chlorination through chlorine atoms involves inversion of the configuration of the carbon atom involved.

It is suggested that certain differences in reactivity between paraffin and cycloparaffin derivatives may be ascribed to differing steric factors for a carbon atom in a chain as compared with one in a ring in reactions proceeding by a bimolecular inversion mechanism.

URBANA, ILLINOIS RECEIVED FEBRUARY 28, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY, NATIONAL MEDICAL COLLEGE OF SHANGHAI. AND THE DEPARTMENT OF CHEMISTRY, GREAT CHINA UNIVERSITY]

The Alkaloids of *Fritilaria Roylei*. II. Isolation of Peiminine[1]

BY YUOH-FONG CHI, YEE-SHENG KAO AND KOU-JEN CHANG[2]

In the previous communication (I)[3] on this subject we showed that the formula for peimine is $C_{26}H_{43}O_3N$ rather than $C_{19}H_{30}O_2N$ which was assigned to it by Chou and Chen.[4] A sample of peimine which Dr. Chou has now kindly sent to us, mixed with some of our material, melts at 221–223°, which does not differ significantly from the melting point (224°) of our peimine, indicating that the two samples are identical.

Chou and Chen's[4] opinion regarding the second crystalline alkaloid (peiminine) isolated from *Fritilaria* also was not in agreement with that of Fukuda[5] and others. Through Dr. Chou's kindness we have received a sample of *peiminine*, for which we determined again its true melting point. Fukuda's *Verticillin* sintered at 130°, melted at 148–50°, solidified again at 157–159°, and finally decomposed at 212–213°. The behavior of our preparation agrees better with that of Fukuda's observation, sintering at 140°, melting at 147–148°, resolidifying at 157°, and finally melting at 212–123° to a brown oil. After drying in a vacuum at 110°, our preparation melted sharply at 212–213°. The analytical data applying to this crystalline base, its methiodide, and its salts proved it to be represented by formula $C_{26}H_{43}NO_3$, instead of formula $C_{18}H_{28}NO_2$ assigned to peiminine by Chou.

Furthermore, the formula of the first crystalline alkaloid, *peimine*, was further substantiated by the results of analysis of its hydriodide, its nitrate and the methyl chloride addition compound of peimine and the platinic chloride salt.

Experimental Part

Peiminine hydrochloride was separated from peimine hydrochloride by fractional crystallization in an alcohol–ether mixture, as described in our previous communication, peiminine hydrochloride being the more soluble. The peiminine was then liberated from its hydrochloride by means of sodium carbonate and separated in colorless needles from a mixture of alcohol and petroleum ether. These needles sintered at 140°, melted at 147–148°, resolidified at 157° and finally melted at 212–213° to a brown oil. A specific rotation determination gave the value $[\alpha]^{13}_{D}$ $-65.8°$.

Peimine Hydriodide.—One hundred milligrams of peimine was neutralized with a dilute hydriodic acid. On concentration in a vacuum desiccator, the hydriodide separated in long needles. It was recrystallized from a mixture of alcohol and ether, and melted at 282–283°. It was dried for analysis over phosphorus pentoxide at 80° in a vacuum.

Anal. Calcd. for $C_{26}H_{43}NO_3{\cdot}HI$: C, 57.22; H, 8.13. Found: C, 57.72, 57.49; H, 81.4, 7.95.

Peimine Nitrate.—One hundred milligrams of peimine was neutralized with dilute nitric acid. This was concentrated in a vacuum desiccator, whereupon the nitrate separated in long needles, m. p. 265–267°. It was recrystallized from a mixture of alcohol and ether and melted at 268–269°. It was dried for analysis over phosphorus pentoxide at 80° in a vacuum.

Anal. Calcd. for $C_{26}H_{43}NO_3{\cdot}HNO_3$: C, 64.95; H, 9.19, N, 5.83. Found: C, 65.08; H, 8.95; N, 5.66.

Peimine Methiodide.—Two-tenths gram of peimine, dissolved in a small volume of acetone, was treated with 0.3 cc. of methyl iodide. The mixture was then allowed to stand for twenty-four hours. The acetone solution was evaporated to dryness on a water-bath, leaving behind a yellow residue which solidified on cooling. This residue was

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[2] The authors wish to express their thanks to Mr. Yao-tseng Huang for his assistance in making the micro-analyses recorded in this paper.

[3] Chi, Kao and Chang, THIS JOURNAL, **58**, 1306 (1936).

[4] Chou and Chen, *Chinese J. Physiol.*, **6**, 265 (1932).

[5] Fukuda, *Science Repts., Tôhoku Imp. Univ.*, (Japan 1), **18**, 323 (1929); *Chem. Zentr.*, **1**, 88 (1930).

readily soluble in water, ethyl and methyl alcohol; difficultly soluble in cold acetone; but insoluble in chloroform and ether. In order to prove the above material to be a methiodide of formula $C_{66}H_{43}NO_3 \cdot CH_3I$, it was transformed into the addition compound of *peimine methochloride* with platinic chloride, $(C_{26}H_{43}NO_3 \cdot CH_3Cl)_2 \cdot PtCl_4$, as follows.

The above solid residue was repeatedly washed with ether to remove any organic impurities and dissolved in 2 cc. of water, and the solution filtered. The filtrate was then treated with freshly prepared silver chloride and heated in a boiling water-bath for one hour. After the mixture of silver chloride and bromide was filtered off, 2% aqueous H_2PtCl_6 was added to the filtrate, whereupon the orange platinum salt separated at once. It was dissolved in dilute hydrochloric acid, from which the pure salt finally separated after concentration of the solution in a vacuum desiccator. This salt softened at 230° and melted at 240° with decomposition.

Anal. Calcd. for $(C_{26}H_{43}NO_3 \cdot CH_3Cl)_2 \cdot PtCl_4$: Pt, 15.34. Found: Pt, 15.45, 14.96.

Amorphous Alkaloids.—The chloroform extract (described in our previous communication),[3] after removing the solvent, weighed 45 g., which represented about 0.042% of the total quantity of the crude drug. Various methods have been tried to obtain some crystalline alkaloid or its crystalline salts from this fraction, but all attempts have thus far been unsuccessful.

Summary

Peiminine has finally been obtained in a very pure condition and showed the following properties: it sintered at 140°, melted at 147–148°, solidified at 157°, and remelted at 212–213° to a brown oil. Its specific rotation is $[\alpha]^{13}_{\text{D}}$ −65.8°. Its formula is $C_{26}H_{43}NO_3$ instead of $C_{18}H_{28}NO_2$, which was assigned to it by Chou. The present formula is substantiated by the results of analysis of the methiodide and several of its salts, namely, the hydrochloride, hydrobromide, hydriodide, acid sulfate, nitrate and platinichloride.

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[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

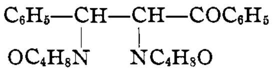
α,β-Unsaturated Aminoketones. II. α- and β-Morpholinobenzalacetophenones*

BY NORMAN H. CROMWELL

In the first paper of this series[1] two known reactions were extended to the preparation of α- and β-N-diethylamino-α,β-unsaturated ketones. One of these, the reaction of amines with 1,2-dibromoketones, has been studied extensively by Dufraisse, *et al.*[2] These workers studied the action of piperidine on several 1,2-dibromoketones, and with the corresponding α-bromo-α,β-unsaturated ketones.

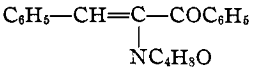
Since the results obtained using diethylamine in the first paper in this series[1] were somewhat different from those experienced by Dufraisse, it seemed important to reinvestigate these reactions using morpholine in place of piperidine.

The rapid reaction of benzalacetophenone dibromide with morpholine has been found to give mostly α,β-dimorpholinobenzalacetophenone I, with small amounts of α-morpholinobenzalacetophenone II.



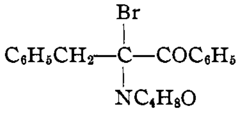
$$C_6H_5-\underset{OC_4H_8N}{CH}-\underset{NC_4H_8O}{CH}-COC_6H_5$$

I



$$C_6H_5-CH=\underset{NC_4H_8O}{C}-COC_6H_5$$

II



$$C_6H_5CH_2-\underset{NC_4H_8O}{\overset{Br}{C}}-COC_6H_5$$

III

When α-bromobenzalacetophenone was treated with morpholine in the cold, the intermediate, α-bromo-α-morpholinobenzylacetophenone, III, was obtained. This compound III was found to give a slow reaction with morpholine, resulting in the formation of approximately equal amounts of I and II. However, when III was treated with a stronger base, sodium ethoxide, a 96% yield of II was obtained. It was not possible to convert II into I by heating II with an excess of morpholine, although this might have been expected in view of the work of Pollard,[3] in which it was shown that morpholine adds quite readily to benzalacetophenone.

The structure of I seems evident since hydrolysis gave a 70% yield of ω-morpholinoacetophenone, which has been prepared recently by Rubin,[4] and of benzaldehyde. Only traces of benzylphenyl diketone were noted. Reactions (1) and (2) seem to be likely ways to account for these results.

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* Presented before the Division of Organic Chemistry, American Chemical Society, Detroit, Mich., September 12, 1940.

(1) Cromwell, THIS JOURNAL, **62**, 1672 (1940).

(2) Dufraisse and Moureu, *Bull. soc. chim.*, (4^e) **41**, 457, 850, 1370 (1927); Dufraisse and Netter, *ibid.*, (4^e) **51**, 550 (1932).

(3) Stewart and Pollard, THIS JOURNAL, **59**, 2702 (1937).

(4) Rubin and Day, *J. Org. Chem.*, **5**, 54 (1940).