

but undoubtedly in proportions quite different from thiolacetic acid. These should be interesting in comparison with the data in Table II and it is our hope to consider them in a later communication.

### Summary

The products of the reaction of thiolacetic acid with a number of alcohols have been studied quantitatively. Isopropyl alcohol yields only hydrogen sulfide and the normal ester; triphenylcarbinol only water and the thiol ester; methyl and ethyl alcohol give about 78% hydrogen sulfide and 22% water. The question of the mechanism of esterification in general is considered and an explanation of certain anomalies is attempted.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF KITASATO INSTITUTE]

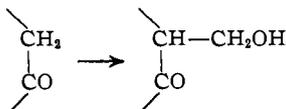
## CONDENSATIONS BETWEEN FORMALDEHYDE AND MONOKETONES. I. CONDENSATION OF 5-ACETYL-8-HYDROXYQUINOLINE WITH ALDEHYDES

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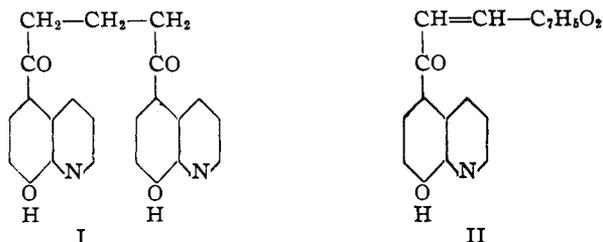
Many researches relating to the condensation between a methyl or methylene group adjacent to a ketone and aromatic or cyclic aldehyde have been published, whereas, as far as the authors are aware, except in the case of the pyrazolone series, there are only a few previous records of condensation with formaldehyde. K. Goto and his co-workers,<sup>1</sup> in the course of investigations of sinomenine, an alkaloid from *sinomenium acutum*, have found that on refluxing sinomenine, which contains a methylene group adjacent to a carbonyl in its molecule, with an excess of formaldehyde a condensation between them results in the formation of an hydroxy-methyl compound in accordance with the scheme



In the present investigation, on treating 5-acetyl-8-hydroxyquinoline with formaldehyde (40%) in a manner similar to that used for sinomenine, it is found that a condensation has taken place between them, but contrary to expectation, resulting in the formation of  $\omega$ -methylene-bis-5-acetyl-8-hydroxyquinoline (I).

Furthermore, the reaction of 5-acetyl-8-benzoyloxyquinoline and formaline gives  $\omega$ -methylene-bis-5-acetyl-8-benzoyloxyquinoline. It is evident in view of the latter fact that the presence of a free hydroxyl

<sup>1</sup> Goto, Shishido and Inaba, *Bull. Chem. Soc., Japan*, 5, 315 (1930).



group in the molecule would not have any necessary part in the condensation. On the other hand, on treating acetophenone with formaldehyde in the same way or even in the presence of pyridine, acetophenone can be recovered without any notable loss (the identification is confirmed by the melting point and mixed melting point test of its oxime (m. p. 160–161.5°)). This last failure makes it seem likely that the presence of an amino group in the molecule may serve to facilitate the condensation in any way. A search of the literature reveals that the reaction of salicylaldehyde with acetophenone<sup>2</sup> gives chiefly salicylidene-diacetophenone, while under similar conditions, with indanone,<sup>3</sup> it gives salicylidene-indanone. The reaction of 5-acetyl-8-hydroxyquinoline and piperonal, in the present work, is found to afford  $\omega$ -piperonylidene-5-acetyl-8-hydroxyquinoline (II), following the course of the latter kind of condensation.

### Experimental

**$\alpha$ -Methylene-bis-5-acetyl-8-hydroxyquinoline.**—A mixture of 0.5 g. of 5-acetyl-8-hydroxyquinoline and 2.5 cc. of formaldehyde (40%), which contains an appreciable amount of a precipitate of paraformaldehyde, is refluxed for two hours. The resulting white precipitate is filtered, on cooling, and washed; yield, 0.5 g. It is recrystallized from nitrobenzene into colorless columns, m. p. >315°. It is sparingly soluble in boiling benzene and alcohol. Its alcoholic solution gives a green coloration with ferric chloride.

*Anal.* Subs., 5.325 mg.: CO<sub>2</sub>, 13.942; H<sub>2</sub>O, 2.014. Subs., 4.200: CO<sub>2</sub>, 11.019; H<sub>2</sub>O, 1.893. Subs., 5.554: N<sub>2</sub>, 0.368 cc. (28°, 753.5 mm.). Calcd. for C<sub>23</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub>: C, 71.50; H, 4.66; N, 7.25. Found: C, 71.41, 71.55; H, 4.20, 5.01; N, 7.17.

The hydrochloride gives yellow needles from hydrochloric acid (10%). It is insoluble in water and does not melt at 300°, decolorizing at 170–220°.

*Anal.* (Water of crystallization). Subs., 0.0830: H<sub>2</sub>O, 0.0168. Calcd. for C<sub>23</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub>·HCl·6 H<sub>2</sub>O: H<sub>2</sub>O, 20.36. Found: H<sub>2</sub>O, 20.24. Subs., 4.640: AgCl, 1.553. Calcd. for C<sub>23</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub>·HCl: Cl, 8.40. Found: Cl, 8.28.

The monoxime gives colorless prisms from nitrobenzene, m. p. 295–300° (decomp.).

*Anal.* Subs., 3.777: N<sub>2</sub>, 0.327 cc. (13.5°, 768 mm.). Calcd. for C<sub>23</sub>H<sub>18</sub>O<sub>4</sub>N<sub>3</sub>: N, 10.47. Found: N, 10.29.

**$\omega$ -Methylene-bis-5-acetyl-8-acetoxyquinoline.**—A mixture of 0.2 g. of  $\omega$ -methylene-bis-5-acetyl-8-hydroxyquinoline, 8 g. of acetic anhydride and 0.5 g. of sodium acetate is

<sup>2</sup> Cornelson and Kostanecki, *Ber.*, **29**, 242 (1896).

<sup>3</sup> Feuerstein, *ibid.*, **34**, 413 (1901).

warmed for two and one-half hours on the water-bath. On pouring into crushed ice, after being cooled, the reaction product separates as oily drops which soon turn to a colorless solid (0.2 g.). It crystallized from ethyl acetate into colorless prisms, m. p. 234–235°. It is easily soluble in chloroform, hot alcohol (with a partial hydrolysis), and moderately in hot benzene, but sparingly in ether.

*Anal.* Subs., 4.783: CO<sub>2</sub>, 12.130; H<sub>2</sub>O, 2.075. Subs., 3.842: N<sub>2</sub>, 0.218 cc. (31°, 760 mm.). Calcd. for C<sub>27</sub>H<sub>22</sub>O<sub>4</sub>N<sub>2</sub>: C, 68.94; H, 4.68; N, 5.96. Found: C, 69.16; H, 4.82; N, 6.10.

**5-Acetyl-8-benzoyloxyquinoline** gives colorless columns from hot alcohol, m. p. 168°. It is easily soluble in benzene and chloroform but sparingly in ether.

*Anal.* Subs., 5.037: N<sub>2</sub>, 0.212 cc. (15°, 767.5 mm.). Calcd. for C<sub>18</sub>H<sub>13</sub>O<sub>3</sub>N: N, 4.81. Found: N, 4.95.

**ω-Methylene-bis-5-acetyl-8-benzoyloxyquinoline.**—A mixture of 0.6 g. of 5-acetyl-8-benzoyloxyquinoline, 7 cc. of formaldehyde and some alcohol is refluxed for fourteen hours. On cooling, the separated solid (0.3 g.) is filtered and recrystallized from nitrobenzene. It gives colorless prisms, m. p. >315°.

*Anal.* Subs., 6.738: N<sub>2</sub>, 0.282 cc. (15°, 772 mm.). Calcd. for C<sub>37</sub>H<sub>26</sub>O<sub>6</sub>N<sub>2</sub>: N, 4.71. Found: N, 4.95.

**ω-Piperonylidene-5-acetyl-8-hydroxyquinoline.**—A solution of 0.4 g. of sodium hydroxide in the same quantity of water is added to the warm solution of 0.19 g. of 5-acetyl-8-hydroxyquinoline and 0.15 g. of piperonal in 2 g. of alcohol with stirring. The resulting yellow paste, after standing for twenty-four hours with some water added, is acidified with dilute hydrochloric acid, and then an excess of sodium acetate is added. The resulting yellow precipitate is filtered and washed; yield, 0.3 g. It crystallizes from alcohol into yellow needles, m. p. 178–179°.

It is soluble in alcohol, benzene and ether, but insoluble in dilute mineral acid and alkali. The alcoholic solution gives a green color reaction with ferric chloride and the solution in concd. sulfuric acid assumes a purple-red color but decolorizes on addition of water.

*Anal.* Subs., 3.284: CO<sub>2</sub>, 8.600; H<sub>2</sub>O, 1.291. Subs., 5.475, 6.115: N<sub>2</sub>, 0.214 cc. (30.5°, 762 mm.), 0.233 cc. (25.5°, 760 mm.). Calcd. for C<sub>19</sub>H<sub>16</sub>O<sub>4</sub>N: C, 71.47; H, 4.08; N, 4.39. Found: C, 71.42; H, 4.37; N, 4.07, 4.21.

The writers, hereby, desire to express their hearty thanks to Professor Hata for the interest which he has kindly taken in this work and to Professor Kakuji Goto for the suggestion at which this work was done.

### Summary

1. Condensation of 5-acetyl-8-hydroxyquinoline with formaldehyde gives ω-methylene-bis-5-acetyl-8-hydroxyquinoline.

2. Condensation of 5-acetyl-8-hydroxyquinoline with piperonal gives ω-piperonylidene-5-acetyl-8-hydroxyquinoline.

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