CCLIV.—*The Alkaloids of Ergot. Part II. Ergotinine and ψ-Ergotinine.*

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IN Part I (J., 1930, 1390) we described some properties of ergotoxine and ergotinine, two alkaloids obtained from ergot. The isolation of a third alkaloid, having a close relationship to these, enables us to clear up some discrepancies between the experimental results of earlier workers and those obtained by ourselves. The specific rotation recorded in our first paper for ergotinine is $[\alpha]_{5461}$ + 513° (c = 1 in chloroform), that given by Barger and Carr (J., 1907, **91**, 337) being $[\alpha]_D$ + 396° (c = 0·514 in chloroform), which corresponds to $[\alpha]_{5461}$ + 495°. The alkaloid now described has the specific rotations $[\alpha]_D$ + 365° and $[\alpha]_{5461}$ + 459° (c = 0·4 in chloroform). It is evident that the specific rotation for the solution in chloroform recorded by Barger and Carr corresponds with that of a mixture consisting predominantly of the alkaloid with the specific rotation $[\alpha]_{5461}$ + 513°. On the other hand, the specific rotation recorded by these authors for the solution in alcohol is + 338°, a figure that is close to the value + 348° which we find for the alcoholic solution of the alkaloid now described. This figure, moreover, is near to the specific rotations of + 334° and + 336° (in alcohol) given by Tanret, who first isolated ergotinine.

On this ground, and because of the analytical data, we think it desirable to describe the alkaloid of lower rotation as ergotinine, and to give the name ψ-ergotinine to the alkaloid of higher rotation described in our first paper. ψ-Ergotinine, like ergotinine, is converted into ergotoxine by boiling with alcohol and phosphoric acid, and the relationship is further established by the partial conversion of ψ-ergotinine into ergotinine by boiling with methyl alcohol. Elementary analysis suggests that the two alkaloids differ in composition by the elements of one molecule of water. It seems probable that ψ-ergotinine is isomeric with ergotoxine, whilst ergotinine contains the elements of one molecule of water less, as first suggested by Kraft and confirmed by Barger and Carr. The

formula $C_{35}H_{41}O_6N_5$ proposed for ergotoxine by Barger and Carr requires N, 11·2%; for ψ-ergotinine we find N, 11·8%, and a similar value (11·8—12·0%) for ergotoxine. These analyses being regarded as correct, the formula $C_{35}H_{41}O_6N_5$ requires modification. In view of the difficulties of the experimental work, we postpone discussion of alternative formulæ to a later communication.

The two alkaloids when heated melt and decompose at the same temperature; both give the colour reaction of Keller and the recent modification of the Van Urk test described by M. I. Smith (*U.S. Public Health Reports*, 1930, **45**, 1466), and both have similar absorption spectra showing a well-defined band with a maximum at 318 μμ, and a hitherto unrecorded less pronounced inflexion with a maximum at 242 μμ. The two alkaloids are best distinguished by their specific rotations and by the solubility differences.

EXPERIMENTAL.

Crude ergotinine, separated as described in Part I (*loc. cit.*), was purified by fractional crystallisation from dilute acetone. The less soluble fractions with the lower specific rotation were fractionally crystallised from dilute acetone until specimens of constant specific rotation were obtained. The fractions containing the alkaloid of higher rotation may be purified by solution in chloroform and fractional precipitation with ether.

The relative proportions of the two alkaloids vary in different specimens of ergot, some containing mainly ergotinine and others mainly ψ-ergotinine as the subsidiary alkaloid, ergotoxine being invariably the predominant alkaloid.

Ergotinine crystallises in long, stout, colourless prisms free from solvent; 1 g. is soluble in 471 g. of absolute alcohol or in 34 g. of acetone, at 15·5° in each case. Barger and Carr (*loc. cit.*) record the following solubilities for ergotinine: 1 g. in 312 g. of absolute alcohol at 10°, 1 g. in 26 g. of acetone at 18°. The specific rotations in various solvents are compared in the following table with those of Barger and Carr for ergotinine.

	Barger and Carr.	Smith and Timmis.	
Solvent.	D line.	D line.	Hg-green line.
Chloroform	+396° (*c* = 0·514)	+365°	+459° (*c* = 0·35)
Alcohol (absolute)	+338 (*c* = 0·257)	+348	+439 (*c* = 0·15)
Acetone	+367 (*c* = 0·234)	+381	+478 (*c* = 1·13)

Tanret (*J. Pharm. Chim.*, 1906, **24**, 397) also gives a specific rotation in chloroform, $[\alpha]_D$ + 357·5° (*c* = 0·42), and states that this varies with the concentration. We confirm this observation, our results being as follows:

c, in chloroform ...	3·358	1·69	0·8472	0·4195	0·2180
$[\alpha]_D$	377·5°	373·3°	369·2°	364·8°	365·9°
$[\alpha]_{5461}$	473·2	467·7	463·4	459·2	457·6

For analysis the substance was crystallised from dilute acetone (Found : * C, 69·05; H, 6·5; N, 11·9%). The figures are close to those recorded by Barger and Carr, *viz.*, C, 68·7; H, 6·5; N, 11·6%.

The Conversion of ψ-Ergotinine and Ergotinine to Ergotoxine.—2·0 G. of each alkaloid were suspended in 25 c.c. of absolute alcohol, the mixture was heated to boiling, and in each case 0·30 c.c. of phosphoric acid (*d* 1·75) was added slowly. The solutions were boiled under reflux for 1½ hours, a trace of ergotoxine phosphate was added to promote precipitation, and boiling was continued for another ½ hour. After 16 hours' standing, the precipitates from ψ-ergotinine and ergotinine amounted to 1·3 g. and 1·4 g. respectively. Their decomposition points and that of a mixture of the two were respectively 195°, 196°, 196°. The corresponding bases were isolated by basification with sodium bicarbonate and extraction with ether, and had $[\alpha]_{5461}$ − 210° and $[\alpha]_{5461}$ − 207° respectively. The two bases were then converted to the ethanesulphonates, which were recrystallised twice and then reconverted to the bases, which had respectively $[\alpha]^{20°}_{5461}$ − 226° and $[\alpha]^{20°}_{5461}$ − 225°, identical with that of ergotoxine ($c = 1$ in chloroform). The two samples of base were recrystallised from benzene, and each formed the characteristic prisms of the benzene compound of ergotoxine.

The Conversion of ψ-Ergotinine to Ergotinine.—1 G. of ψ-ergotinine ($[\alpha]^{20°}_{5461}$ + 512°, $c = 1$ chloroform) was boiled with 75 c.c. of methyl alcohol for 1½ hours. After standing for 16 hours, well-formed needles (0·15 g.) were deposited, and after two recrystallisations from acetone had $[\alpha]^{20°}_{5461}$ + 466° ($c = 0·8$ in chloroform). The crystals had the same m. p. as ψ-ergotinine and ergotinine; their identity was confirmed by the solubility in acetone and by analysis (Found : C, 69·0; H, 6·2%).

ψ-Ergotinine.—The specific rotation has been determined in acetone (that in chloroform for the green line was reported in our previous paper) :

Solvent.	D line.	Hg-green line.
Chloroform	+410°	+513° ($c = 0·353$)
Acetone	+403	+509 ($c = 1·04$)

ψ-Ergotinine is considerably more soluble than ergotinine in the common organic solvents. For analysis the substance was crystallised from dilute alcohol [Found (mean of 7 analyses for C and H and 3 for N, extremes being given in parentheses) : C, 66·6 (66·3—67·1); H, 6·7 (6·5—7·0); N, 11·8 (11·7—11·9)%].

* Mean of 2 macro-analyses for C, H, and N, and 6 micro-analyses for C and H and 2 for N; extremes for C, 68·8—69·3; for H, 6·3—6·6; for N, 11·8—12·0%.

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