The Condensations of Furfural with Methyl Isobutyl Ketone and Phenylacetone by Aqueous Sodium Hydroxide

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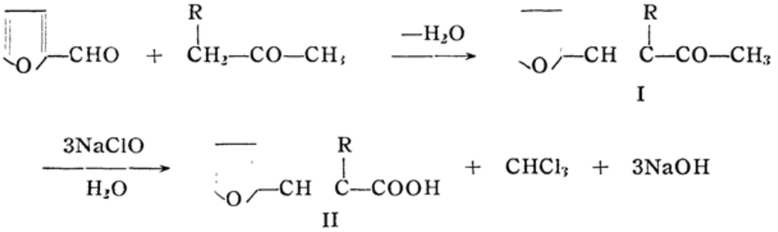
In the previous reports$^{1)}$ were represented the following facts: At the lowered reaction temperature 0–5°, methyl ethyl ketone tends to condense with furfural or benzaldehyde by alkali at its α-methylene group, and methyl propyl ketone, though slightly, has such a tendency in the condensation with furfural by alkali. At the elevated reaction temperature 60–65°, methyl ethyl ketone, as well as methyl propyl ketone, condenses with furfural chiefly at their α-methyl groups. In the condensation with benzaldehyde at the elevated reaction temperature 60–65°, methyl ethyl ketone reacts exclusively at its α-methyl group.

The present work consists in studying whether methyl isobutyl ketone and phenylacetone, on the condensation with furfural by aqueous sodium hydroxide, react at their α-methylene groups or not. In the reaction of furfural with methyl isobutyl ketone by alkali, there are few reports$^{2,3,4)}$. But those appear to have no such consideration.

When the condensation of furfural with the ketone CH_3—CO—CH_2—R takes place at its α-methylene group, the resulting furfurylidene ketone (I) must be oxidised by sodium hypochlorite to α-R-2-furanacrylic acid (II), as in all cases so far examined$^{1)}$. The reaction is represented in the following formulae.



On the condensation of furfural with methyl isobutyl ketone by aqueous sodium hydroxide, both condensation products at the lowered and at the elevated reaction temperatures gave only one species (m.p. 177–178°) of semicarbazone, which was considered to be identical with the semicarbazone (m.p. 175–176°) of the condensation product obtained by Wienhaus and Leonhardi$^{3)}$. On suspension of these condensation products in sodium hypochlorite solution for 2 days with occasional shaking, no α-isopropyl-2-furanacrylic acid and no smell of chloroform were detected. Consequently, it seemed certain that the condensation products were composed of 1-(2-furyl)-5-methyl-1-hexen-3-one (III) resulting from the condensation of furfural at the α-methyl group of methyl isobutyl ketone irrespective of the reaction temperatures, as illustrated below.

This semicarbazone (m.p. 177–178°) was converted into two species of 2,4-dinitrophenylhydrazone. One was reddish-orange, flattened needles (m.p. 196–197°) and the other red, long needles (m.p. 144–145°). These two forms also were directly obtained from both the condensation products at the lowered and elevated reaction temperatures. Furthermore, it was of interest that the red, long needles shifted readily to the reddish-orange needles in dilute alcoholic sulfuric acid. Probably, these two forms of 2,4-dinitrophenylhydrazone may be the syn- and antiisomers as two *o*-tolyhydrazones of N-phenacyl-*p*-anisidine.$^{5)}$

Refluxion of the condensation product at the reaction temperature 60–65° with alcoholic hydrochloric acid and subsequent hydrolysis gave a dioxocarboxylic acid (m.p. 79–80°) in a good yield, which was considered to be γ,ζ-dioxo-ϑ-methylcapric acid (IV), as reported by Breusch and Ulusoy$^{4)}$. The reaction sequence is illustrated in the accompanying formulae.

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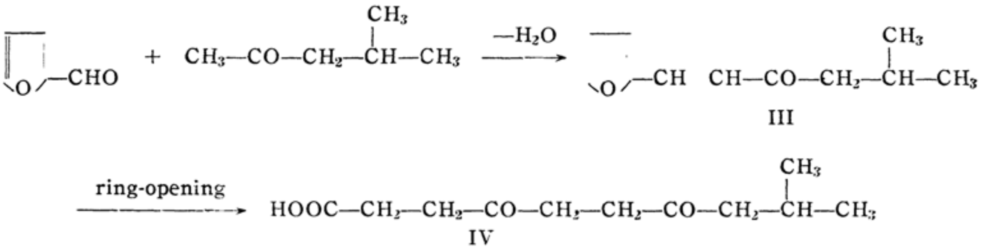
1) H. Midorikawa, This Bulletin, **26**, 460 (1953); **27**, 131 (1954), **27**, 143 (1954); **27**, 149 (1954).

2) J. T. Thurston, *C. A.*, **39**, 5023 (1945); H. Wachs and O. F. Hedenburg, *J. Am. Chem. Soc.*, **70**, 2695 (1948).

3) H. Wienhaus and H. Leonhardi, *C. A.*, **24**, 2127 (1930).

4) F. L. Breusch and E. Ulusoy, *C. A.*, **42**, 5850 (1948).

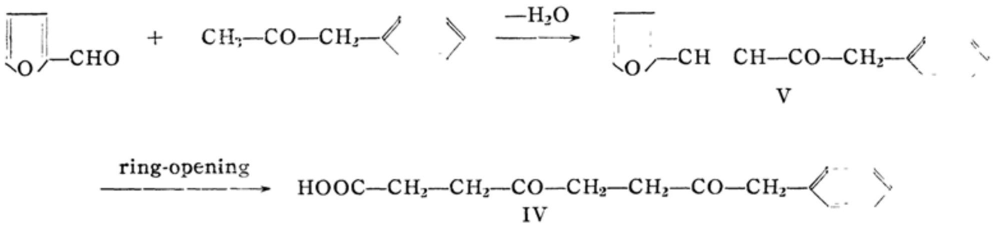
5) M. Busch, G. Friedenberger and W. Tischbein, *Ber.*, **56**, 999 (1926).



Phenylacetone was also condensed with furfural at the lowered and elevated reaction temperatures, 5° and 60–70°. Neither of the condensation products at the lowered and elevated reaction temperatures, on sodium hypochlorite oxidation, gave any α-phenyl-2-furanacrylic acid nor any smell of chloroform. It seemed certain that the condensation of phenylacetone with furfural gave 4-(2-furyl)-1-phenyl-3-buten-2-one (V), reacting at the α-methyl group of the ketone irrespective of the reaction temperatures, as illustrated below.

On the other hand, both condensation products at the lowered and elevated reaction temperatures gave two species of semicarbazone, colourless prisms (m.p. 210–212°) and colourless prisms (m.p. 163-164°), which were converted respectively into 2,4-dinitrophenylhydrazones of red, flattened needles (m.p. 183–184°) and reddish-orange leaflets (m.p. 178–179°). The condensation product at the elevated reaction temperature gave these two semicarbazones in equal proportions, and the condensation product at the lowered reaction temperature gave the semicarbazone of prisms (m.p. 210–212°) chiefly.

Moreover, both condensation products at the lowered and elevated temperatures afforded a dioxocarboxylic acid in nearly equal yields on the ring-opening in alcoholic hydrochloric acid, which was considered to be γ,ζ-dioxo-η-phenylcaprylic acid (VI). From these results, it may be supposed that the compound (V) obtained here consists of the cis- and trans-isomers. The reaction sequence is illustrated by the following formulation.



Ultimately, methyl isobutyl ketone and phenylacetone appeared difficult to condense with furfural at their α-methylene groups, in contrast with methyl ethyl ketone and methyl propyl ketone. This fact may perhaps be attributed to the presence of the bulky group adjacent to the α-methylene group of these ketones, such as isopropyl and phenyl groups.

Experimental

Condensation of Methyl Isobutyl Ketone with Furfural Into a stirred suspension of furfural (15 g.) and methyl isobutyl ketone (30 g.) in water (200 cc.) was at once introduced 5% aqueous sodium hydroxide (10 cc.) at 60°, with stirring. After prolonged stirring for 2 hrs. at 60–65°, the reaction mixture was neutralised with dilute hydrochloric acid and the oily layer separated. The aqueous solution was extracted twice with ether and the ether extract combined with the oil. Fractionation of the ether solution gave a yellow oil (12.7 g.) distilling at 124–126°/6 mm., which was considered to consist of 1-(2-furyl)-5-methyl-1-hexen-3-one (III), $C_{11}H_{14}O_2$. (Found: C, 73.84; H, 7.61%; Calcd. for $C_{11}H_{14}O_2$: C, 74.11; H, 7.96%).

This fraction gave a semicarbazone crystallising from methanol-water as colourless needles, (m.p. 177–178°; lit[3]., m. p. 175∼176°.) (Found: C, 61.09; H, 6.94; N, 17.65%; Calcd. for $C_{12}H_{17}O_2N_3$; C, 61.24; H, 7.29; N, 17.86%).

This fraction gave nearly equal amounts of two 2,4-dinitrophenylhydrazones, reddish-orange, flattened needles (m.p. 196–197°) and red, long needles (m.p. 145–146°). The former 2,4-dinitrophenylhydrazone was comparatively sparingly soluble in pyridine and the latter fairly soluble in pyridine. Those isomers were separated by the solubility difference. Needles (m.p. 196–197°) (Found: C, 57.09; H, 4.79; N, 15.22%; Calcd. for $C_{17}H_{18}O_5N_4$: C, 56.96; H, 5.07; N, 15.63%). Needles (m.p. 145–146°) (Found: C, 57.12; H, 4.74; N, 15.50%; Calcd. for $C_{17}H_{18}O_5N_4$: C, 56.96; H, 5.07; N, 15.63%).

The latter needles (m.p. 145–146°) were readily transformed into the former (m.p. 196–197°), being suspended in hot dilute methanolic sulfuric acid for a short time.

The semicarbazone (m.p. 177–178°) was also converted into a mixture of these two 2,4-dinitrophenylhydrazones, reacting with 2,4-dinitrophenylhydrazine in alcoholic sulfuric acid.

The condensation of furfural with methyl isobutyl ketone at the reaction temperature 0–5° was carried out by stirring a mixture of furfural (15 g.), methyl isobutyl ketone (30 g.), water (250 cc.) and 10% aqueous sodium hydroxide (30 cc.) for 6 hrs. The reaction mixture was worked up in the same manner as in the case of the foregoing condensation, and a fraction (20 g.) distilling at 121–124°/5 mm. was collected. This fraction also gave the same semicarbazone and 2,4-dinitrophenylhydrazones as in the case of the condensation at the reaction temperature 60–65°.

Both condensation products at the reaction temperatures, 60–65° and 0–5° were suspended in the sodium hypochlorite solution[6], but no heat was generated and no α-isopropyl-2-furanacrylic acid detected.

Condensation of Furfural with Phenylacetone Furfural (15 g.) and phenylacetone (30 g.) were suspended in water (200 cc.), and 5% aqueous sodium hydroxide was at once run in at about 60° with stirring. After prolonged stirring for 5.5 hrs. at 60–70°, the reaction mixture was worked up in the same manner as in the foregoing condensation, and a fraction (22 g.) distilling at 172–177°/5 mm. was obtained, which was considered to be 4-(2-furyl)-1-phenyl-3-buten-2-one (V), $C_{14}H_{12}O_2$. (Found: C, 78.71; H, 5.69%; Calcd. for $C_{14}H_{12}O_5$: C, 79.28; H, 5.71%).

This fraction afforded nearly equal amounts of two semicarbazones, colourless prisms (m.p. 163–164°) fairly soluble in methanol and colourless needles(m.p. 210–212°)sparingly soluble in methanol. These isomers were separated by the solubility difference. Prisms (m.p. 163–164°)(Found: C, 66.48; H, 5.50; N, 15.45%; Calcd. for $C_{15}H_{15}O_2N_3$: C, 66.88; H, 5.62; N, 15.61%). Needles (m.p. 210–212°) (Found: C, 66.68; H, 5.61; N, 15.43%; Calcd. for $C_{15}H_{15}O_2N_3$: C, 66.88; H, 5.62; N, 15.61%).

The former semicarbazone was converted to a 2,4-dinitrophenylhydrazone crystallising from pyridine as reddish-orange, lustrous leaflets (m.p. 178–179°), and the latter semicarbazone to a 2,4-dinitrophenylhydrazone crystallising from pyridine as red, flattened needles (m.p. 183–184°). Orange leaflets (m.p. 178–179°) (Found: C, 60.90; H, 4.04; N, 13.94%; Calcd. for $C_{20}H_{16}O_5N_4$: C, 61.20; H, 4.12; N, 14.28%). Red, flattened needles (m.p. 183–184°) (Found: C, 60.88; H, 4.03; N. 14.17%; Calcd. for $C_{20}H_{16}O_5N_4$: C, 61.20; H, 4.12; N, 14.28%).

Furfural (15 g.) and phenylacetone (30 g.) were suspended in a mixture of alcohol (50 cc.) and water (250 cc.), whereupon 10% aqueous sodium hydroxide was run in at about 5° with stirring. After prolonged stirring for 6.5 hrs. at 5°, the reaction mixture was worked up as described above, and a fraction (8 g.) distilling 170–178°/5 mm. obtained. This fraction gave the red flattened needles (m.p. 183–184°) mainly.

Both condensation products at the reaction temperatures 60–70° and 5° were suspended in the sodium hypochlorite[6], but no heat was generated and no α-phenyl-2-furanacrylic acid detected.

Ring-opening The condensation product (III) (2 g.) of furfural with methyl isobutyl ketone at the reaction temperature 60–65° was refluxed with conc. hydrochloric acid (1.5 cc.) and alcohol (5 cc.) on the water-bath for 3 hrs. The reaction mixture, after addition of an equal volume of dilute hydrochloric acid, was evaporated to dryness on the water-bath. The residue was extracted with a sufficient quantity of water, and the extract evaporated on the water-bath to give an oily matter which on cooling formed a crystalline mass (1 g.). It was recrystallised from ligroin as colourless leaflets, m.p. 79–80°. This specimen was considered to be γ,ζ-dioxo-ϑ-methylcapric acid (IV)[4], $C_{11}H_{18}O_4$. (Found: C, 61.57; H, 8.23%; Calcd. for $C_{11}H_{18}O_4$: C, 61.64; H, 8.47%).

The condensation product (V) (2 g.) of furfural with phenylacetone at the reaction temperature 60–70° was refluxed with conc. hydrochloric acid (1.5 cc.) and alcohol (5 cc.) for 3 hrs. The reaction mixture, after being worked up as described above, gave a crystalline mass (0.3 g.), which was recrystallised from ligroin-ethyl acetate as colourless rhombic plates, m.p. 88–89°.

By the same procedure, the condensation product (V) (2 g.) of furfural with phenylacetone at the reaction temperature 0–5° yielded the same crystals (0.3 g.). This specimen was considered to be γ,ζ-dioxo-η-phenylcaprylic acid (VI), $C_{14}H_{16}O_4$. (Found: C, 67.37; H, 6.62%; Calcd. for $C_{14}H_{16}O_6$: C, 67.71; H, 6.49%).

Summary

Methyl isobutyl ketone and phenylacetone, unlike methyl ethyl ketone[1], condensed with furfural by sodium hydroxide at their α-methyl groups irrespective of the reaction temperature, giving 1-(2-furyl)-5-mthyl-1-hexen-3-one (III) and 4-(2-furyl)-1-phenyl-3-buten-2-one (V) respectively.

1-(2-Furyl)-5-methyl-1-hexen-3-one (III) gave the two forms of 2,4-dinitrophenylhydrazone. One (m.p. 145–146°) shifted readily to the other (m.p. 196–197°) in dilute alcoholic sulfuric acid, and those may be the syn- and anti-isomers.

4-(2-Furyl)-1-phenyl-3-buten-2-one (V) obtained here gave the two species of semicarbazone which were converted into the respective two species of 2,4-dinitrophenylhydrazone. It may perhaps be composed of the cis- and trans-isomers. This furfurylidene ketone gave γ,ζ-dioxo-η-phenylcaprylic acid (VI) by the ring-opening in alcoholic hydrochloric acid.

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[6] H. Midorikawa, This Bulletin, **26**, 462 (1953).