Acetylformoin. I. Its Preparation.

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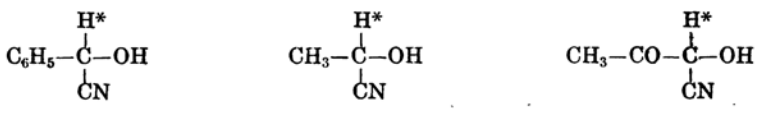
Benzoylformoin[1] has long been known, but acetylformoin (a provisional formula $CH_3COCHOHCOCOCH_3$) has not previously been reported. It may be anticipated to be an interesting substance not only from the point of view of its structure, but also of sugar chemistry, being a possible dehydration product of the hexoses. In the present work, the preparation was effected by applying the principle of benzoin condensation to methylglyoxal.

From the condensation product of methylglyoxal in the presence of potassium cyanide, a yellow crystalline substance was isolated by means

(1) H. G. Söderbaum, *Ber.* **24** (1891), 1386, 3033.
P. H. Abenius and H. G. Söderbaum, *Ber.*, **25** (1892), 3470.
W. Abenius, *Ber.*, **27** (1894), 706.
P. Karrer and A. v. Segesser, *Helv. Chim. Acta*, **18** (1935), 273.
P. Karrer and C. Musande, *Helv. Chim. Acta*, **18** (1935), 1140.
P. Karrer and F. Litwant, *Helv. Chim. Acta*, **19** (1936), 829.
A. H. Blatt, *J. Am. Chem. Soc.*, **57** (1935), 1103; **58** (1936), 1894.

of vacuum distillation. On recrystallization from cold benzene, it formed pale yellow needles and melted at 81–82°. This substance has a molecular formula $C_6H_8O_4$ and may be either acyloin or aldol of methylglyoxal. Under similar experimental conditions, however, it was not formed by the action of hydroxyl ion alone—a proper catalyst for aldolization, indicating that the simultaneous presence of cyanide ion is essential for its formation. It was also observed that its hebaviour towards various oxidizing agents—Fehling's solution, ferric chloride and potassium permanganate, was quite similar to that of benzoylformoin. From these evidence, it may be concluded that it has a structure analogous to benzoylformoin and may properly be called acetylformoin.

By the action of aqueous alkali cyanide, aliphatic aldehydes, in general, give aldols, but no acyloin. The success in synthesizing acetylformoin seems at first sight to be somewhat surprising. In the previous articles,[2] however, we showed that it may be an essential condition for benzoin condensation that the hydrogen atom H* of a well accepted



(I) (II) (III)

intermediate—benzaldehyde cyanhydrine (I) is sufficiently acidic. The failure in the acyloin condensation of aliphatic aldehyde may, therefore, be attributed to a lack of acidity of the typical hydrogen in the intermediate, e.g., (II) being CH_3 a group far inferior to the C_6H_5 group in acidifying effect. On the other hand, the hydrogen atom of methylglyoxal cyanhydrine (III) would be sufficiently acidic, taking into consideration a powerful electromeric effect—an acidifying effect—of the CH_3-CO group. Methylglyoxal should therefore condense to acetylformoin, as it did in the actual case.

It should be noted that the aqueous solution of acetylformoin was fermented by Fleischmann's yeast, leaving the solution laevo-rotatory.

Experimental Part. *Methylglyoxal.* This was prepared from acetone by oxydation with selenium dioxide[3]. 850 c.c. of pure acetone was refluxed with 250 g. selenium dioxide for about 3 hours during which the liquid gradually became clear. After cooling the reaction liquid, the selenium powder deposited was filtered off and the filtrate distilled on a boiling water bath. The distillation residue was again distilled under reduced pressure and the fraction b.p. 39–41°/15 mm. was taken as methylglyoxal (yield 40 g.).

Acetylformoin. A methylglyoxal solution (40 g. in 200 c.c. water) and a potassium cyanide (3.1 g. mol ratio to methylglyoxal 0.083) solution were both cooled in ice water and then mixed. The mixture was made

(2) R. Nodzu and co-workers, *J. Chem. Soc. Japan*, **58** (1937), 313; **59** (1938), 1237.
(3) H. L. Riley, *J. Chem. Soc.*, **1932**, 1875.
J. Hahn and O. Schales, *Ber.*, **67** (1934), 1821.
T. Bersin, *Ber.*, **69** (1936), 560.

just alkaline (pH = 7.3) by addition of solid sodium bicarbonate, and kept for 30 minutes in ice water. After acidifying with syrupy phosphoric acid, it was evaporated under reduced pressure until inorganic salt began to crystallize out and then absolute alcohol (ca. 150 c.c.) was added. The deposited inorganic crystals were filtered off and the filtrate was evaporated to a syrup under reduced pressure. To the syrup, ether (ca. 350 c.c.) was added and the solution was filtered. The filtrate was dehydrated with anhydrous sodium sulphate and the ether driven away. The yellow syrupy residue was now subjected to a vacuum (5 mm.) distillation. At first an oily substance (ca. 4 g., b.p. 35–50°) distilled and as the thermometer rose from 60° to 70°, yellow crystals appeared in the condenser and on cold parts of the distilling flask. The crystals were gathered, and found to amount to about 4.5 g. They were recrystallized from cold benzene in fine pale yellow needles (m.p. 82.° Found: C, 50.1; H, 5.6; M, (in acetic acid) 142. Cal. for $CH_3COCHOHCOCOCH_3$: C, 50.0; H, 5.6%; M, 144.)

So far as studied under various conditions—of temperature, times and pH,—the reaction conditions described above were the best.

It was very auto-oxidizable, quickly darkened and liquefied in the course of 2 hours, when exposed to the air. It reduced Fehling's solution in the cold, and on addition of ferric chloride solution gave a greenish blue coloration which instantaneously faded when the solution was shaken.

Oxidation of acetylformoin. A solution of acetylformoin (0.12 g.) in 5% sulphuric acid (25 c.c.) was warmed on a boiling water bath, adding drop by drop 3% solution of potassium permanganate until no more decoloration of the oxidant took place. 8 c.c. of the permanganate solution was used. The reaction product was distilled, keeping its volume constant by the addition of water and the distillate was received in N/10 sodium hydroxide solution (25 c.c.). The distillation was continued until the distillate no longer reddened methylorange. On titration, it was found that it contained acid amounting to 0.0945 g. as acetic acid which corresponds to about 95% of the value calculated by the following equation

$$CH_3CO\cdot CHOH\cdot CO\cdot CO\cdot CH_3 \xrightarrow{+4O} 2\,CH_3COOH + 2\,CO_2$$

The amount of permanganate solution used was almost equal to what the theory requires (7.3 c.c.). From another experiment with 0.554 g. acetylformoin similar results were obtained, i.e., 34 c.c. (theoretically 33 c.c.) of the potassium permanganate solution was consumed and 0.425 g. acetic acid (92% of the theoretical) was formed. The distillates gave acetotoluidide (m.p. 147°).

Benzoylformoin (1 g.) was similarly oxidized (35 c.c. of 3% potassium permanganate solution) and benzoic acid (0.81 g.) was obtained with a yield of 96% of the theoretical value.

Action of potassium carbonate upon methylglyoxal. A solution of methylglyoxal (30–50 g. in 200 c.c. water) was made alkaline (pH 7.4–9.0) by potassium carbonate and kept for various intervals (0.5–15 hours) at 0–2°. After acidifying the reaction product with phosphoric acid, it was evaporated and extracted with ether. The ether extract was

evaporated and the residue was then distilled under reduced pressure without any sign of the appearance of acetylformoin. With ferric chloride the distillate (36–60°/3–5 mm.) did not show the characteristic greenish blue coloration of acetylformoin but rather a persistent red.

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