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THE ALKALOIDS OF CHINESE CORYDALIS AMBIGUA, CHAM. ET SCH. (YEN-HU-SO). PART III. CORYDALIS I AND MONOMETHYL ETHERS OF CORYDALIS F AND G

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In two previous communications on Chinese Corydalis (1, 2), the writer reported the isolation of Corydalis A, B, C, D and E from fraction "2", Corydalis F and G from fraction "3" and Corydalis H from fraction "4". Corydalis A is identical with corydaline in all respects. Corydalis C is similar to protopine in its molecular formula and general properties, but melts constantly at 201°C instead of 207°C, the melting point of protopine. The other alkaloids remain to be identified and further investigated. The present communication describes the isolation of another new alkaloid, Corydalis I from fraction "2" and the identification of Corydalis F and G by means of their monomethyl ether. Corydalis I crystallises out from a mixture of alcohol and petroleum ether in the form of prisms, melting at 104°C and having a specific rotation +112.5°. It has the lowest melting point of the series. In 1923, Späth, Mosettig and Trothändl (3), isolated from Corydalis tuberosa, corypalmine, $C_{20}H_{23}O_4N$, a phenolic base, having a melting point 235-236° and a specific rotation +280°, and its monomethyl ether d-tetrahydropalmatine, $C_{21}H_{25}O_4N$, melting at 142° and having a specific rotation +295.5°. Corydalis F resembles corypalmine in its molecular formula and general properties, but is levo-rotatory. Its monomethyl ether has now been prepared. It has a molecular formula $C_{21}H_{25}O_4N$ and is in turn similar to d-tetrahydropalmatine in general respects besides its optical activity. This suggests that Corydalis F is most probably l-corypalmine isolated for the first time. Corydalis G

has now been identified to be corybulbine, as on methylating with nitrosomethyl urethane in the presence of sodium hydroxide, it gives rise to the formation of corydaline which can also be obtained from corybulbine by methylation.

EXPERIMENTAL

(1) Corydalis I.

This was isolated from the basic residue of fraction "2" by means of its hydrochloride. It was non-phenolic and crystallised out from a mixture of alcohol and petroleum ether in the form of prisms, (see fig. 1) melting at 104°C. It was easily soluble in most organic solvents except petroleum ether in which it was almost insoluble. A 0.4 per cent solution in alcohol gave a specific rotation in 1 dm tube of +0.45°; $[\alpha]_{D}^{25} = +112.5°$. It showed the following colour reactions; conc. H_2SO_4, colourless; Froehde's reagent, green and then blue; Erdmann's reagent, green, orange and reddish brown. On account of the small amount of substance in hand, its molecular formula has not yet been determined. The following salts have been prepared.

(a) *Hydrogen oxalate.* This is the most characteristic salt of Corydalis I, melting at 185°C. It crystallised out from alcohol in clusters of prisms and was easily soluble in warm water. Its aqueous solution was acid to litmus.

(b) *Hydrochloride.* It separated out from alcohol or water as a jelly but could usually be made crystalline in the form of soft silky needles by warming the liquid carefully; melting point 236°C.

(c) *Hydrobromide.* It crystallised out from water or alcohol also in the form of soft silky needles, melting at 241°C. Like the hydrochloride, it has the tendency to become a jelly.

Preliminary tests of the physiological properties of Corydalis I by Dr. C. Pak gave the following results:—With doses varying from 0.19 to 0.35 mg per gm body weight subcutaneously, Corydalis I, in the form of its hydrobromide, produced in mice and rats, a slight depression of the central nervous system (drowsiness) followed within one hour by severe convulsions ending in death. In frogs, the depression was followed by exaggerated reflexes and increased extensor tonus, but no convulsions.

(2) Monomethyl ether of Corydalis F, $C_{21}H_{25}O_4N$.

0.62 gm of Corydalis F was dissolved in 30 cc of methyl alcohol in the presence of 1 gm of sodium hydroxide. The solution was cooled

with freezing mixture and gradually treated while shaking with 4 cc of nitrosomethyl urethane. After being allowed to stand at room temperature for two days, the methyl alcohol was evaporated off and the residue taken up with dilute H_2SO_4, made alkaline with NaOH and extracted with ether. The ethereal extract, when dried and distilled, left behind the monomethyl ether required. It crystallised out from alcohol in large prisms (see fig. 2), melting at 140°C. It was easily soluble in chloroform, less so in ether and insoluble in petroleum ether. Unlike corydaline, the crystals fall rapidly into an amorphous powder on keeping and become highly coloured when exposed to the air. A 0.4 per cent solution in alcohol gave a specific rotation of −1.1° in 1 dm tube, 25/D = −275°.

Analysis: — 0.1122 gm substance gave 0.2912 gm CO_2 and 0.0707 gm H_2O,

C = 70.78; H = 7.00

$C_{21}H_{25}O_4N$ requires C = 70.98; H = 7.04.

Its hydrochloride and hydrobromide crystallised out from alcohol in the form of prismatic needles, easily soluble in water. The following table shows the resemblance of Corydalis F to corypalmine on the one hand and its monomethyl ether to d-tetrahydropalmatine on the other.

	Corydalis F	Corypalmine
Mol. formula M. P. Sp. R.	$C_{20}H_{23}O_4N$ 237° −259°	$C_{20}H_{23}O_4N$ 235–236° +280°
	Monomethyl ether of Corydalis F.	d-tetrahydropalmatine
Mol. formula M. P. Sp. R.	$C_{21}H_{25}O_4N$ 140° −275°	$C_{21}H_{25}O_4N$ 142° +295.5°

(3) Monomethyl ether of Corydalis G, (corydaline).

Prepared in a way similar to the above method.

The methylated base crystallised out from alcohol in six-sided prisms just like those of corydaline (see fig. 3). It melted at 135°C; when mixed with corydaline (Corydalis A), its melting point remained unchanged. A 0.1 per cent solution in alcohol gave a specific rotation +0.30° in 1 dm tube, $[\alpha]$ 25/D = +300°. Its salts showed the same

melting points as those of corydaline; platinichloride, brown crystals, m.p. 227°; nitrate, prisms, m.p. 197°. This proves that Corydalis G is corybulbine, an alkaloid isolated from commercial corydaline by Freund an Josephi (4). Corybulbine, besides its similarity to Corydalis G in its melting point, specific rotation and general properties it also yields corydaline on methylation.

DISCUSSION

Chinese Corydalis (Yen-Hu-So) is very rich in alkaloids. Besides the nine alkaloids already isolated and described, there are still some others left in the residue, the complete isolation and full investigation of which can only be successfully made by working on a large quantity of raw material. The following table gives a summary of the nine alkaloids already described.

Name	Molecular formula	Melting point	Specific rotation	Identification
Corydalis A.	$C_{22}H_{27}O_4N$	135°	+295°	Corydaline
,, B.	$C_{20}H_{23}O_4N$	148-149°	0°	—
,, C.	$C_{20}H_{19}O_5N$	201°	0°	Protopine (?)
,, D.	$C_{19}H_{16}O_4N$ or $C_{19}H_{17}O_4N$	204°	-295°	—
,, E.	—	219°	—	—
,, F.	$C_{20}H_{23}O_4N$	237°	-250°	—
,, G.	—	237°	+300°	Corybulbine
,, H (HBr salt)	—	235°	0°	—
,, I.	—	104°	+112.5	—

Of these nine alkaloids, three are dextro-rotatory, two are levo-rotatory, three are optically inactive and one has not yet been determined. Their melting points range from 104°C to 237°C. Corydalis B and F have the same molecular formula, but show entirely different properties. Corydalis A and Corydalis G are identified as corydaline and corybulbine respectively. Corydalis C is probably protopine and the others are new. They have generally interesting physiological properties and deserve some detailed investigations pharmacologically. As shown by Chu and Pak (1), Corydalis B has narcotic and local anaesthetic properties and a cardiac augmentor action. Corydalis C is apparently a cerebral stimulant and Corydalis I a nerve depressant.

SUMMARY

From the tubers of Chinese Corydalis (Yen-Hu-So), besides the eight alkaloids (Corydalis A–H) already reported, another new alkaloid,

Corydalis I has now been isolated from fraction "2". It crystallises out in prisms; m.p. 104°; specific rotation +112.5°. It forms well crystallised salts; oxalate, prisms, m.p. 185°; hydrochloride, needles, m.p. 236°; hydrobromide, needles, m.p. 241°. Corydalis I produces a slight depression of the central nervous system in mice and rats, followed by severe convulsions ending in death. In frogs, the same depression is observed, but no convulsions.

Corydalis F forms a monomethyl ether having a molecular formula $C_{21}H_{25}O_4N$, m.p. 140°C and specific rotation −275°. Corydalis F is probably l-corypalmine isolated for the first time.

Corydalis G gives rise to the formation of corydaline (Corydalis A) when methylated. This proves that Corydalis G is corybulbine.

LITERATURE

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中國延胡索之研究

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在中國之延胡索中,作者曾提出八種 鹼性物質幷定名爲延胡索甲,乙,丙,丁,戊,己,庚及辛,(參觀本報第二卷第二期二百零三至二百十八頁及本報第三卷第一期六十九至七十四頁)今又提出一新鹼性物質,定名爲延胡索素壬,關于此物之提取方法化學性質,物理性質及生理性質等,請閱西文原文.延胡索庚今已證明爲前人已發明之 Corybulbine.