The Condensation of Benzaldehyde with Methyl Ethyl Ketone by Aqueous Sodium Hydroxide

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Harries and Müller[1] demonstrated that, when aqueous sodium hydroxide was employed as the condensing agent, benzaldehyde condensed with methyl ethyl ketone at the α-methyl group of the ketone at ordinary temperature, forming 1-phenyl-1-penten-3-one, and, when hydrogen chloride was employed as the condensing agent, benzaldehyde reacted with methyl ethyl ketone at its α-methylene group, giving 3-methyl-4-phenyl-3-buten-2-one.

In the preceding report[2], it was indicated that furfural condensed with methyl ethyl ketone chiefly by aqueuos sodium hydroxide at its methylene group at the lowered reaction temperature 0~5°, giving the chief product 4-(2-furyl)-3-methyl-4-butanol-2-one, whereas furfural condensed with the ketone chiefly at its α-methyl group at the elevated reaction temperature 60~65°, giving 1-(2-furyl)-1-penten-3-one.

In the present experiment, the condensation of benzaldehyde with methyl ethyl ketone by aqueous sodium hydroxide at lowered and elevated reaction temperatures was studied in order to compare it with the result of furfural in the preceding report[2].

At the elevated reaction temperature 60~65°, the condensation of benzaldehyde with methyl ethyl ketone gave only 1-phenyl-1-penten-3-one (I) as illustrated below, since this condensation product afforded an oxime melting at 86~87° which was identical with that of 1-phenyl-1-penten-3-one obtained by Harries and Müller.[1] The semicarbazone of this ketone melted at 181~182°.

At the lowered reaction temperature 3~5°, benzaldehyde and methyl ethyl ketone underwent aldol condensation by sodium hydroxide, giving a mixture of 3-methyl-4-phenyl-4-butanol-2-one (II) and 1-phenyl-1-pentanol-3-one (III), as illustrated below. The mixture of these condensation products gave no semicarbazone, but, after the dehydration with acetic anhydride, gave a mixture of a semicarbazone melting at 218~219° in a larger proportion and the semicarbazone (m.p. 181~182°) of 1-phenyl-1-penten-3-one in a smaller proportion. The semicarbazone melting at 218~219° was identified with that of 3-methyl-4-phenyl-3-buten-2-one obtained by condensing benzaldehyde with methyl ethyl ketone by hydrogen chloride. Consequently, it was confirmed that the condensation products at the reaction temperature 3~5° were a larger amount of 3-methyl-4-phenyl-4-butanol-2-one (II) and a smaller amount of 1-phenyl-1-pentanol-3-one (III), and, on the dehydration with acetic anhydride, gave the corresponding unsaturated ketones, 3-methyl-4-phenyl-3-buten-2-one (IV) and 1-phenyl-1-penten-3-one (I).

Furthermore, 3-methyl-4-phenyl-3-buten-2-one was oxidized by sodium hypochlorite to α-methylcinnamic acid (V), while 1-phenyl-1-penten-3-one (I) was not acted upon by this oxidizing agent.

The overall reactions are illustrated by the following formulation.

3-Methyl-4-phenyl-3-buten-2-one (IV) and 1-phenyl-1-penten-3-one (I) obtained here gave respective 2,4-dinitrophenylhydrazones. It was of interest that the mixture of the aldol condensation products at the reaction temperature 3~5°, on the reaction with 2,4-dinitrophenylhydrazine in methanolic sulfuric acid, gave the 2,4-dinitrophenylhydrazones of 1-phenyl-1-penten-3-one (I) and benzaldehyde, but no 2,4-dinitrophenylhydrazone of 3-methyl-4-phenyl-3-buten-2-one (IV). This result appeared to indicate that, under such a reaction condition, 1-phenyl-1-pentanol-3-one (III) gave 2,4-dinitrophenylhydrazone of 1-phenyl-1-penten-3-one (I) with simultaneous dehydration, and 3-methyl-4-phenyl-4-butanol-2-one (II) initially dissociated to methyl ethyl ketone and benzaldehyde, which subsequently gave its 2,4-dinitrophenylhydrazone.

Experimental

Condensation at Reaction Temperature 3~5° Into a stirred suspension of benzaldehyde (20 g.) and methyl ethyl ketone (40 g.) in water (300 cc.) was at once introduced 10% aqueous sodium hydroxide (15 cc.) at 3°. The reaction was complete after prolonged stirring for 6 hrs. at 3~5°. The reaction mixture was neutralized with dilute sulfuric acid, the oily layer separated and the aqueous solution extracted twice with ether. The oily layer and the ether extract were combined and dried over anhydrous sodium sul-

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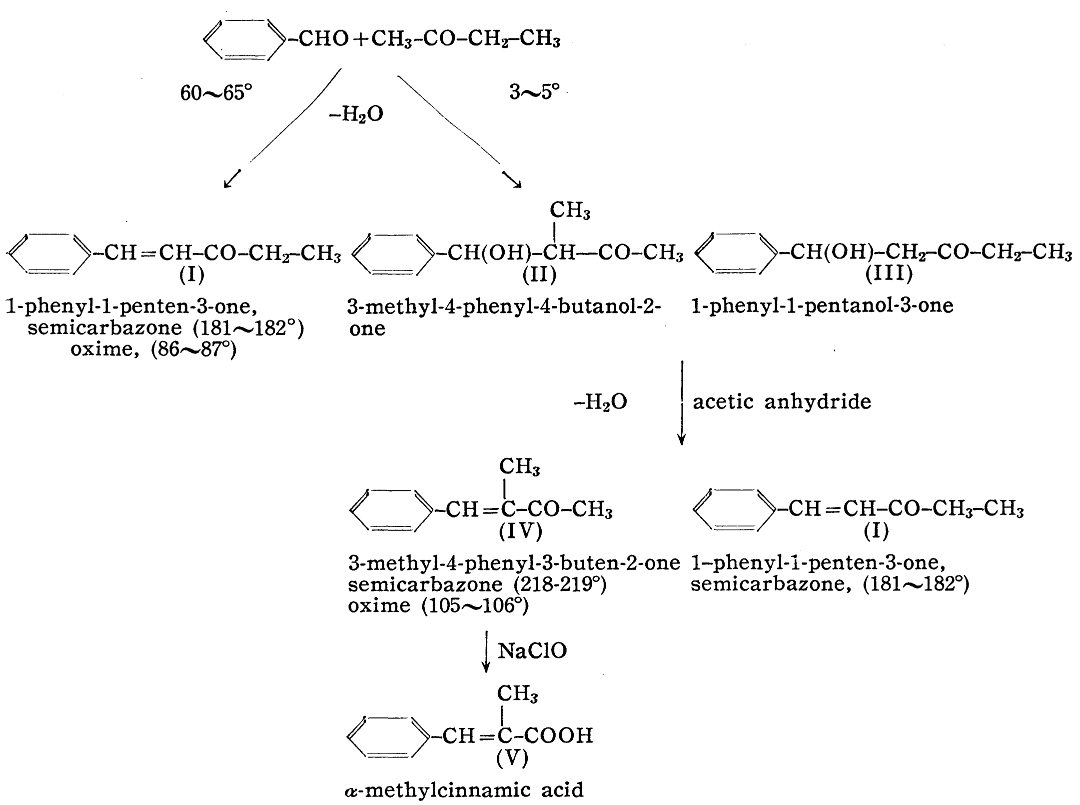
[1] C. Harries and G. H. Müller, *Ber.*, **35**, 966 (1902).

[2] H. Midorikawa, This Bulletin, **26**, 460 (1953).



fate. Fractionation of the ethereal solution gave a pale yellow liquid (25 g.), b.p. 122~129°/6 mm. This fraction was considered to consist of 3-methyl-4-phenyl-4-butanol-2-one (II) in a larger proportion and 1-phenyl-1-pentanol-3-one (III) in a smaller proportion. Calcd. for $C_{11}H_{14}O_2$: C, 74.11 H, 7.92; Found: C, 72.22, H, 7.67%.

This analysis appeared to show that this fraction contains a small quantity of the dehydrated ketones $C_{11}H_{12}O$, but the fraction gave no semicarbazone. From this fraction were obtained two 2,4-dinitrophenylhydrazones in equal proportions, which were readily separable from each other by the difference of the solubility in nitrobenzene. The more soluble one crystallised in red needles, m.p. 212~213°, undepressed on admixture with 2,4-dinitrophenylhydrazone of 1-phenyl-1-penten-3-one (I) as indicated below. The less soluble one formed orange prisms melting at 235~236°, undepressed on admixture with benzaldehyde 2,4-dinitrophenylhydrazone.

Dehydration of the Condensation Product at the Reaction Temperature 3~5C° The foregoing aldol condensation product (5 g.) at the reaction temperature 3~5° was refluxed with acetic anhydride (15 g.) for 16 hrs. Fractionation of the reaction mixture gave a pale yellow oil (4 g.), b.p. 112~114°/6 mm.

This oil (0.5 g.) was suspended in an aqueous semicarbazide-sodium acetate solution, and methanol added until a clear solution was obtained. The solution, after heating on the water-bath for a short time and standing for 3 hrs., gave colourless crystals (0.4 g.), which was recrystallised from methanol as plates, m.p. 218~219°, undepressed on admixture with the semicarbazone of 3-methyl-4-phenyl-3-buten-2-one (IV) indicated below. The filtrate on standing overnight gave colourless crystals (0.1 g.), which were recrystallised twice from methanol in needles, m.p. 181~182°. This specimen was identical with the semicarbazone of 1-phenyl-1-penten-3-one (I).

The oil (1 g.), above mentioned was suspended in an aqueous sodium hypochlorite solution[2] (8 cc.) at ordinary temperature with occasional shaking for 2 days. The reaction mixture was freed of oily matter by extraction with ether, and acidified with dilute hydrochloric acid to yield crystals (0.3 g.) on cooling, which were recrystallised from water as colourless prisms, m.p. 77~78°. This specimen was identified with α-methylcinnamic acid (V); lit[3]., m.p. 78°. Calcd. for $C_{10}H_{10}O_2$: C, 74.04, H, 6.22%; Found: C, 73.96, H, 6.11%.

Cndensation at the Reaction Temperature 60~65° Into a stirred suspension of benzaldehyde (15 g.) and methyl ethyl ketone (30 g.) in water (200 cc.) was at once introduced 10% aqueous sodium hydroxide (7 cc.) at about 60°. After prolonged stirring for 3 hrs. at 60~65°, the reaction was over. The reaction mixture was worked up as described above. Fractionation of the ether solution, after drying over calcium chloride, gave a pale yellow oil (19 g.), b.p. 117~118°/6 mm., which solidified at ordinary temperature. This fraction was composed of 1-phenyl-1-penten-3-one (I). Calcd. for $C_{11}H_{12}O$: C, 82.45 H, 7.55%; Found:

C, 82.29 H, 7.70%.

This fraction gave the oxime melting at 86~87°, which was identical with the oxime (m.p. 85~86°) of 1-phenyl-1-penten-3-one (I) obtained by Harries and Müller1). Its semicarbazone formed colourless needle crystals melting at 181~182° (lit4)., m.p. 173°), and its 2,4-dinitrophenylhydrazone, carmine rhombic crystals, melting at 212~213° on crystallisation from pyridine. Calcd. for $C_{17}H_{16}O_4N_4$: C, 59.97, H, 4.74, N, 16.46 %; Found: C, 59.78, H, 4.59, N, 16.50 %.

3-Methyl-4-phenyl-3-buten-2-one (IV) was synthesised from benzaldehyde and methyl ethyl ketone by the use of hydrogen chloride as the condensing agent, as reported by Harries and Müller1). This ketone gave the oxime melting at 105~106° (lit1)., m.p. 103~104°), the semicarbazone melting at 218~219° (lit4., m.p. 204°) and a 2,4-dinitrophenylhydrazone, red needles, melting at 199~200°. Calcd. for $C_{17}H_{16}O_4N_4$: C, 59.97, H, 4.74, N, 16.46%; Found: C, 59.52, H, 4.56, N, 16.51%.

Summary

In the condensation of benzaldehyde with methyl ethyl ketone by aqueous sodium hydroxide, the lowered reaction temperature (3~5°) favored the aldol condensation at the α-methylene group of the ketone as in the condensation of furfural with the ketone2). On the other hand, the elevated reaction temperature (60~65°) conducted exclusively the condensation at the α-methyl group of the ketone, giving 1-phenyl-1-penten-3-one (I).

3-Methyl-4-phenyl-4-butanol-2-one (II), obtained by the aldol condensation at the lowered reaction temperature (3~5°), was dehydrated with acetic anhydride to 3-methyl-4-phenyl-3-buten-2-one (IV), which was oxidized by sodium hypochlorite to afford α-methylcinnamic acid (V).

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3) R. Stoermer and R. Wehlu: *Ber.*, 35, 3552 (1902).

4) C. V. Gheroghiu and B. Arwentiew: *Bull. Soc. Chim.*, 47, 195 (1930).