same selective activity toward double bonds activated by phenyl groups as does sodium. Any mechanism to account for the activity of the alkali metals will possibly have to be extended to calcium.

Some of the hydrogenation observed when sodium is used as a catalyst is due to hydrogenolysis of the product of addition of sodium to a double bond, since sodium hydride was obtained in some of these reactions, and not in appreciable quantities by heating metallic sodium alone with high pressure hydrogen under the same conditions.[6]

Some of the hydrogenation must be due to specific catalytic activity of the sodium hydride, as observed in experiments of Hugel and co-workers.[1,2] The assumption could be made that sodium hydride adds to the double bond, and is then regenerated by hydrogenolysis, leaving a reduced organic compound. Certainly this cannot always be true, since metallic calcium is comparable with sodium as a catalyst and yet both calcium hydride and metallic calcium should add to a double bond much less readily than sodium hydride or sodium.

Summary

1. A number of organic compounds have been hydrogenated with high pressure hydrogen at 130–260°, in the presence of lithium, sodium, potassium or calcium metals as catalysts.

2. The only substances so far found that can be hydrogenated are those to which the alkali metals add. This suggests a connection with the work of Hugel and co-workers[1,2] who found that sodium hydride similarly catalyzes the hydrogenation of unsaturated compounds which form sodium addition products.

3. The mechanism of the hydrogenations is discussed.

STANFORD UNIVERSITY, CALIFORNIA
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(6) McCurdy, unpublished observations, Stanford University, 1941. Hugel and Friess claim to have prepared sodium hydride by heating sodium with high pressure hydrogen at 235–425°, but McCurdy was unable to duplicate their results at temperatures of 200–300° and pressures up to 2000 lb./sq. in. (no absorption of hydrogen), with the use of the apparatus of the present article. Some unknown catalyst must have influenced the work of Hugel and Friess.

[CONTRIBUTION FROM THE INSTITUTE OF MATERIA MEDICA, SHANGHAI, CHINA]

The Preparation and Properties of Peimine and Peiminine

BY T. Q. CHOU AND T. T. CHU

In 1932, one of us[1] reported the isolation from the Chinese drug, Pei-Mu, identified as *Fritillaria Roylei*, two alkaloids, peimine and peiminine, to which the formulas $C_{19}H_{30}O_2N$ and $C_{18}H_{28}O_2N$, respectively, wereas signed. Peimine melted at 223°, being optically inactive, while peiminine had a melting point of 135° and a specific rotation of $[\alpha]^{24}\text{D}$ $-62.5°$. Their pharmacological action was subsequently studied.[2] Chi, Kao and Chang[3] later assigned the formula $C_{26}H_{43}O_3N$ to both peimine and peiminine and the melting point of the latter was stated by them to be indefinite, sintering at 140°, melting at 147–148°, resolidifying at 157° and finally melting at 212–213°, whereas a specimen of peiminine dried at 110° in a vacuum melted directly at 212–213°. More recently Li[4] confirmed, however, the formula $C_{19}H_{30}O_2N$ for peimine and gave the melting point of peiminine as 130–133°. This discrepancy led us to reinvestigate these two alkaloids with the object of establishing more conclusively their composition and properties and at the same time working out a practical process for their isolation.

The present analytical data indicate that the composition of peimine agrees well with the formula $C_{26}H_{43}O_3N$ assigned to it by Chi, instead of $C_{19}H_{30}O_2N$ which resulted from an error in its nitrogen determination; but that of peiminine is better represented by $C_{26}H_{41}O_3N$, differing from peimine by two atoms of hydrogen. This is substantiated by the fact that peimine and peiminine are convertible into each other by oxidation in one case and reduction in the other, details of which will be described later in a separate paper. The indefinite nature of the melting point of peiminine as observed by Chi can be attributed to its water of crystallization. When freshly prepared and air-dried, peiminine melts at 135–137° to a clear liquid, no change taking place on further heating to about 200°; on drying at 110°

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(1) Chou, *Chin. J. Physiol.*, **6**, 265 (1932).

(2) Chen, Chen and Chou, *J. Am. Pharm. Assoc.*, **22**, 638 (1933).

(3) Chi, Kao and Chang, THIS JOURNAL, **58**, 1306 (1936); **62**, 2896 (1940).

(4) Li *J. Chin. Pharm. Assoc.*, **2**, 235 (1940).

TABLE I

PHYSICAL CHARACTERISTICS AND CHEMICAL COMPOSITION OF PEIMINE, PEIMININE AND DERIVATIVES

Substance	M. p., °C.	Formula	Analyses, anhydrous											
			Crystn. Water, %		Carbon, %		Hydrogen, %		Nitrogen, %		Chlorine, %		Platinum or gold, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
Peimine	223	$C_{26}H_{43}O_3N$	2.12	2.16 2.13	74.76	74.66 74.77	10.38	10.42 10.47	3.36	3.48 3.40				
Peimine hydrochloride	300	$C_{25}H_{43}O_3N \cdot HCl \cdot 3H_2O$	10.63	9.50	68.75	68.84 68.81	9.77	9.81 9.98	3.08	3.06 2.95	7.81	7.81 7.56		
Peimine platinichloride	...	$(C_{26}H_{43}O_3N \cdot HCl)_2 \cdot PtCl_4$											15.68	15.56 15.47
Peimine aurichloride	...	$C_{26}H_{43}O_3N \cdot HCl \cdot AuCl_3$											26.04	25.92 25.92
Diacetylpeimine	Indef.	$C_{26}H_{41}(CH_3CO)_2O_3N$			71.67	71.65 71.49	9.43	9.66 9.70	2.78	3.02 3.00				
Diacetylpeimine·HCl	293	$C_{26}H_{41}(CH_3CO)_2O_3N \cdot HCl \cdot 2H_2O$	6.30	6.60	66.94	67.12 67.11	9.00	9.18 9.25	2.66	2.90 2.88	6.59	6.48 6.32		
Diacetylpeimine·platinichloride	...	$[C_{26}H_{41}(CH_3CO)_2O_3N \cdot HCl]_2 \cdot PtCl_4$											13.81	13.66 13.51
Peiminine	135–137	$C_{26}H_{41}O_3N \cdot {}^1/_2H_2O$	2.12	2.16 2.13	75.12	74.90 74.86	9.95	10.08 10.08	3.37	3.40 3.28				
Peiminine hydrochloride	298	$C_{26}H_{41}O_3N \cdot HCl \cdot 3H_2O$	10.67	10.34	69.06	68.84 68.98	9.37	9.40 9.52	3.10	3.31 3.18	7.85	7.76 7.76		
Peimine platinichloride	...	$(C_{26}H_{41}O_3N \cdot HCl)_2 \cdot PtCl_4$											15.73	15.72 15.64
Peiminine aurichloride	...	$C_{26}H_{41}O_3N \cdot HCl \cdot AuCl_3$											26.11	26.12 26.06
Monoacetylpeiminine	174	$C_{26}H_{40}(CH_3CO)O_3N$			73.48	73.39 73.29	9.48	9.62 9.68	3.06	3.29 3.29				
Monoacetylpeiminine·HCl	294	$C_{26}H_{40}(CH_3CO)O_3N \cdot HCl$			68.04	67.96 67.88	8.98	9.04 9.19	2.83	3.05 3.01				
Peiminine oxime	108 dec.	$C_{26}H_{42}O_3N_2$			72.51	72.34 72.42	9.84	10.10 9.98	6.51	6.54 6.60				
Peiminine oxime·HCl	...	$C_{26}H_{42}O_3N_2 \cdot HCl \cdot H_2O$	3.71	3.50	66.84	66.50 66.60	9.28	9.31 9.40	6.00	6.20 6.18				

in a vacuum, it loses weight corresponding to a half molecule of water of crystallization and melts sharply at 212–213°. The characteristic feature of resolidifying at 157° as described by Chi occurs only with the substance partially dried at 80° in vacuum. The optical activity of peiminine either air-dried or dried at 110° shows no change and that of peimine has now been found to be slightly levorotatory instead of being inactive as reported previously, thus confirming Li's observation.[4] Both peimine and peiminine are tertiary monoacidic bases. Peimine contains two alcoholic hydroxyl groups, and on acetylation it gives a diacetyl derivative. Peiminine contains one alcoholic hydroxyl group and one carbonyl group, forming easily a monoacetyl derivative and an oxime.

Experimental

I. **Isolation.**—A quantity of 10 kilograms of the Chinese drug, Pei-Mu, of Chekiang variety, is finely powdered, moistened with a 5% solution of sodium carbonate and percolated with benzene at room temperature for two days. The benzene extract is separated and washed well with 1% hydrochloric acid to remove any basic substance present. The acid solution is made alkaline with sodium carbonate and the precipitate extracted with chloroform. The chloroform solution, when dried and distilled, leaves behind the crude alkaloid, weighing 13 g. and representing 0.13% of the drug used. The residue so obtained is dissolved in 20 cc. of warm absolute alcohol on a water-bath, and neutralized with a mixture of equal volumes of concentrated hydrochloric acid and alcohol. On the addition of a sufficient quantity of ether, the peimine hydrochloride crystallizes out in white soft needles; yield, 4.5 g. Its mother liquor is concentrated to 7–8 cc., diluted with about an equal volume of acetone and then a sufficient quantity of ether, whereupon peiminine hydrochloride crystallizes out rapidly as hard rhombic prisms; yield, 3.3 g. The hydrochlorides so obtained are almost pure and can be used directly for working up their respective alkaloids. From the final mother liquor a further quantity of peimine and peiminine, together with a small amount of other crystalline alkaloids, can be isolated. The latter will be reported on later.

II. **Peimine.**—It is prepared by treating the hydrochloride with sodium carbonate and extracting with sufficient ether. It crystallizes from acetone in minute crystals and from dilute alcohol in colorless long needles, m. p. 223°, $[\alpha]^{26}\text{D}$ −25° in absolute alcohol. It is easily soluble in alcohol or chloroform, but much less so in ether or benzene. Its hydrochloride, prepared by neutralizing the pure alkaloid with hydrochloric acid in alcohol, forms needles which are anhydrous, m. p. 300°, $[\alpha]^{26}\text{D}$ −19° in water; when recrystallized from water, it forms colorless rhombic prisms, having no sharp melting point and containing 3 molecules of water of crystallization which are lost when dried at 120–130° for one hour. The analytical results obtained with the alkaloid, its hydrochloride, platinichloride and aurichloride agree well with the formula $C_{26}H_{43}O_3N$ assigned to peimine by Chi, as shown in Table I.

Diacetylpeimine.—One-half gram of peimine is warmed with 5 cc. of acetic anhydride in the presence of a trace of pyridine on a water-bath for three hours. The resulting product is treated with powdered ice until, with shaking, a homogeneous liquid is obtained. As soon as the acid solution is made alkaline with sodium carbonate, a precipitate is obtained; this is extracted with ether in which it is easily soluble. The ethereal solution, when dried and distilled, leaves behind the required product which is converted into its hydrochloride by neutralizing with hydrochloric acid in alcohol. Diacetylpeimine hydrochloride crystallizes from an alcohol–ether mixture in silky, shining plates, melting at 293° and containing 2 molecules of water of crystallization. It becomes anhydrous when dried at 135–140°. Diacetylpeimine is recovered from its pure hydrochloride by action of sodium carbonate. It separates from its alcoholic solution on addition of water as a crystalline powder, possessing no definite melting point. Its platinichloride is obtained as an orange amorphous powder by precipitation in aqueous solution in the presence of hydrochloric acid. The analytical data as given in Table I indicate the compound to be a diacetyl derivative.

III. **Peiminine.**—It is liberated from its hydrochloride with sodium carbonate and extracted with ether containing 10% chloroform. The ether–chloroform solution is dried and distilled and the residue is taken up with a little acetone. On addition of a sufficient quantity of ether, peiminine crystallizes out in fine needles, containing $^1/_2$ molecule of water of crystallization. When air-dried, it melts at 135–137° to a clear liquid which undergoes no change on further heating to 200°. Resolidifying at 157°, first observed by Chi, occurs only when the substance has been dried at 80° in a vacuum. If dried over phosphorus pentoxide at 110° in a vacuum, it becomes anhydrous and melts sharply at 212–213°, $[\alpha]^{26}\text{D}$ −68°. Its hydrochloride crystallizes from an alcohol–ether mixture in rhombic prisms (anhydrous), m. p. 298°; and from water, also in rhombic prisms, but with 3 molecules of water of crystallization, which are lost when dried at 140–150°. Its platinichloride and aurichloride are obtained as amorphous powders by precipitation in aqueous solution with one drop of hydrochloric acid. The composition of peiminine is determined to be $C_{26}H_{41}O_3N$ according to the analytical results listed in Table I.

Monoacetylpeiminine.—It is prepared in a similar manner to diacetylpeimine. It crystallizes from acetone in needles, m. p. 174°. Its hydrochloride crystallizes from an alcohol–ether mixture in prisms, and melts at 294°. The analytical data shown in Table I agree with the composition of a monoacetyl derivative.

Peiminine Oxime.—A mixture of 0.4 g. of peiminine hydrochloride, 0.1 g. of hydroxylamine hydrochloride, and 0.2 g. of potassium acetate is dissolved in 20 cc. of water and warmed on the water-bath for about one hour. Peiminine oxime separates out in the form of hydrochloride in large rhombic prisms as heating proceeds. The hydrochloride so obtained is slightly soluble in water, but crystallizes easily from an alcohol–ether mixture in prisms, containing one molecule of water of crystallization and possessing no sharp melting point. The anhydrous salt is obtained by drying at 130–145° for two hours. The oxime is liberated from its hydrochloride with sodium carbonate, and extracted with ether in which it is easily soluble. After the ethereal solution is dried with potassium carbonate and distilled to a small volume, peiminine oxime separates out as an amorphous powder which has no definite melting point, but decomposes at 108°. Analyses confirm its composition as given in Table I.

Summary

Peimine and peiminine have been reinvestigated regarding their composition and properties. The composition of peimine agrees with the empirical formula $C_{26}H_{43}O_3N$ assigned to it by Chi, Kao and Chang, but that of peiminine fits better with $C_{26}H_{41}O_3N$, differing from peimine by 2 atoms of hydrogen. Peimine contains 2 alcoholic hydroxyl groups, and, on acetylation, it yields a diacetyl derivative. Peiminine contains one alcoholic hydroxyl group and one carbonyl group, forming easily a monoacetyl derivative and an oxime. A simple and practical process for isolating these two alkaloids has been described.

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