

decomposition. The substance was dried over phosphorus pentoxide in a vacuum at 80°.

Anal. Calcd. for $C_8H_{13}ON_3$: C, 57.44; H, 7.84. Found: C, 57.81; H, 7.92.

Hydrochloride.—The above cytosine derivative dissolved in dilute hydrochloric acid, and on cooling the hydrochloride separated in prisms, melting at 235°.

Anal. Calcd. for $C_8H_{13}ON_3 \cdot HCl$: C, 47.15; H, 6.93. Found: C, 46.78; H, 6.65.

Summary

1. Ethyl *n*-propylacetoacetate condenses with thiourea in alcohol solution in the presence of sodium ethylate to give 2-thio-4-methyl-5-*n*-propyl-6-oxypyrimidine.

2. 2-Thio-4-methyl-5-*n*-propyl-6-oxypyrimidine is alkylated on sulfur by treatment with methyl iodide, ethyl bromide, *n*-propyl bromide

and ethyl monochloroacetate to form the corresponding 2-mercaptopyrimidine derivatives, respectively.

3. 2-Ethylmercapto-4-methyl-5-*n*-propyl-6-chloropyrimidine is obtained from its corresponding 6-oxypyrimidine compound by heating the latter with phosphorus oxychloride.

4. This chloropyrimidine interacts with alcoholic ammonia to form 2-ethylmercapto-4-methyl-5-*n*-propyl-6-aminopyrimidine.

5. Treatment with concentrated hydrobromic acid converts 2-ethylmercapto-4-methyl-5-*n*-propyl-6-aminopyrimidine into 4-methyl-5-*n*-propyl-cytosine hydrobromide, from which the free base is obtained by neutralization with ammonia.

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The Alkaloids of Chinese Gelsemium, Kou Wen¹

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Chou² has isolated the following alkaloids from the plant Kou Wen: (A) koumine $C_{20}H_{22}N_2O$, m. p. 170°, (B) kouminine, (C) kouminicine and (D) kouminidine. Of these four alkaloids, koumine only was obtained in a good crystalline state and kouminidine was probably not very pure on account of small traces of impurity present, while kouminine and kouminicine were only obtained in an amorphous condition. Recently, Chou³ isolated the following alkaloids from Ta-Cha-Yeh: (Z) koumine $C_{20}H_{22}N_2O$, m. p. 170°; (B) kouminine in the form of its hydrochloride; (C) gelsemine, $C_{20}H_{22}N_2O_2$, m. p. 178°; and kouminidine $C_{21}H_{24}N_2O_5$. In this short paper the authors give a report of their investigation of the alkaloids of Kou Wen. Besides koumine, m. p. 168°, they succeeded in separating Chou's kouminine into gelsemine and other impure bases. From the kouminidine fraction, they isolated a base, m. p. 299° (instead of 200°), to which the original name, kouminidine, was assigned.

Experimental Part

Twenty-two and seven-tenths kilograms of Kou Wen in the form of stems, roots and leaves was powdered and per-

colated with cold 95% alcohol. The alcoholic extract was evaporated under diminished pressure, and the resin left over was taken up with a sufficient quantity of 2% hydrochloric acid. When the insoluble resinous matter was filtered off the acid extract was allowed to stand for about two weeks, when there deposited a further quantity of neutral resinous material. The clear solution, obtained after removing the insoluble non-basic resinous matter, was finally neutralized with sodium carbonate and extracted thoroughly, first with ether several times (A), and then with chloroform (B).

Isolation of Koumine.—After removing the solvent from the ethereal solution (A), the crude basic residue weighed 38 g. This was dissolved in a small quantity of acetone, and the solution allowed to stand in an ice-box for several days; whereupon koumine deposited in the form of colorless prisms. This was recrystallized from acetone several times or until the melting point became constant at 168°. It was readily soluble in alcohol, chloroform and benzene and slightly soluble in hot water.

Anal. Calcd. for $C_{20}H_{22}N_2O$: C, 78.38, H, 7.24; N, 9.15. Found: C, 78.52, 78.37; H, 7.31, 7.39; N, 9.37, 9.35.

Acetylation of Koumine.—When Koumine was treated with acetic anhydride, the original alkaloid melting at 168° was recovered.

Isolation of Gelsemine.—The acetone mother liquid, from which the base, koumine, had been separated, was evaporated to dryness. The residue was dissolved in ethyl alcohol and acidified with the desired amount of alcoholic hydrochloric acid. The solution was then allowed to stand for several days, whereupon the mixed hydrochlorides separated in the form of a crystalline pow-

(1) The authors desire to express their thanks to Professor Treat B. Johnson of Yale University for his personal help in arranging this report for publication in THIS JOURNAL.

(2) Chou, *Chinese J. Physiol.*, **5**, 345-352 (1931).

(3) Chou, *ibid.*, **10**, 79-84 (1936).

TABLE I
 PROPERTIES OF KOUMINE DERIVATIVES

Compound	Cryst. from	Crystal form	M. p., °C.	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
Hydrochloride	Alc.-ether	Cubes	258	$C_{20}H_{22}N_2O \cdot HCl$	70.04	69.40	69.43	6.77	7.20	6.97
Hydrobromide	Alc.-ether	Cubes	268-269	$C_{20}H_{22}N_2O \cdot HBr$	62.00	62.56	62.22	5.99	6.29	6.03
Sulfate			261-262							
Nitrate	Alcohol		249-250	$C_{20}H_{22}N_2O \cdot HNO_3$	65.00	65.56		6.28	6.19	11.38
Platinichloride	Dil. HCl	Brown ppt.	>310							10.62
				$C_{20}H_{27}N_2O \cdot CH_3I$	56.23			5.62		
Methiodide	Dil. acetone	Needles,	230 dec.			54.21	54.24		5.79	5.92
				$C_{20}H_{22}N_2O \cdot CH_3I \cdot H_2O$	54.06			5.84		

der. They were repeatedly purified by recrystallization from ethyl alcohol, and melted at 303°.

The free base was liberated from an aqueous solution of the crystallized mixed hydrochlorides by adding sodium carbonate just to neutrality. The resulting amorphous base was then filtered off and dried in a vacuum desiccator. It was soluble in most of the common organic solvents with the exception of petroleum ether and water, and refused to crystallize from any of the common solvents tried. This amorphous base, melting approximately at 108°, was extracted with hot benzene (b. p. 80-90°), and after filtering off the insoluble part and cooling, the benzene solution deposited a colorless amorphous solid. This amorphous base was then digested with petroleum ether (b. p. 40-60°) for twenty-four hours, whereupon the base gradually changed into a crystalline condition. It was then filtered and the base purified further by recrystallization from acetone. It separated in the form of long shining needles, melting at 176-178°. It contained acetone of crystallization. When 0.0735 g. of the substance was dried in a vacuum over phosphorus pentoxide at 117°, it was found that the weight lost was equal to 0.0111 g., where from the percentage of acetone of crystallization was 15.1, the calculated value for $C_{20}H_{22}O_2N_2 \cdot CH_3COCH_3$ being 15.27. A sample dried at room temperature was used for analysis.

Anal. Calcd. for $C_{20}H_{22}O_2N_2 \cdot CH_3COCH_3$: C, 72.58; H, 7.42; N, 7.37. Found: C, 73.41, 73.10; H, 7.52, 7.67; N, 7.56.

Color Test.—A few crystals of the base were dissolved in a small quantity of concentrated sulfuric acid, to which a few crystals of potassium dichromate were then added. The solution first became violet, and then turned to a red color. On standing it changed to green.

Nitrate.—The pure base was dissolved in dilute nitric acid, and the solution evaporated to dryness in a vacuum desiccator. The residue was then recrystallized from ethyl alcohol and melted at 288°.

Anal. Calcd. for $C_{20}H_{22}O_2N_2 \cdot HNO_3$: C, 62.31; H, 6.02; N, 10.91. Found: C, 62.17, 62.70; H, 6.28, 6.17; N, 10.42.

Methiodide.—The pure base dissolved in warm acetone, to which an excess of methyl iodide was then added and

the mixture heated for about one to two hours. The methiodide separated on cooling in colorless shining scales and melted at 284°.

Anal. Calcd. for $C_{20}H_{22}O_2N_2 \cdot CH_3I$: C, 54.29; H, 5.43. Found: C, 54.17, 53.91; H, 5.46, 5.59.

The alcoholic mother liquid, from which the crude gelsemine hydrochloride had been separated, was evaporated to dryness, and the residue dissolved in 1% hydrochloric acid. This acid solution was repeatedly washed with chloroform, and then made alkaline with sodium carbonate. The resulting solution was first extracted with ether to remove koumine and gelsemine, and then extracted with chloroform. When the solvent was distilled off an amorphous basic product was obtained and nothing crystalline could be isolated.

Isolation of Kouminidine.—The chloroform extract (B) was evaporated to dryness, and the crude base left over weighed 22 g. It dissolved in warm acetone, from which a small quantity of a neutral substance, melting at 62-64°, separated. The mother liquid was concentrated and allowed to stand for several days, whereupon a small quantity of a basic substance separated. This was then purified by recrystallization from a methyl alcohol-ethyl ether mixture and separated in colorless prisms, melting at 299° with decomposition. It was soluble in water and most organic solvents.

Anal. Calcd. for $C_{19}H_{23}N_2O_4$: C, 66.04; H, 7.30; N, 8.12. Found: C, 66.88, 66.42; H, 7.18, 7.29; N, 8.20.

Summary

1. The authors have repeated the work of Chou and have isolated from Kou Wen the alkaloid koumine, $C_{20}H_{22}N_2O$.
2. The alkaloid kouminine obtained from Kou Wen by Chou has been separated by the authors into gelsemine, $C_{20}H_{22}N_2O_2$, and other impure bases.
3. Gelsemine is also found in the plant Ta-Cha-Yeh.

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