PYRROLIZIDINE ALKALOIDS. XXI.*

ALKALOIDS FROM *Senecio fluviatilis* WALLR.

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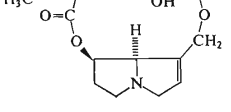
In this paper, the isolation of seneciphylline (*I*), othosenine (*II*) and florosenine (*III*) from *Senecio fluviatilis* WALLR. has been described.

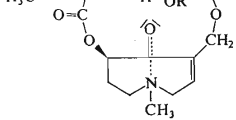
During a systematic investigation of pyrrolizidine alkaloids, we have carried out the isolation of alkaloids from *S. fluviatilis* WALLR. (*Asteraceae*). At the time of collection (in September), the flowers and leaves of most of the plants were already withered.

An analysis of *S. fluviatilis* showed that the dry material contained 0·12% of a crude mixture of free alkaloids and 0·026% of a crude mixture of alkaloids which originally were present as N-oxides and were obtained only after previous reduction with zinc dust[2]. Thin-layer chromatography revealed that these two portions differed in their content of alkaloids and, therefore, they were worked up separately.

The crude mixture of free alkaloids was purified and subjected to column chromatography on aluminium oxide to give othosenine (*II*) in pure state. Thin-layer chromato-



I



II, R = H
III, R = Acetyl

* Part XX: see ref.[1].

graphy of the less polar fractions showed mainly a substance of hR_F 24 ($hR_F = R_F \times 100$) which was obtained in pure state by purification of its picrate and identified as florosenine (*III*). So far, this substance was isolated[3] only from *Cacalia floridana* (*Asteraceae*). The amounts of the other substances in the mixture were so small that they could not be isolated or identified. By thin-layer chromatography, only seneciphylline (*I*) was detected.

The crude mixture of alkaloids from N-oxides was purified and subjected to column chromatography on aluminium oxide. The less polar fractions gave seneciphylline (*I*) and the more polar fractions again othosenine (*II*). The other substances in the mixture could not be isolated or identified.

It is of interest to compare the alkaloidal content in the individual portions. Florosenine (*III*) is present only in the portion obtained by direct extraction; it does not occur in the plant in form of an N-oxide. According to thin-layer chromatography, seneciphylline (*I*) occurs in both portions, its content in the plant in form of an N-oxide is, however, much higher; it was isolated only from the latter portion. Othosenine (*II*) is dominant in both portions.

EXPERIMENTAL

The melting points have been determined on the Kofler block and are not corrected. The IR spectra were measured on an Infrascan (Hilger), the NMR spectra on a T-60 (Varian) in deuteriochloroform using tetramethylsilane as an internal standard. Thin-layer chromatography was carried out on silica gel G with the solvent system benzene–ethyl acetate–diethylamine, 7 : 2 : 1, detection by spraying with the Dragendorff reagent.

Isolation of Alkaloids

The dry, ground plant (4·10 kg) (collected in September 1972 in the environs of Lomnice near Rýmařov) was extracted continually with methanol (60 l). After evaporation of the solvent under reduced pressure, the residue was mixed with 3 liters of 15% citric acid and filtered. The filtrate was washed 3 times with 300 ml portions of light petroleum and then 3 times with 300 ml portions of ether. After evaporation of the solvent, the residue (5·3 g) did not contain any alkaloids and was, therefore, discarded. The aqueous solution was made alkaline with ammonia to pH 10·5 and extracted 5 times with 400 ml portions of chloroform. After drying over anhydrous sodium sulphate and removal of the solvent by distillation, a crude mixture of alkaloids (4·9 g) was obtained (portion *A*). The aqueous solution was acidified with diluted hydrochloric acid to Kongo-red, zinc dust (50 g) was added, and the mixture left standing for 2 days at room temperature. After filtration, the solution was made alkaline with ammonia to pH 10·5 and extracted 5 times with 400 ml portions of chloroform. After drying over anhydrous sodium sulphate and removal of the solvent by distillation a crude mixture of alkaloids from N-oxides (1·1 g) was obtained (portion *B*).

Separation of the portion A: The crude mixture of alkaloids (4·9 g) was extracted with 2% sulphuric acid, filtered, the filtrate washed with ether, made alkaline with ammonia and extracted with chloroform. The extract was worked up to afford a mixture of alkaloids (1·4 g) of hR_F 91, 82, 73, 57, 45, 24 and 16 which was chromatographed on aluminium oxide (45 g, activity II, Reanal) in a column of 20 mm i.d.; collection of 8 ml fractions. The fractions 1—23 (benzene)

gave 115 mg of a Dragendorff-negative residue and the fractions 24—45 (benzene–ethanol, 99:1) 98 mg of a non-crystallizing mixture of alkaloids of hR_F 91, 82, and 73. Thin-layer chromatography of the fractions 46—55 (benzene–ethanol, 99 : 1) (180 mg) showed that they contained mainly a substance of hR_F 24 besides trace amounts of substances of hR_F 82, 73, 57 and 45. The fractions 56—61 (benzene–ethanol, 98 : 2) yielded 90 mg of an alkaloid of hR_F 24 with traces of a substance of hR_F 16. Since the alkaloid of hR_F 24 could not be crystallized from the mixture, the fractions 46—55 and 56—61 were combined and treated with an ethanolic solution of picric acid. The precipitated picrate was recrystallized from ethanol (150 mg) and converted into a free base which crystallized from a mixture of benzene–cyclohexane. Yield 45 mg of a substance of hR_F 24, m.p. 102—104°C, $[\alpha]_D^{24}$ +33° ± 2° (*c* 0·30 in chloroform). The adduct of florosenine (*III*) with benzene is reported[3] to have m.p. 100—103°C $[\alpha]_D$ +31·9° (chloroform). The NMR spectrum of the isolated substance corresponds to the values reported[3] for florosenine (*III*). The fractions 62—69 (benzene–ethanol, 95 : 5) yielded 425 mg of a residue which crystallized from ethanol 265 mg to give a substance of hR_F 16, m.p. 233—234°C, $[\alpha]_D^{24}$ +15° ± 2° (*c* 0·46 in chloroform). For othosenine (*II*), m.p. 231—232°C, $[\alpha]_D^{24}$ +14° ± 2° (chloroform) have been reported[4]. The infrared spectrum of the isolated substance was identical with that of authentic othosenine (*II*). Washing of the column with ethanol (50 ml) gave additional 265 mg of a residue which on crystallization from ethanol yielded 120 mg of othosenine, m.p. 232—234°C.

Separation of the portion B: The crude mixture of alkaloids from N-oxides (1·1 g) was purified as sub *A*) to afford 0·45 g of a mixture of alkaloids of hR_F 91, 82, 73, 57 and 16. The mixture was chromatographed on aluminium oxide (15 g, activity II, Reanal) in a column of 12 mm i.d.; collection of 7 ml fractions. The fractions 1—5 (benzene) yielded 53 mg of a Dragendorff-negative residue, the fractions 6—9 (benzene–ethanol, 99 : 1) 40 mg of a non-crystallizing mixture of alkaloids of hR_F 91 and 82, and the fractions 10—12 (benzene–ethanol, 99 : 1) 62 mg of a substance of hR_F 57 with traces of a substance of hR_F 82 and 73. Crystallization from ethyl acetate gave 37 mg of a substance of hR_F 57, m.p. 215—216°C. For seneciphylline (*I*), the reported[5] m.p. is 217°C. The infrared and the NMR spectra of the isolated substance were identical with those of authentic seneciphylline (*I*). The fractions 13—25 (benzene–ethanol, 98 : 2) afforded 37 mg of a non-crystallizing mixture of substances of hR_F 73, 57, and 16, and the fractions 26—42 (benzene–ethanol, 95 : 5) 160 mg of a residue of hR_F 16 which crystallized from ethanol to give 95 mg of othosenine (*II*), m.g. 232—233°C. By washing the column with ethanol (30 ml), additional 57 mg of a residue were obtained which crystallized from ethanol to yield 31 mg of othosenine (*II*), m.p. 233—234°C.

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