On the Ring-opening Reactions of the Furan Compounds. III. On the Condensation of Furfural with Methyl Ethyl Ketone by Alkali

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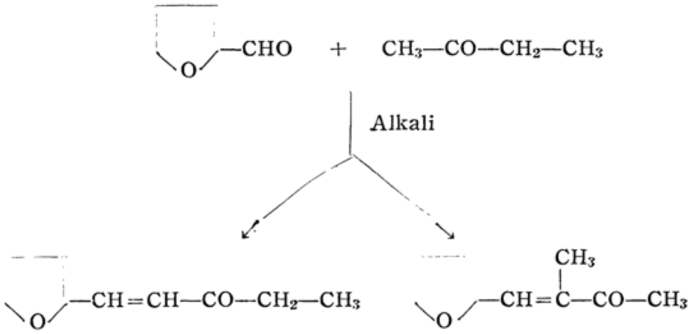
In the case of condensation of furfural with methyl ethyl ketone by alkali, there are two possibilities, as illustrated in the accompanying equation:



1-(2-furyl)-1-penten-3-one

(I)

4-(2-furyl)-3-methyl-3-buten-2-one

(II)

Kashiwagi[1] and the other[2] indicated that the condensation product was II. But they gave no satisfactory confirmation of its structure.

On the other hand, Hunsdiecker[3] and the others[5] reported that the condensation product which they assumed to be I afforded γ, ζ-dioxopelargonic acid by ring-opening in alcoholic hydrochloric acid. The work done to date seems to be not yet clear.

In the present experiment, the condensation was carried out at reaction temperatures 0° and 60°.

At reaction temperature 0°, furfural underwent principally the aldol condensation with methyl ethyl ketone. The resulting aldol was easily dehydrated with acetic anhydride or dilute hydrochloric acid to yield the unsatu-

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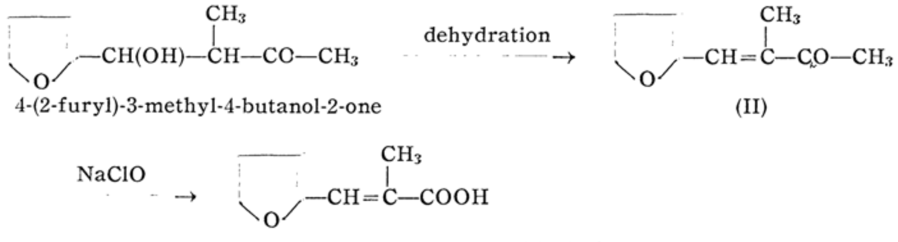
[1] I. Kashiwagi: This Bulletin, **2**, 310 (1927).

[2] D. M. Al'vin Gutzatz: *C. A.*, **30**, 3591 (1936).

[3] H. Hunsdiecker: *Ber.*, **75B**, 447 (1942).

ated ketone, which gave a semicarbazone of foliated crystals melting at 212~4°. This unsaturated ketone was smoothly oxidised to α-methyl-2-furanacrylic acid III by sodium hypochlorite. It is undoubted, therefore, that this unsaturated ketone is II and the reaction sequence is shown as follows:



4-(2-furyl)-3-methyl-4-butanol-2-one

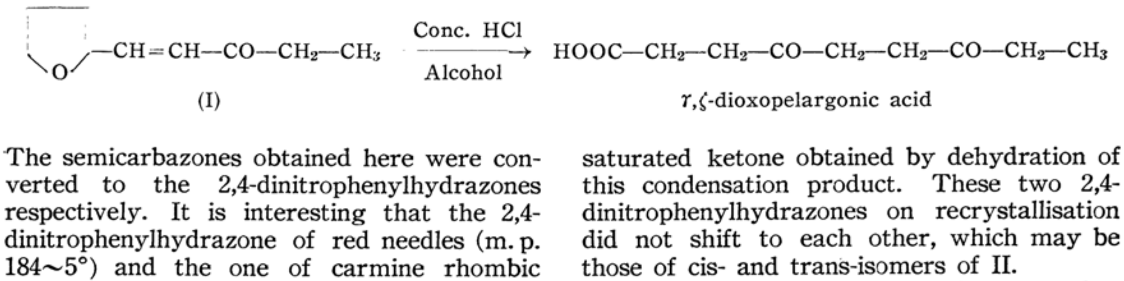
(II)

α-methyl-2-furanacrylic acid (III)

From the condensation product at reaction temperature 60° was obtained a mixture of two semicarbazones, which consisted of a larger part of needles melting at 182~4° and a smaller part of foliated crystals melting at 212~4°. The latter was identical with the semicarbazone of II. This condensation product, on sodium hypochlorite oxidation, afforded III in a very poor yield. It seems certain that the semicarbazone of needles melting at 182~4° is that of I. Furthermore, this condensation product, on ring-opening in alcoholic hydrochloric acid, gave a dioxocarboxylic acid in a fairly good yield.

On the other hand, the condensation product at reaction temperature 0°, after dehydration with acetic anhydride, gave the same dioxocarboxylic acid by ring-opening in alcoholic hydrochloric acid as the condensation product at reaction temperature 60°, but its yield was very poor.

From these results, it may be inferred that the dioxocarboxylic acid was γ,ζ-dioxopelargonic acid arising from the ring-opening of I as illustrated below, and the condensation product at reaction temperature 0° contained a small amount of I accompanying 1-(2-furyl)-1-pentanol-3-one, and II failed to give a dioxocarboxylic acid by ring-opening in alcoholic hydrochloric acid.



(I)

γ,ζ-dioxopelargonic acid

The semicarbazones obtained here were converted to the 2,4-dinitrophenylhydrazones respectively. It is interesting that the 2,4-dinitrophenylhydrazone of red needles (m.p. 184~5°) and the one of carmine rhombic plates (m.p. 212~3°) were detected to be those of II. The former was obtained directly from the condensation product at reaction temperature 0°, and the latter from the unsaturated ketone obtained by dehydration of this condensation product. These two 2,4-dinitrophenylhydrazones on recrystallisation did not shift to each other, which may be those of cis- and trans-isomers of II.

The semicarbazones of I and II, together with their 2,4-dinitrophenylhydrazones, are shown in the accompanying table.

	Semicarbazone	2,4-dinitrophenyl-hydrazone
1-(2-furyl)-1-penten-3-one	colourless needles, m.p. 182~4°	red needles m.p. 205~6°
4-(2-furyl)-3-methyl-3-buten-2-one	colourless leaflets, m.p. 212~4°	carmine rhombic plates, m.p. 212~3°
		red needles, m.p. 184~5°

Detection of the 2,4-dinitrophenylhydrazones obtained from the condensation product at reaction temperature 25° indicated the presence of I, II and 4-(2-furyl)-3-methyl-4-butanol-2-one.

Experimental

Condensation at 60∼5°.—A solution of furfural (12 g.) and methyl ethyl ketone (24 g.) in water (200 cc.) was mechanically stirred at 60∼5° and 5% aqueous caustic soda (20 cc.) was at once run in. After stirring for 1.5 hrs., the reaction mixture was neutralised with dil. sulfuric acid, the oily layer separated, and the aqueous solution extracted twice with benzene. The separated oil and the benzene extract were combined. The benzene solution was dried over calcium chloride and the benzene removed. From the remaining oil was collected a fraction (10 g.) distilling at 128∼9°/22 mm.

	H	C
Anal. Calcd. for $C_9H_{10}O_2$:	6.71%	71.96%
Found:	6.72%	71.31%

This fraction gave a mixture of two semicarbazones which consisted of a larger part of needle crystals (m.p. 182∼4°) and a smaller part of foliated crystals (m.p. 212∼4°). The former was more soluble in methanol than the latter.

The needles (this was considered to be 1-(2-furyl)-1-penten-3-one semicarbazone)

	H	C	N
Anal. Calcd. for $C_{10}H_{13}O_2N_3$:	6.32%	57.94%	20.28%
Found:	6.27%	57.90%	20.08%

The foliated crystals (4-(2-furyl)-3-methyl-3-buten-2-one semicarbazone)

	H	C	N
Anal. Calcd. for $C_{10}H_{13}O_2N_3$:	6.32%	57.94%	20.28%
Found:	6.42%	58.12%	19.85%

The semicarbazone of needle crystals was converted to a 2,4-dinitrophenylhydrazone of carmine needle crystals (m.p. 205∼6°).

	H	C	N
Anal. Calcd. for $C_{15}H_{14}O_5N_4$:	4.27%	54.53%	16.96%
Found:	4.05%	54.43%	17.09%

The semicarbazone of foliated crystals was converted to a 2,4-dinitrophenylhydrazone of carmine rhombic crystals (m.p. 212∼3°).

	H	C	N
Anal. Calcd. for $C_{15}H_{14}O_5N_4$:	4.27%	54.53%	16.96%
Found:	4.10%	54.84%	17.14%

Aldol Condensation at 0∼3°.—Into a stirred solution of furfural (15 g.) and methyl ethyl ketone (20 g.) in water (350 cc.) was at once introduced 10% aqueous caustic soda (10 cc.) at 0∼3°, after stirring for 4.5 hrs. at 0∼3°, the reaction mixture was neutralised with dil. sulfuric acid, the oily layer was separated and the aqueous solution extracted twice with ether. The separated oil and the ether extract were combined. Fractionation of the ether solution, after drying over calcium chloride for a brief time, gave a pale yellow oil (10 g.), b.p. 117∼8°/10mm., which was considered to chiefly contain 4-(2-furyl)-3-methyl-4-butanol-2-one.

	H	C
Anal. Calcd. for $C_9H_{12}O_3$:	7.19%	64.24%
Found:	6.79%	65.13%

This fraction afforded a 2,4-dinitrophenylhydrazone of unsaturated ketone $C_9H_{10}O_2$, which was recrystallised from pyridine-methanol; microscopic carmine needles; m.p. 184∼5°. This was considered to be the 2,4-dinitrophenylhydrazone of 4-(2-furyl)-3-methyl-3-buten-2-one.

	H	C	N
Anal. Calcd. for $C_{15}H_{14}O_5N_4$:	4.27%	54.53%	16.96%
Found:	4.14%	55.03%	16.93%

Dehydration of Aldol.—The foregoing aldol (6 g.) was gently refluxed with acetic anhydride (6 g.) for 3 hrs. Fractionation of the reaction mixture gave a yellow oil (4 g.), b.p. 124∼5°/20 mm.

	H	C
Anal. Calcd. for $C_9H_{10}O_2$:	6.71%	71.96%
Found:	6.43%	71.00%

This fraction gave the semicarbazone of foliated crystals (m.p. 212∼4°) and the 2,4-dinitrophenylhydrazone of rhombic crystals (212∼3°).

The aldol was also dehydrated by heating with 5% hydrochloric acid on the water-bath for a short time, giving the same semicarbazone and 2,4-dinitrophenylhydrazone.

Oxidation by Sodium Hypochlorite.—Anhydrous sodium carbonate (7 g.) and bleaching powder (10 g.) were mixed in water (30 cc.) After a brief time, the resulting calcium carbonate was filtered off, the filtrate was diluted to 40 cc. with water and 1 g. caustic soda was added.

The oil (1 g.) obtained by the dehydration of the aldol was suspended in the sodium hypochlorite solution (8 cc.) prepared above and the vessel was kept for two days in water at room temperature, with occasional shaking. Then, the reaction mixture was acidified with dil. hydrochloric acid to yield α-methyl-2-furanacrylic acid (0.35 g.) It was recrystallised from hot water; colourless needles; m.p. 116∼7°; lit.[4] m.p. 116°.

	H	C
Anal. Calcd. for $C_8H_8O_3$:	5.29%	63.13%
Found:	5.34%	63.15%

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[4] I. Kashiwagi: This Bulletin, **2**, 318 (1927).

The condensation product at reaction temperature 60∼5° gave a trace of α-methyl-2-furanacrylic acid under the same conditions.

Ring-opening in Alcoholic Hydrochloric Acid.—The condensation product (2 g.) at reaction temperature 60∼5° was refluxed with alcohol (4 cc.) and conc. hydrochloric acid (1.5 cc.) on the water-bath for 3 hrs. The reaction mixture, after addition of water, was evaporated to dryness on the water-bath. The residue was extracted with a sufficient quantity of boiling water; the extract, after decoloursing with active charcoal, was evaporated up. The dioxocarboxylic acid which was considered to be γ,ζ-dioxopelargonic acid was obtained as a crystalline mass (0.35 g.) on cooling and recrystallised twice from ligroin; colourless hexagonal plates; m.p. 83∼4; lit.[5] m.p. 84∼5°.

	H	C
Anal. Calcd. for $C_9H_{14}O_4$:	7.58%	58.03%
Found:	7.55%	57.54%

The dehydration product from the aldol gave a very small amount of colourless tabular crystals by the same procedure; m.p. 83∼4°. The mixed melting point of the specimen with the foregoing dioxocarboxylic acid showed no depression.

Condensation at Ordinary Temperature (25°).—A mixture of furfural (10 g.), methyl ethyl ketone (20 g.), 10% aqueous caustic soda (10 cc.) and water (250 cc.) was stirred for 5 hrs. at about 25°. By the same procedure as described above, a pale yellow oil (8 g.) distilling at 131∼5°/22 mm. was obtained, which gave a mixture of the three species of 2,4-dinitrophenylhydrazone mentioned above. These 2,4-dinitrophenylhydrazones were separable from the mixture by virtue of their pyridine solubility. The 2,4-dinitrophenylhydrazone of m.p. 212∼3° was the least soluble and that of m.p. 185∼6° was the most soluble.

Summary

It seems that furfural can react with methyl ethyl ketone in two ways by alkali.

In the condensation at 0∼3°, the main product was 4-(2-furyl)-3-methyl-4-butanol-2-one. This aldol was easily dehydrated to 4-(2-furyl)-3-methyl-3-buten-2-one, which was oxidised to α-methyl-2-furanacrylic acid by sodium hypochlorite.

In the condensation at 60∼3°, the main product was the furfurylidene ketone, which gave the semicabazone melting at 182∼4° and the dioxocarboxylic acid by ring opening in alcoholic hydrochloric acid. It is presumed that this ketone is 1-(2-furyl)-1-penten-3-one, and the dioxocarboxylic acid resulting from it is γ,ζ-dioxopelargonic acid.

It is also interesting that two species of 2,4-dinitrophenylhydrazone were obtained with respect to 4-(2-furyl)-3-methyl-3-buten-2-one.

The author wishes to thank Messrs. K. Furuhashi and K. Muto for micro-analyses.

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[5] F. L. Breusch and E. Ulusoy: *C. A.*, **42**, 5850 (1948).