<sub>3</sub>-gypsum (9:1)] in the ethyl acetate-methanol (9:1) system,  $R_f$  0.4.

Found, %: C 68.9, 68.8; H 5.34, 5.59; N 5.81, 5.77; mol. wt. 241.9 (by titration), 243 (by mass spectroscopy). Calculated for  $C_{14}H_{13}O_3N$ , %: C 69.1; H 5.4; N 5.8; mol. wt. 243.

Oxidation of prangosine with chromic acid. 0.25 g of prangosine was dissolved in an oxidizing mixture consisting of 4 g of chromic anhydride and 6 ml of concentrated sulfuric acid in 25 ml of water. The mixture was heated for 4 hr. Acetone was trapped in a 0.1% hydrochloric acid solution of 2.4-dinitrophenylhydrazine. A mixture of the hydrazone that precipitated (mp  $124^{\circ}-125^{\circ}$  C) with acetone 2,4-dinitrophenylhydrazone gave no depression of the melting point.

<u>Hemiprangosine (II)</u>. A solution of 1.877 g of prangosine in 20 ml of freshly distilled acetic anhydride was boiled for 2 hr. The crystals of hemiprangosine (II) that deposited after cooling had mp  $184^{\circ}-185^{\circ}$  C (from acetone). Yield 1.735 g.

The yellowish crystals were soluble in methanol and chloroform, and sparingly soluble in ether. On a paper chromatogram they gave a single spot in the n-hexane-benzene-methanol (5:4:1) system with  $R_f$  0.84. UV spectrum:  $\lambda_{max}$  270, 326 mµ (log  $\varepsilon$  4.45, 3.97).

Found, %: C 74.90, 74.80; H 4.85, 4.87. Calculated for C<sub>14</sub>H<sub>10</sub>O<sub>3</sub>, %: C 74.3; H 4.4; mol. wt. 226.

The mother liquor was evaporated, and the residue was dissolved in 10% caustic potash and heated in the water bath. The volatile products were trapped in an aqueous solution of picric acid. A picrate with mp  $258^{\circ}-260^{\circ}$  C

(decomp. from alcohol), identical with ammonium picrate, was isolated.

The hydrogenation of hemiprangosine absorbed 3 moles of hydrogen per mole. The hexahydrohemiprangosine formed a glassy mass.

The oxidation of hexahydrohemiprangosine with chromic acid was carried out under the conditions for the oxidation of prangosine. Acetone was isolated in the form of the 2, 4-dinitrophenylhydrazone.

Methylation of prangosine by Hess's method. A mixture of 1 g of prangosine, 1.13 ml of formic acid (fivefold amount) and 1 ml of formaldehyde (threefold amount) was heated for 3 hr; 0.6 g of hemiprangosine (II) separated out.

After the removal of the hemiprangosine the mother liquor was diluted with a small amount of water and the solution was neutralized with aqueous caustic soda. The volatile amine was absorbed in a solution of hydrochloric acid, and then evaporated to dryness. The yield of amine hydrochloride was 250 mg, mp  $273^{\circ}-275^{\circ}$  C (acetone + alcohol).

The amine hydrochloride (200 mg) was neutralized with alkali and the volatile amine was trapped in an alcoholic solution of picric acid. The picrate that deposited melted at  $218^{\circ}-219^{\circ}$  C (ethanol). A mixture of it with trimethylamine picrate gave no depression of the melting point. After the elimination of the trimethylamine, the alkaline solution was acidified with 10% sulfuric acid, made alkaline again with 25% ammonia solution, and shaken with ether. The ethereal extract was distilled to give 0.11 g of N-dimethylprangosine (III) with mp 160°-162° C. The substance was readily soluble in acetone and methanol and sparingly soluble in ether. It gave only one spot,  $R_f$  0.9, on a paper chromatogram in butan-1-ol-acetic acid- water (4:1:5) system. On a thin-layer chromatogram [Al<sub>2</sub>O<sub>3</sub>- gypsum (9:1)] in the methanol- ethyl acetate system it had  $R_f$  0.67. UV spectrum:  $\lambda_{max}$  250, 290, 330 mµ (log  $\varepsilon$  4.58, 4.10, 3.90); mol. wt. 273 (by mass spectrometry).

N-Dimethylprangosine was converted into hemiprangosine (II) under the conditions of obtaining the latter from prangosine.

<u>N-Dimethylprangosine methiodide (IV)</u>. A mixture of 0.2 g of N-dimethylprangosine in 3 ml of methanol and 2 ml of methyl iodide was boiled for 5 min. This gave crystals of a methiodide mp  $180^{\circ}-181^{\circ}$  C (from methanol). On a paper chromatogram, the substance showed one spot with  $R_f$  0.8 in the isopropyl alcohol-acetic acid-water (5:1:5) system.

Hofmann degradation of N-dimethylprangosine methiodide (IV). The methiodide obtained from 0.2 g of N-dimethylprangosine was dissolved in 8 ml of 30% alcoholic caustic potash and heated for 3 hr. The volatile amine was trapped in 2% hydrochloric acid, and acid solution evaporated to dryness. Crystals with mp  $273^{\circ}-275^{\circ}$  C remained, giving no depression of the melting point with trimethylamine hydrochloride. Then the alkaline solution was concentrated and the dry residue was dissolved in 10% sulfuric acid and extracted with ether. This gave 0.16 g of hemiprangosine (II).

The acid solution was made alkaline with ammonia and extracted with ether. This yielded 15 mg of the initial N-dimethylprangosine.

Oxidation of prangosine with nitric acid. With heating on a boiling water bath, 20 ml of concentrated nitric acid was added in portions of 1-2 ml to 0.3 g of prangosine. After evaporation to dryness, a solid yellow mass remained which was recrystallized from aqueous alcohol; yellow crystals with mp  $174^{\circ}-175^{\circ}$  C deposited. The substance was readily soluble in water, alcohol, and ether; litmus was colored red by its aqueous and alcoholic solutions.

Found, %: C 29.25, 29.30; H 1.73, 1.73; N 17.2, 17.25. Calculated for C<sub>6</sub>H<sub>3</sub>O<sub>8</sub>N<sub>3</sub>, %: C 29.3, H 1.2; N 17.1; mol. wt. 245.

A mixture of this substance with synthetic trinitroresorcinol (styphnic acid) gave no depression of the melting point. The IR spectra were also identical.

## Summary

From the results of the UV and IR spectra of prangosine and its conversion products and of oxidation, acetylation, methylation, and Hofmann degradation reactions, it has been established that prangosine has the structure 2'-isopropyl amino-4', 5': 6, 7-furocoumarin.

## REFERENCES

1. S. Yu. Yunusov, S. T. Akramov, and G. P. Sidyakin, DAN UZSSR, no. 7, 23, 1957.

2. M. E. Perel'son, Apt. delo, 3, 70, 1964.

3. E. Spath and K. Klader, Ber., 67, 859, 1934.

4. E. Spath and K. Klader, Schlösser, Ber., 64, 2210, 1931.

5. A. P. Prokopenko, KhPS [Chemistry of Natural Compounds], 215, 1965.

24 April 1966

Institute of the Chemistry of Plant Substances, AS UzSSR