399. *Formaldehyde Condensations with Aliphatic Ketones. Part I.*

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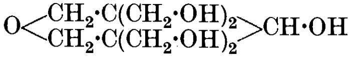
The present investigation was undertaken in order to elucidate the chemical changes involved in the formation of resins from formaldehyde condensations with acetone or its homologues. In general, one molecular proportion of acetone, methyl ethyl or diethyl ketone was heated with two molecular proportions of formaldehyde, present as 40% formalin solution, and 2*N*-sodium hydroxide added in varying amounts according to the ketone employed. With acetone, 0·5 molecular percentage of alkali was sufficient to initiate a vigorous reaction, and 3% produced a yellowish-brown viscous oil insoluble in water. The reaction with methyl ethyl ketone was induced by 2% of the alkali, whereas 10% precipitated a yellow viscous oil. Diethyl ketone needs 6% of alkali for initial condensation and even with 20% there is no sign of resin formation. An exact comparison is, however, not possible, since the alkaline catalyst undergoes partial or even complete neutralisation during these condensations.

A vigorous reaction between formaldehyde and acetone was first recorded by E. Werner (P., 1904, **20**, 196), who obtained a red, infusible and amorphous material. Müller (*Ber.*, 1921, **54**, 1142), using similar conditions, isolated a paler product. Reference should be made to early researches by Apel and Tollens (*Annalen*, 1896, **289**, 46), who prepared anhydro-enneaheptitol,

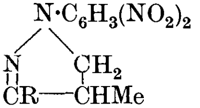


$$\mathrm{O}{<}\begin{matrix}\mathrm{CH_2\cdot C(CH_2\cdot OH)_2}\\ \mathrm{CH_2\cdot C(CH_2\cdot OH)_2}\end{matrix}{>}\mathrm{CH\cdot OH}$$

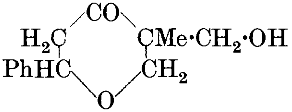
from acetone by a complex condensation, including reduction of the carbonyl group to CH(OH), wherein the six hydrogen atoms of the two methyl groups become replaced by hydroxymethyl radicals, two of which lose water so as to close the ring. The Bayer Company (D.R.-P. 223,207; B.P. 19,087/1909) isolated an intermediate compound, γ-ketobutyl alcohol, representing the first stage of formaldehyde–acetone condensation and they also produced its homologue from methyl ethyl ketone. We have now succeeded in isolating a third intermediate, produced by condensing one molecule of acetone with four of formaldehyde.

Carleton Ellis (Amer. Pats. 1502945, 1514509, and 1716542), who regarded acetone–formaldehyde condensations as potential sources of resins, used sodium carbonate, or phosphate, as catalyst, and on evaporating the resulting solution isolated a water-white viscous syrup, which we have obtained with much smaller proportions of sodium hydroxide. In his book " Synthetic Resins and their Plastics " (1923, p. 227) this investigator refers to a condensation of methyl ethyl ketone and formaldehyde, which, however, offers little promise of favourable resin formation.

By fractional distillation of the acetone condensation product we have isolated γ-ketobutyl alcohol and 3 : 3- or 3 : 5-*bishydroxymethyltetrahydro-γ-pyrone*, a liquid distillable only under reduced pressure. The non-volatile residue amounts to more than 90% of the condensation product, a proportion which is in marked contrast to that obtained in the methyl ethyl ketone condensations, which yield about 95% of volatile products, including the liquid γ-keto-β-methylbutyl alcohol and *γ-keto-β-hydroxymethyl-β-methylbutyl alcohol*, a solid, m. p. 60°.* The former yields a characteristic 1-(2′ : 4′-*dinitrophenyl*)-3 : 4-*dimethyl*-4 : 5-*dihydropyrazole* (I; R =



(I; R = Me or Et).



(II.)

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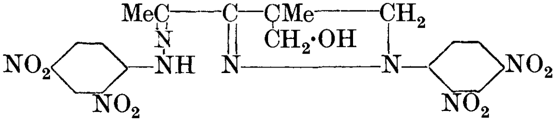
* This compound was originally mentioned by one of us (G. T. M.) in the Presidential Address to Section B (Chemistry) at the British Association Meeting in September, 1930. It has since been described in Eng. Patent 361,597 as melting at 62°.

Me) when condensed with 2 : 4-dinitrophenylhydrazine, and the latter condenses with benzaldehyde to form 6-*phenyl*-3-*hydroxymethyl*-3-*methyltetrahydro*-γ-*pyrone* (II).

With diethyl ketone condensations there is very little resin formation; the main products are volatile and include mono-, di-, and tri-hydroxymethyl derivatives, namely, γ-*keto*-β-*methyl*-n-*amyl alcohol*, γ-*keto*-β-*hydroxymethyl*-β-*methyl*-n-*amyl alcohol*, and γ-*keto*-βδ-*bishydroxymethyl*-β-*methyl*-n-*amyl alcohol*. The first two are liquids and the third is a solid, m. p. 91°. The first gives a characteristic *pyrazole* derivative (I; R = Et), whereas with the same reagent the second yields a more complex compound giving analytical data agreeing with the composition of a *hydrazone-dihydropyrazole* (III).

(III.)



In the presence of alkaline catalysts the tendency to form resinous formaldehyde–ketone condensation products diminishes considerably as the homologous series of aliphatic ketones is ascended.

EXPERIMENTAL.

I. *Acetone Condensations.*—Acetone (220 g.), aqueous formaldehyde (500 g. of 40% solution), and 20 c.c. of 2*N*-sodium hydroxide were warmed to about 40°; a reaction then ensued which kept the solution boiling for 10 minutes. On cooling, the alkali was found to be neutralised. After removal of water on the steam-bath the residual colourless viscous syrup (Ellis, *loc. cit.*) was distilled under 20—50 mm. to about 250° and yielded a small distillate; the remainder darkened and finally frothed into an insoluble, infusible, yellowish-brown resin which is still under examination. On fractionation the distillate yielded water and two colourless liquids, b. p. 100—120°/20 mm. (8 g.) and b. p. 164—165°/20 mm. (4 g.).

The former, redistilled (b. p. 90—92°/11 mm.), was identified as γ-ketobutyl alcohol (the Bayer patent gives b. p. 110—120°/30 mm.) and characterised by the following derivatives: (1) γ-ketobutyl acetate, COMe·CH$_2$·CH$_2$·O·COMe, prepared by heating the alcohol (27 g.) and acetic anhydride (35 g.) with one drop of pyridine for 4 hours at 100°, was isolated as a colourless liquid on distillation (12 g.), b. p. 125—130°/30 mm.; much resinous material was formed (Found: C, 55·4; H, 7·5. Calc. for $C_6H_{10}O_3$: C, 55·4; H, 7·7%). The Bayer Company (*loc. cit.*) mention this acetate and give b. p. 96°/15 mm., but no further details. (2) *γ-Ketobutyl acetate semicarbazone*, $COMe{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2$, separated as a solid when the acetate (2·5 g.), semicarbazide hydrochloride (2·5 g.), and 2*N*-sodium hydroxide (10 c.c.) were shaken together; it crystallised from methyl alcohol in stout colourless prisms decomposing at 207° (Found : C, 45·2; H, 7·0; N, 22·7. $C_7H_{13}O_3N_3$ requires C, 44·9; H, 7·0; N, 22·5%).

The less volatile liquid, b. p. 164—165°/20 mm., was identified as 3 : 3- or 3 : *5-bishydroxymethyltetrahydro-γ-pyrone* (Found : C, 52·6; H, 7·7. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5%) and was characterised by the following derivatives : (1) the *oxime*, isolated by extracting with benzene the residue obtained on evaporating in a vacuum a solution of molecular proportions of the pyrone, hydroxylamine, and 2*N*-sodium hydroxide, crystallised from methyl alcohol in colourless prisms, m. p. 134—135° (Found : C, 48·6; H, 7·65; N, 8·05. $C_7H_{13}O_4N$ requires C, 48·6; H, 7·4; N, 8·0%). (2) The pyrone (4 g.) by the pyridine or the Schotten-Baumann reaction yielded an equal weight of the *monobenzoate*, which crystallised from petroleum (b. p. 60—80°) in colourless needles, m. p. 107—107·5° (Found : C, 63·6, 63·9; H, 6·0, 5·9. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·05%). This and phenylhydrazine (1 mol.) in alcoholic solution slowly deposited the *phenylhydrazone*, which crystallised from alcohol in small colourless needles, m. p. 137°; it darkened slowly on exposure (Found : C, 67·9; H, 6·0; N, 7·9. $C_{20}H_{22}O_4N_2$ requires C, 67·8; H, 6·2; N, 7·9%). The 2 : *4-dinitrophenylhydrazone* of the benzoate crystallised from benzene in yellow needles, m. p. 180° (Found : N, 12·9. $C_{20}H_{20}O_8N_4$ requires N, 12·6%).

II. *Methyl Ethyl Ketone Condensations.*—When methyl ethyl ketone (108 g.), 40% aqueous formaldehyde (225 g.), and 2*N*-sodium hydroxide (25 c.c.) were warmed, a reaction ensued with generation of sufficient heat to keep the liquid boiling for some minutes. After being heated under reflux for ½ hour, the solution was cooled and treated as in the acetone condensation; the residue of non-volatile resin was only 5 g. Besides unchanged ketone (30—40 g.), three main fractions were obtained : (A) b. p. 90—110° (35 g.); (B) b. p. 138—140° (21 g.), which solidified; and (C) b. p. 160—200° (8 g.), all under 15 mm.

Fraction A, redistilled (b. p. 89—90°/11 mm. and 186—187°/760 mm.), was identified as γ-keto-β-methylbutyl alcohol (D.R.-P. 223,207 gives b. p. 90—95°/15 mm.) and was characterised by the following derivatives : the *acetate*, $COMe{\cdot}CHMe{\cdot}CH_2{\cdot}O{\cdot}COMe$, a colourless limpid liquid, b. p. 99—100°/20 mm. (Found : C, 58·1; H, 8·4. $C_7H_{12}O_3$ requires C, 58·3; H, 8·3%), and its *semicarbazone*, $COMe{\cdot}O{\cdot}CH_2{\cdot}CHMe{\cdot}CMe{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2$, stout colourless prisms,

m. p. 134·5°, from benzene (Found : C, 48·0; H, 7·6; N, 21·2. $C_8H_{15}O_3N_3$ requires C, 47·8; H, 7·5; N, 20·95%); the p-*nitrobenzoate* (prepared by the pyridine method), pale straw-coloured needles, m. p. 54°, from alcohol (Found : C, 57·4; H, 5·5; N, 5·8. $C_{12}H_{13}O_5N$ requires C, 57·4; H, 5·2; N, 5·6%); and 1-(2′ : 4′-*dinitrophenyl*)-3 : 4-*dimethyl*-4 : 5-*dihydropyrazole* (I; R = Me), prepared by heating γ-keto-β-methylbutyl alcohol (3 g.), alcohol (20 c.c.), 2 : 4-dinitrophenylhydrazine (6 g.), and concentrated hydrochloric acid (0·5 c.c.) until solution was complete. The pyrazole separated on cooling and crystallised from ethyl acetate in dark red prisms, m. p. 191° (Found : C, 49·7, 49·8; H, 4·5, 5·0; N, 21·2. $C_{11}H_{12}O_4N_4$ requires C, 50·0; H, 4·55; N, 21·2%).

Fraction B separated from chloroform–petroleum (b. p. 60—80°) in large colourless plates, m. p. 60°, b. p. 138°/16 mm. (Found : C, 54·5; H, 9·0. $C_6H_{12}O_3$ requires C, 54·5; H, 9·0%). These data agree with a compound in which the ketone (1 mol.) has condensed with formaldehyde (2 mols.), namely, γ-*keto*-β-*hydroxymethyl*-β-*methylbutyl alcohol*, $COMe{\cdot}CMe(CH_2{\cdot}OH)_2$, a substance very soluble in water, alcohol, ketones, benzene or chloroform but dissolving only slightly in light petroleum; it was characterised by the following derivatives : the *dibenzoate*,

$$COMe{\cdot}CMe(CH_2{\cdot}O{\cdot}CO{\cdot}C_6H_5)_2$$

(prepared by the pyridine and Schotten–Baumann methods), colourless needles, m. p. 78—79°, from petroleum (b. p. 60—80°) (Found : C, 70·5; H, 5·7. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%); the *di*-p-*nitrobenzoate*, very pale straw-coloured needles, m. p. 177—178°, from alcohol–acetone (Found : C, 56·4; H, 4·2; N, 6·4. $C_{20}H_{18}O_9N_2$ requires C, 55·8; H, 4·2; N, 6·5%); the *diacetate*, a colourless liquid, b. p. 140—145°/10 mm. and 166—168°/30 mm. (Found : C, 55·8; H, 7·4. $C_{10}H_{16}O_5$ requires C, 55·6; H, 7·4%), and its *semicarbazone*, stout colourless prisms, m. p. 132·5°, from benzene (Found : C, 48·4; H, 6·8; N, 15·7. $C_{11}H_{19}O_5N_3$ requires C, 48·4; H, 6·95; N, 15·4%); and 6-*phenyl*-3-*hydroxymethyl*-3-*methyltetrahydro*-γ-*pyrone* (II), which was obtained in flat colourless needles, m. p. 103°, by shaking the keto-glycol and benzaldehyde (1 mol.) with concentrated hydrochloric acid and crystallising the solid produced from petroleum (b. p. 60—80°) (Found : C, 70·8; H, 7·3. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The last compound only slowly absorbed bromine with evolution of hydrogen bromide and production of a viscous uncrystallisable oil.

Fraction C was accumulated from successive condensations and redistilled into narrower fractions consisting of brownish viscid oils which had carbon contents higher than those of simple products arising from condensations of formaldehyde and ketone in molecular proportion. Elimination of the elements of water intramolecularly would yield more volatile materials.

B. p./22 mm.	150—180°	180—200°	200—210°	210—240°
C, %	58·6	60·55	60·8	66·8
H, %	8·5	8·7	8·0	8·3

These results accord best with intermolecular condensation and the products are regarded as resin intermediates, since they are convertible into resins by heating with excess of alcoholic sodium hydroxide.

III. *Diethyl Ketone Condensations.*—Since diethyl ketone is not miscible with aqueous formaldehyde, it was necessary to add alcohol to secure a uniform reaction. Comparative experiments in alcohol with the lower ketones showed that in those cases the course of the reaction was unchanged.

Diethyl ketone (50 g.), 40% aqueous formaldehyde (75 g.), 2*N*-sodium hydroxide (15 c.c.), and methyl alcohol (12 c.c.) were warmed for 30 minutes; the initial reaction was exothermic. Distillation of the resulting solution yielded the following fractions: (A) b. p. 92—94°/10 mm., (B) b. p. 140—150°/10 mm., and (C) b. p. 160—200°/10 mm.

Fraction A was identified as *γ-keto-β-methyl-*n*-amyl alcohol*, $CH_2Me\cdot CO\cdot CHMe\cdot CH_2\cdot OH$, a limpid colourless liquid, b. p. 191—192°/760 mm. (Found: C, 62·2; H, 10·1. $C_6H_{12}O_2$ requires C, 62·1; H, 10·3%), and was characterised by the following derivatives: the p-*nitrobenzoate*, pale yellow needles, m. p. 50—51°, from methyl alcohol (Found: C, 59·1; H, 5·95; N, 5·4. $C_{13}H_{15}O_5N$ requires C, 58·9; H, 5·7; N, 5·3%); and 1-(2′ : 4′-*dinitrophenyl*)-4-*methyl*-3-*ethyl*-4 : 5-*dihydropyrazole* (I; R = Et), red plates, m. p. 149—150°, from petroleum (b. p. 60—80°) or ethyl acetate (Found: C, 51·9; H, 5·2. $C_{12}H_{14}O_4N_4$ requires C, 51·8; H, 5·0%).

Fraction B, although only an impure *γ-keto-β-hydroxymethyl-β-methyl-*n*-amyl alcohol* (Found: C, 58·4; H, 9·5. $C_7H_{14}O_3$ requires C, 57·5; H, 9·4%), nevertheless gave the following crystalline derivatives of that compound: (1) the *di*-p-*nitrobenzoate* crystallised from acetone–alcohol in almost white needles, m. p. 147—148° (Found: C, 57·2; H, 4·7; N, 6·2. $C_{21}H_{20}O_9N_2$ requires C, 56·8; H, 4·5; N, 6·2%). (2) 2 : 4-Dinitrophenylhydrazine gave a small yield (20% by weight) of a material crystallising from methyl alcohol in reddish-brown flakes very similar to shellac, m. p. 123—124°. The following analyses pointed to a compound into which two substituted hydrazines had condensed and its constitution is suggested tentatively by formula (III), that is, 3-*acetyl*-1-(2′ : 4′-*dinitrophenyl*)-4-*hydroxymethyl*-4-*methyl*-4 : 5-*dihydropyrazole*-2″ : 4″-*dinitrophenylhydrazone* (Found:

C, 45·7, 45·6; H, 3·9, 4·0; N, 22·6, 22·4. $C_{19}H_{18}O_9N_8$ requires C, 45·4; H, 3·6; N, 22·3%).

Fraction C gradually deposited a solid, which crystallised from chloroform in colourless hard prisms, m. p. 91°, and was identified as *γ-keto-βδ-bishydroxymethyl-β-methyl-*n*-amyl alcohol* (*γ-keto-ββδ-trishydroxymethyl-*n*-pentane*), $CHMe(CH_2{\cdot}OH){\cdot}CO{\cdot}CMe(CH_2{\cdot}OH)_2$ (Found: C, 54·7; H, 9·2. $C_8H_{16}O_4$ requires C, 54·5; H, 9·1%). It was very readily soluble in water and the lower alcohols and was characterised by the following derivatives: the *tribenzoate*, colourless needles, m. p. 79—80°, from methyl alcohol (Found: C, 71·0; H, 5·9. $C_{29}H_{28}O_7$ requires C, 71·3; H, 5·7%), and the *tri*-p-*nitrobenzoate*, small, pale yellow prisms, m. p. 147—148°, from acetone–alcohol (Found: C, 56·1; H, 4·3; N, 6·9. $C_{29}H_{25}O_{13}N_3$ requires C, 55·9; H, 4·0; N, 6·7%).

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