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A STUDY OF THE ALKALOIDS OF SAUSSUREA SALSA AND S. ELEGANS

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From the epigeal part of S. salsa Ldb. collected in the Pamir in the region of the village of Murgab in June, 1966, we have obtained, by chloroform extraction, 0.35% of total substances with a basic nature from which we have isolated, in the form of the oxalate, an amorphous substance consisting of the adduct of a neutral substance with ammonia. The neutral substance is readily soluble in caustic alkalies and carbonates and is not extracted from them by organic solvents. The ethereal extraction of the acidified alkaline solutions restores the initial substance. Consequently, the latter possesses the nature of a lactone. We have called it lactone A.

The chloroform extraction of the raw material without its moistening with alkali yielded 0.02% of total alkaloids (acid solution made alkaline with sodium carbonate). From the mother liquor, after the addition of ammonia, we obtained 0.27% of extractive substances of a basic nature from which the same adduct of lactone A with ammonia was isolated [1].

Thus, the large amounts of substances of a basic nature obtained on treating the plant with ammonia arise from the formation of condensation products of neutral substances with ammonia.

From the epigeal part of S. elegans M.B., Spreng, prepared in the Pamir in the gorge of the Karagaitugaya in June, 1965, extraction without the use of ammonia isolated 0.055% of total alkaloids. The chloroform extracts, after the elimination of the alkaloids, yielded a mixture of neutral and acidic substances from which lactone A was isolated. From this it is obvious that lactone A is contained in the plant in the free state.

The richest alkaloids were found in the epigeal part of S. elegans collected in the Pamir in the region of Daraut-kurgan in July, 1965. The plant was extracted with chloroform without previous moistening with alkalies. This gave 0.15% of total alkaloids. Ethanolic extraction isolated 0.5% of total alkaloids. The ethereal fraction yielded a white crystalline alkaloid with mp 190–192° C; $[\alpha]_D^{20}$ + 75° (dimethylformamide) with the composition $C_{23}H_{29}O_5N$. UV spectrum: $\lambda_{max}^{ethanol}$ 224, 276 mμ (log ε 3.24; 2.56). IR spectrum: 3250 cm^{-1} (active hydrogen), 1765 (lactone carbonyl), 1595, 1520 (benzene ring with substituents), 1640, 910 cm^{-1} (terminal double bond.) The integral intensity corresponded to one carbonyl. Since this base has not been described in the literature, we have called it elegantine. Elegantine is a natural base obtained from the plant without the use of ammonia; elegantine was not detected in the chloroform mother liquors after their treatment with ammonia.

When the base was reduced catalytically by Adams' method, six hydrogen atoms were absorbed (three double bonds). No $N—CH_3$ and $O—CH_3$ groups were found.

Elegantine is saponified by 10% alkali to a nitrogen-containing and a neutral fraction. The nitrogen-containing fraction is a crystalline base with mp 161–162° C and the composition $C_8H_{11}ON$. IR spectrum: doublet at 3340, 3290 cm^{-1} (primary amino group), 2950 (hydroxyl), 1620, 840, 780 cm^{-1} (disubstituted aromatic ring). The substances are optically inactive. The hydroxyl has a phenolic nature. The developed formula of the amino phenol may be given as $C_6H_4(—NH_2)(OH)(C_2H_4)$.

By comparing the composition, developed formula, and physical constants of the amino phenol and its salts with those of tyramine, we concluded that they were identical.

Not having an authentic sample of tyramine for comparison, we methylated the amino phenol by Hess's method and obtained the alkaloid hordenine.

The neutral fraction was identical with lactone A obtained previously from S. salsa and S. elegans. Lactone A has the composition $C_{15}H_{18}O_4$; IR spectrum: 1755 cm^{-1} (lactone carbonyl), 3450 (hydroxyl), 1650, 910 cm^{-1} (vibrations of a double bond); IR spectrum: $\lambda_{max}^{ethanol}$ 203 mμ (log ε 4.26). As in the case of elegantine, the integral intensity corresponds to one carbonyl.

Since tyramine does not contain hydrogenatable double bonds, it may be assumed that lactone A contains three double bonds. In fact, when lactone A was catalytically hydrogenated by Adams' method it absorbed six hydrogen atoms forming a noncrystalline product.

On the basis of composition, the presence of a lactone group and double bonds, and also the isolation of sesquiterpene lactones from other species of Saussurea [2–4], we assume that lactone A belongs to the group of sesquiterpene lactones.

Experimental

Isolation of the amorphous base. Ten kilograms of the epigeal part of S. salsa was wetted with 8% ammonia and extracted with chloroform. The concentrated chloroformic extracts were treated with 10% sulfuric acid; the acid solution was made alkaline with ammonia and the mixture of bases was extracted with ether and chloroform. This gave 1.40 g of ethereal and 20.2 g of chloroformic alkaloids. From them was obtained 6.95 g of one and the same oxalate of a base with mp 194–196° C [ethanol–water (5 : 1)], the decomposition of which gave an amorphous substance with a basic nature with mp 60–62° C; $[\alpha]_D^{20}$ + 79.8° (c 0.61; ethanol).

For saponification, 1 g of this substance was boiled in 15 ml of 5% caustic soda for 5 hr, the ammonia liberated being trapped with an ethanolic solution of picric acid. The reaction mixture was acidified with sulfuric acid and the lactone A was extracted with ether. Yield 0.5 g.

Isolation of bases from S. salsa. The epigeal part of S. salsa (220 g) was extracted with chloroform, the alkaloids were back-extracted with sulfuric acid, and the acid solution was made alkaline with sodium carbonate and re-extracted with ether. The yield of combined alkaloids was 0.04 g. To the chloroform free from alkaloids was added ammonia to pH 10, and it was left for a day and was then again treated with acid and the acid extract was made alkaline with ammonia. Ethereal and chloroform fractions (0.31 and 0.29 g) of the total substances of a basic nature were isolated. From them was obtained an oxalate (0.09 and 0.13 g) identical with the preceding compound.

Isolation of alkaloids and of lactone A from S. elegans. The epigeal part of the plant from Karagaitugaya (4.5 kg) was moistened with 5% sodium carbonate solution and extracted with chloroform. The plant was aerated and then extracted with ethanol. The concentrated chloroform extract was washed with sulfuric acid. The latter was made alkaline with sodium carbonate and the alkaloids were extracted with ether (1.04 g) and chloroform (0.14 g). The chloroform extract freed from alkaloids was treated with 5% alkali which, after acidification, was extracted with ether. This gave 2.3 g of lactone A.

The methanolic extracts were evaporated to dryness, the residue was dissolved in chloroform, and the alkaloids were extracted with acid. After the acid had been made alkaline with sodium carbonate and extracted with ether, the combined ethereal (0.93 g) and chloroform (0.56 g) fractions of alkaloids were obtained.

Isolation of elegantine. The epigeal part of S. elegans from Darautkurgan (500 g) was extracted with methanol. The ethereal (1.5 g) and chloroformic (1 g) alkaloids were isolated from the methanolic extract by the method described above. From the chloroform fraction, pre-extraction yielded 0.14 g of elegantine. The ethereal alkaloids were chromatographed on alumina, and the ethyl acetate fractions yielded an additional 0.46 g of elegantine.

Elegantine. The substance had mp 190–192° C (methanol); $[\alpha]_D^{20}$ +75.4° (c 0.87; dimethylformamide). It is sparingly soluble in all organic solvents.

Found, %: C 68.6; H 7.67; N 3.68. Calculated for $C_{23}H_{29}O_5N$, %: C 69.1; H 7.34; N 3.51; mol. wt. 399.47.

The hydrobromide was formed by the addition of hydrobromic acid to a suspension of elegantine in acetone, mp 210° C (decomp.).

Reduction of elegantine. Elegantine (0.2 g) in concentrated acetic acid was reduced catalytically over platinum, 3 moles of hydrogen being absorbed. It was impossible to obtain a crystalline fraction from the reaction products.

Saponification of elegantine. One gram of elegantine was boiled with 50 ml of caustic soda for 5 hr. The reaction mixture was acidified with sulfuric acid and extracted with ether. This gave 0.6 g of lactone A. The acid solution was made alkaline with ammonia and extracted with ether. After drying, the ether was distilled off to give 0.4 g of a nitrogen-containing fraction.

Tyramine. The nitrogen-containing fraction from the hydrolysis of elegantine formed a white crystalline substance with mp 161–162° C; $[\alpha]_D^{20}$ ± 0° (c 1.21; methanol).

Found, %: C 70.0; H 8.07; N 9.42; mol. wt. 137 (mass spectrometry). Calculated for $C_8H_{11}ON$, %: C 70.4; H 8.37; N 10.21; mol. wt. 137.176.

Tyramine picrate had mp 204–205° C (ethyl acetate), and the oxalate mp 202° C (acetone).

Methylation of tyramine. A mixture of 0.16 g of tyramine, 0.12 g of formic acid, 0.5 g of formaldehyde, and 4 ml of water was boiled for 8 hr and was then made alkaline with ammonia and extracted with ether. The oily mass obtained (0.18 g) did not crystallize. It was chromatographed on paper (Leningrad, slow) in the systems 1) 1-butanol–acetic acid–water (3 : 1 : 4), and 2) 1-propanol–acetic acid–water (5 : 1 : 5). Spots were obtained of hordenine and the reaction product with R_f values 0.61 and 0.61 (1), and 0.90 and 0.90 (2), respectively.

Lactone A. This had mp 148–149° C (ethyl acetate); $[\alpha]_D^{20}$ + 102° (c 0.48; chloroform); mol. wt. 262 (mass spectrometry); $C_{15}H_{18}O_4$. The lactone is readily soluble in polar and sparingly soluble in nonpolar solvents.

Conclusions

1. In the extraction of S. salsa and S. elegans, the condensation of the neutral substances with ammonia takes place with the formation of products of a basic nature.

2. From S. elegans a new alkaloid elegantine $C_{23}H_{29}O_5N$ has been obtained the saponification of which has given tyramine and a sesquiterpene lactone.

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