The relation between conarrhimine, \( \text{C}_{21}\text{H}_{31}\cdot\text{NH} \cdot \text{OH} \) and holarrhimine, \( \text{C}_{21}\text{H}_{31}\cdot\text{NH} \cdot \text{H}_{3}\), suggested in the earlier communication\(^1\) made it desirable to extend the studies in holarrhimine beyond the position arrived at in Part IV, wherein tetra N.methyl holarrhimine and its benzyol and acetyl derivatives were characterised, and the action of nitrous acid on holarrhimine was qualitatively observed to yield a nitrogen-free, oily product. The present paper gives the results of studies in methylation, benzyolation and acetylation of holarrhimine.

On treatment of holarrhime with 4 mols of benzoyl chloride, di- and tri- benzyol derivatives were formed, and with large excess of acetic anhydride and sodium acetate a tri-acetyl derivative was obtained. With 2 mols of methyl iodide, holarrhimine dimethyl iodide was obtained which, however, unexpectedly yielded monomethyl holarrhimine on treatment with caustic soda or silver hydroxide, probably as a result of splitting of one molecule of methyl alcohol in the process of liberation of the base.

\[
\text{C}_{21}\text{H}_{31}\cdot\text{NH}_{2}\cdot\text{CH}_{3}I + 2\text{KOH} \rightarrow \text{C}_{21}\text{H}_{31}\cdot\text{NH}_{2} + 2\text{KI} + \text{CH}_{3}\text{OH} + \text{H}_{2}\text{O}
\]

The analysis of the non-nitrogenous product, obtained through the action of nitrous acid on holarrhimine and expected to correspond to the formula \( \text{C}_{21}\text{H}_{31}\text{O}_{3} \) gave too high carbon value for this formula. This may probably be due to its slight impurity with a product resulting from a subsequent splitting of a molecule of water. As the substance could not so far be obtained in a pure condition, its description is not included in the practical. It may,

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however, be stated here that this product as well as holarrhimine showed, like conessine, the presence of only one double bond, on titration with bromine. But in each case the brominated products gave on isolation and analysis too low bromine value due probably to a subsequent partial splitting of one HBr, as has been noted in the case of conessine.²

It was intended to study holarrhimine more closely but as one of us (R.S.) had to leave for foreign studies, these joint investigations had to be brought to an abrupt close.

2. Experimental.

Benzoylation of holarrhimine: Tri-benzoyl holarrhimine.—To a solution of holarrhimine (0.5 g. 1 mol) in 3 c.c. pyridine was added benzoyl chloride (0.85 g. 4 mols) with ice cooling and stirring and the reaction mixture was left well corked at room temperature for two hours. On dilution with water a non-basic crystalline mass separated out which was well washed with water and acetic acid to remove any unchanged base. On recrystallisation from chloroform it formed snow-white hexagonal rods m.p. 269-70° (yield, 0.85 g.). It is soluble in ethyl acetate, alcohol, chloroform and insoluble in ether and petroleum ether (Found: C, 78.45, 78.20; H, 7.60, 7.64; N, 4.57; C₁₁H₁₃ON₂ (CO.C₆H₅)₃ requires C, 78.26; H, 7.45; N, 4.35 per cent.).

Di-benzoyl holarrhimine.—The mother liquor from tri-benzoyl holarrhimine gave on removal of the solvent the dibenzoyl product as a semi crystalline white powder (0.10 g.) which was easily soluble in ether, petroleum ether and other organic solvents and frothed up at 115° (Found: C, 77.74; H, 7.77; N, 4.64; C₁₁H₁₃ON₂ (CO.C₆H₅)₂ requires C, 77.77; H, 8.14; N, 5.14 per cent.).

Acetylation of holarrhimine: Tri-acetyl holarrhimine.—An intimate mixture of holarrhimine (0.5 g.), anhydrous sodium acetate (2 g.) and acetic anhydride (2 c.c.) was heated on the water-bath for two hours. On dilution and further heating on the water-bath a non-basic mass was obtained, which crystallised out of alcohol and ethyl acetate in clusters of spindle-shaped needles melting at 240-41°. On recrystallisation from methyl alcohol and acetone it formed snow-white spindle-shaped needles melting at 249-50° (yield, 0.75 g.). It is soluble in benzene, chloroform, acetone, alcohol, and insoluble in ethyl acetate, ether and petroleum ether. On dehydration at 100° in vacuo over P₂O₅ it lost 3.7 per cent. water of crystallisation. C₁₁H₁₃ON₂ (CO.C₆H₅)₃ + H₂O requires H₂O, 3.1 per cent. (Found: C, 69.87, 69.90; H, 9.34, 9.20; N, 6.00; C₁₁H₁₃ON₂ (CO.C₆H₅)₃ requires C, 70.74; H, 9.17; N, 6.30 per cent.).

² Arch. Pharm., 1918, 256, 57.
Bromination of holarrhimine: Di-bromo holarrhimine.—0·2 g. holarrhimine dissolved in dry chloroform was titrated against bromine in dry chloroform solution with ice cooling, when it took up 0·10 g. bromine (calculated for one double bond 0·10 g.). The titration was followed by means of potassium iodide starch paper. After titration the bromo compound was completely precipitated by adding ether to the mixture. Well washed with ether it melted at 290-95°. On liberation with caustic soda from its acetic acid solution, the bromo base melted at 226-28° (decomp.). It was soluble in alcohol and water and insoluble in chloroform, acetone, ethyl acetate, ether and petroleum ether (Found: C, 51·99; H, 7·98; N, 5·43; Br, 28·32; C_{21}H_{36}ON_{2}Br_{2} requires C, 51·20; H, 7·33; N, 5·69; Br, 32·5 per cent.).

Methylation of holarrhimine with methyl iodide: Di-methyl holarrhimine hydroiodide.—To a solution of holarrhimine (1 g.) in dry chloroform was added a chloroformic solution of methyl iodide (1 g. 2·3 mols) and the reaction mixture kept overnight at room temperature when a crystalline product separated out, m.p. 276°. On recrystallisation out of alcohol it melted at 278°. It was soluble in warm alcohol and water, insoluble in acetone, ethyl acetate and chloroform (Found: C, 44·84; H, 7·13; N, 4·54; CH_{3}, 5·93; C_{21}H_{38}ON_{2}(CH_{3})_{2} requires C, 44·80; H, 6·82; N, 4·55; CH_{3} for 2 N—CH_{3}, 4·87 per cent.).

Methyl holarrhimine.—The aqueous solution of the hydroiodide gave on liberation with ammonia or caustic soda a very small quantity of a white precipitate which after crystallisation from methyl alcohol and ether formed snow-white needles melting at 170° (Found after dehydration at 100° in vacuo: C, 74·92; H, 10·82; N, 8·33; C_{22}H_{38}ON_{2} requires C, 76·30; H, 9·98; N, 8·09; per cent.). A more quantitative yield was obtained on liberation of the base with freshly precipitated silver hydroxide. The base, thereby obtained, also melted at 169-70° and gave no depression with the base liberated with caustic soda. It showed the presence of only one N—CH_{3} after Herzig and Meyer (Found: CH_{3}, 3·91; C_{22}H_{38}ON_{2} requires for 1 N—CH_{3}, CH_{3}, 4·32 per cent.). (Found in air dried substance: C, 71·9; H, 10·7; N, 7·1; C_{22}H_{38}ON_{2}+H_{2}O requires C, 72·5; H, 11·0; N, 7·7; after dehydrating at 100°: C, 75·0, 75·1; H, 11·0, 11·2; N, 7·8, 7·8; C_{22}H_{38}ON_{2} requires C, 76·3; H, 11·0; N, 8·1 per cent.). The dehydration at 100° was apparently not complete.

—hydrochloride was obtained by adding ethereal hydrochloric acid to a solution of the base in methyl alcohol and acetone as a white semi-crystalline powder which melted at 266° (decomp.) and was soluble in alcohol and water (Found: Cl, 16·16; C_{22}H_{38}ON_{2}.2HCl requires Cl, 16·95 per cent.).
—*chloroplatinate* was obtained as a golden yellow powder, when a 10 per cent. solution of platinic chloride was added to an aqueous solution of the hydrochloride. It was soluble in alcohol and water and melted at 245° with blackening and decomposition (Found: Pt, 25.6; \((\text{C}_{25}\text{H}_{35}\text{O}_4\text{N}_2\cdot2\text{HCl})\) PtCl₄ requires Pt, 25.8 per cent.).

—*picrate* was prepared by adding ethereal picric acid to a solution of the base in methyl alcohol and acetone. It crystallises out of alcohol and water in tufts of lemon-yellow needles, sparingly soluble in hot water, fairly soluble in alcohol and melting at 205°.