172. *Formaldehyde Condensations with Aliphatic Ketones. Part II. Methyl Ethyl Ketone.*

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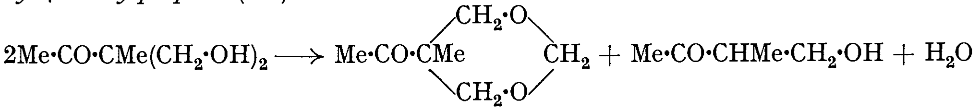
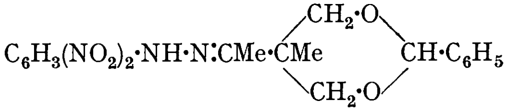
CONDENSATION of methyl ethyl ketone with formaldehyde in presence of alkali has previously been shown to give rise to two main products, γ-keto-β-methylbutyl alcohol (I), b. p. 89—90°/11 mm., and γ-keto-β-hydroxymethyl-β-methylbutyl alcohol (II), m. p. 60° * (Morgan and Holmes, J., 1932, 2667). The present communication, which involves a reconsideration of the structure of the benzaldehyde condensation compound of the latter substance, reveals a novel type of reaction in which formaldehyde produced by partial decomposition of (II) condenses with unchanged material to give *$\alpha\gamma$-methylenedioxy-β-acetyl-β-methylpropane* (III).



(II.) (III.) (I.)

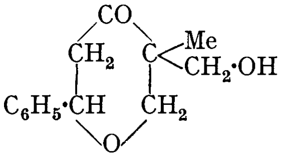
Compound (II) on distillation with potassium hydrogen sulphate yields water, acidic decomposition products, and methyl *iso*propenyl ketone, which on prolonged exposure to light polymerises to a transparent colourless resin as described by Morgan and Holmes (B.P. 404,317). Methyl *iso*propenyl ketone, when condensed with 2 : 4-dinitrophenylhydrazine, gives 1-2′ : 4′-dinitrophenyl-3 : 4-dimethyl-4 : 5-dihydropyrazole identical with that obtained from (I) by Morgan and Holmes (*loc. cit.*). The condensation of (II) with 2 : 4-dinitrophenylhydrazine gives rise to no pyrazole formation, the product being the normal *dinitrophenylhydrazone* (IV), $C_6H_3(NO_2)_2\cdot NH\cdot N\colon CMe\cdot CMe(CH_2\cdot OH)_2$, the constitution of which was established by condensing it with benzaldehyde in the presence of zinc

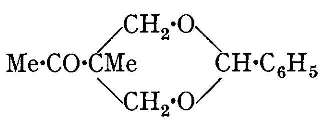


(V.)

chloride. The condensation product is regarded as *$\alpha\gamma$-benzylidenedioxy-β-acetyl-β-methylpropane dinitrophenylhydrazone* (V) for the following reason. Condensation of the parent ketol (II) with benzaldehyde led to a substance described by Morgan and Holmes as 6-phenyl-3-hydroxymethyl-3-methyltetrahydro-γ-pyrone (VI), which, however, has since

(VI.)





(VII.)

been decomposed by N/100-hydrochloric acid with liberation of benzaldehyde. In view of this reaction the tetrahydro-γ-pyrone structure can no longer be maintained, since

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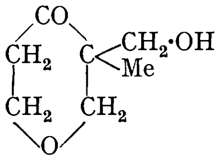
* A melting point of 66° for this substance is cited by Décombe (*Compt. rend.*, 1936, **203**, 1079). Repeated crystallisation from anhydrous benzene has only raised our melting point to 61·5°.

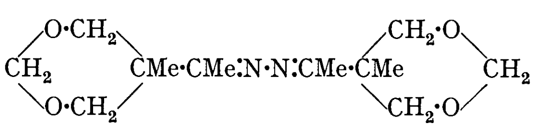
liberation of benzaldehyde would then necessitate rupture of a carbon–carbon linkage, an unlikely occurrence under such comparatively mild conditions (compare Kharasch and Porsche, hydrolysis of phenyldi-1-β-hydroxynaphthylmethane; *J. Org. Chem.*, 1936, **1**, 266). Furthermore it has not been found possible to acetylate or benzoylate the benzaldehyde compound or to obtain its phenyl- or *p*-xenyl-carbamate, even although structure (VI) includes a free hydroxyl group. Accordingly the substance is now regarded as being αγ-benzylidenedioxy-β-acetyl-β-methylpropane (VII).

The condensation of benzaldehyde with phloroglucinol under acidic conditions has been utilised in confirming the constitution of (VII).* The *benzylidenephloroglucide* is an amorphous substance charring above 300° and changing colour from pink to yellow-brown on drying at 130° (cf. Liebermann and Lindebaum, *Ber.*, 1904, **37**, 1179). It has now been found that 1 mol. (106 g.) of benzaldehyde yields 196 g. of condensation product, which is the same amount as that obtained on hydrolysing 1 mol. (220 g.) of αγ-benzylidenedioxy-β-acetyl-β-methylpropane with hydrochloric acid in presence of phloroglucinol.

Compound (II) on heating with iodine yields methyl *iso*propenyl ketone, water, and a ketone $C_7H_{12}O_3$, boiling at 109°/29 mm., which could neither be acetylated, benzoylated, nor hydrogenated at 150° and under 150 atmospheres' pressure with a platinum catalyst. Its molecular refraction (35·69) corresponded closely with that required for αγ-methylenedioxy-β-acetyl-β-methylpropane (III) (35·43), thus precluding the isomeric tetrahydro-γ-pyrone type of structure (VIII), which still contains one hydroxyl group. Further confirmation of these views was supplied by hydrolysis of (III) with dilute hydrochloric acid in presence of phloroglucinol (Clowes, *Ber.*, 1899, **32**, 2841). Estimation of the methylene group as formaldehyde-phloroglucide indicated 98·3% hydrolysis, the other product being (II), which was recovered as its 2 : 4-dinitrophenylhydrazone.

(VIII.)





(IX.)

The formation of (III) by the action of iodine on the ketol appears to be a new type of reaction and it is reasonable to suppose that under the influence of iodine one molecule of this ketol loses a molecular proportion of formaldehyde to give γ-keto-β-methylbutyl alcohol, which is dehydrated to methyl *iso*propenyl ketone. The free formaldehyde then condenses with a molecular proportion of unchanged ketol (II), to give (III).

To confirm this supposition it was necessary to show that the ketol (II) would in fact condense with formaldehyde under similar conditions to yield (III). This proof was established by comparing the yields of (III) obtained by distilling the ketol with 1% of iodine both alone and with one molecular proportion of formaldehyde. In the first case the yield of (III) was 69·8% of that required by the foregoing theory, whereas in the second case the yield of (III) was 80·7% of that required for the direct condensation of one molecular proportion of (II) with one molecular proportion of formaldehyde. It is apparent, therefore, that the condensation of the ketol with formaldehyde takes place readily in presence of iodine, but it should be noted here that, although potassium hydrogen sulphate has been shown to convert the ketol into methyl *iso*propenyl ketone, it does not catalyse the condensation of ketol with formaldehyde, since (III) was not obtained in this reaction.

The 2 : 4-*dinitrophenylhydrazone* and *semicarbazone* of this new ketone (III) are obtainable, but on attempting to prepare its hydrazone only the *ketazine* (IX) could be isolated.

EXPERIMENTAL.

Distillation of γ-Keto-β-hydroxymethyl-β-methylbutyl Alcohol with Potassium Hydrogen Sulphate.—The ketol (50 g.) was distilled with finely powdered potassium hydrogen sulphate (10 g.). The fraction boiling from 98° to 105°/760 mm. separated into two portions, a top layer

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* This method of estimating benzylidene groups is capable of wide application, as, for example, in the case of benzylidene sugar derivatives.

(15·5 g.), which after drying boiled at 96—98°/760 mm. and consisted of methyl *iso*propenyl ketone, b. p. 96—97°, $d^{20°}_{20°}$ 0·8543, $n^{20°}_{\mathrm{D}}$ 1·4224, $[R_L]_{\mathrm{D}}$ 25·00 (calc., 24·81), and a lower aqueous layer (10·5 g.). A second fraction, boiling at 110—120°/760 mm., gave acidic decomposition products and left a tarry residue (28 g.).

1-2′ : *4′-Dinitrophenyl-3 : 4-dimethyl-4 : 5-dihydropyrazole.*—Methyl *iso*propenyl ketone (10 g.) was added to a boiling solution of 2 : 4-dinitrophenylhydrazine (23·5 g.) in methyl alcohol (500 c.c.) containing concentrated hydrochloric acid (3 c.c.) and after refluxing for 1½ hours the liquid was cooled at 0° until microscopic orange-red elongated prisms (26 g.) separated, m. p. 190—191°. Admixture with authentic 1-2′ : 4′-dinitrophenyl-3 : 4-dimethyl-4 : 5-dihydropyrazole, m. p. 191°, showed no depression of melting point.

2 : *4-Dinitrophenylhydrazone of γ-Keto-β-hydroxymethyl-β-methylbutyl Alcohol.*—The ketol (5 g.), m. p. 60—62°, prepared by the method of Morgan and Holmes (*loc. cit.*), was dissolved in methyl alcohol (125 c.c.) and heated with 2 : 4-dinitrophenylhydrazine (7·5 g.) and concentrated hydrochloric acid (2 c.c.) until a homogeneous solution was obtained. On cooling, microscopic orange prisms (7·5 g.) were precipitated, which after recrystallising from ethyl acetate melted at 160—162° (Found : C, 46·8 ; H, 5·1 ; N, 18·3. $C_{12}H_{16}O_6N_4$ requires C, 46·15 ; H, 5·1 ; N, 17·9%).

αγ-Benzylidenedioxy-β-acetyl-β-methylpropane 2 : *4-Dinitrophenylhydrazone.*—On addition of light petroleum and water to a well-shaken mixture of the preceding compound (3 g.), benzaldehyde (15 c.c.), and finely powdered dry zinc chloride (5 g.), a yellow precipitate (2·2 g.) was obtained which, when recrystallised from ethyl acetate, separated in minute flattened orange prisms, m. p. 176—177° (Found : C, 57·2 ; H, 4·8 ; N, 14·3. $C_{19}H_{20}O_6N_4$ requires C, 57·0 ; H, 5·0 ; N, 14·0%).

Condensation of γ-Keto-β-hydroxymethyl-β-methylbutyl Alcohol with Benzaldehyde.—The ketol (20 g.), finely powdered anhydrous zinc chloride (20 g.), and benzaldehyde (50 g.) were shaken together for ½ hour until the mass had solidified (compare Morgan and Holmes, *loc. cit.*). After shaking with water and light petroleum (b. p. 60—80°), a crystalline precipitate (23 g.) was obtained which, when recrystallised from light petroleum, consisted of flattened colourless needles, m. p. 103° alone or mixed with the substance formerly described as 6-phenyl-3-hydroxymethyl-3-methyltetrahydro-γ-pyrone. When the product was warmed with *N*/100-hydrochloric acid, benzaldehyde was evolved readily.

After heating at 100° and cooling to 0°, a solution of this benzaldehyde condensation product (5 g.) in acetic anhydride (3 g.) and pyridine (1 c.c.) gave the unchanged material (4 g.). This failure to acetylate, which would be surprising in the case of a substance containing hydroxyl (VI), is explicable in the case of a substance with the non-hydroxylic structure (VII).

Condensation of Benzaldehyde with Phloroglucinol.—Freshly distilled benzaldehyde (3·587 g.), dissolved in a mixture of 2*N*-hydrochloric acid (20 c.c.) and industrial alcohol (20 c.c.), was refluxed at 100° for 3 hours with phloroglucinol (5·0 g.). Water (100 c.c.) was then added, and the precipitate (6·652 g.) filtered off, washed with water, and dried at 130°. This yellowish-brown amorphous substance was appreciably hygroscopic (Found : C, 72·4 ; H, 5·1. $C_{13}H_{10}O_3$ requires C, 72·9 ; H, 4·7%). The amount of *benzylidenephloroglucide* obtainable from redistilled benzaldehyde corresponds with 91·5% of the calculated quantity.

Hydrolysis of αγ-Benzylidenedioxy-β-acetyl-β-methylpropane.—This benzylidene compound (VII) (4·242 g.), dissolved in a mixture of industrial alcohol (20 c.c.) and 2*N*-hydrochloric acid (20 c.c.), was heated at 100° for 3 hours with phloroglucinol (7·0 g.) ; water (100 c.c.) was then added and the precipitate (3·772 g.) was washed with water (100 c.c.), dried at 130°, and weighed. This amount corresponds with practically complete hydrolysis (99·8%) of the benzylidene compound (VII) on the assumption that benzaldehyde itself gives 91·5% of the insoluble benzylidenephloroglucide, $C_{13}H_{10}O_3$.

The regenerated γ-keto-β-hydroxymethyl-β-methylbutyl alcohol (II) remained in the aqueous-alcoholic filtrate and was characterised by addition to this liquid of 2 : 4-dinitrophenylhydrazine (5 g.) dissolved in hydrochloric acid. When the mixture was left overnight at 0°, a brick-red precipitate (4·5 g.) was obtained ; its m. p. and mixed m. p. with the 2 : 4-dinitrophenylhydrazone of γ-keto-β-hydroxymethyl-β-methylbutyl alcohol was 162—163°.

Action of Iodine on γ-Keto-β-hydroxymethyl-β-methylbutyl Alcohol.—The ketol (50 g.) was distilled under atmospheric pressure with iodine (0·5 g.). The distillate from 98° to 108° consisted of two layers, an upper oily layer A (30·5 g.) and a lower aqueous layer B (9 g.), and a tarry residue (6 g.) was left. When fractions A and B were distilled separately, the following products were obtained. *Fraction A* : αγ-methylenedioxy-β-acetyl-β-methylpropane, b. p. 110°/31 mm., 19·0 g. ; methyl *iso*propenyl ketone, b. p. 96—97°, 9·0 g. ; tarry residue, 0·6 g. *Fraction B* : Water, 7·0 g. ; methyl *iso*propenyl ketone, 0·3 g. ; tarry residue, 1·2 g.

Action of Iodine and Paraformaldehyde on γ-Keto-β-hydroxymethyl-β-methylbutyl Alcohol.—The ketol (50 g.) was distilled with iodine (0·5 g.) and paraformaldehyde (11·3 g.) under atmospheric pressure. The first fraction, b. p. 98—105°, separated into two layers, a top layer (2 g.) which, after drying, distilled at 120—150°/40 mm. and consisted of unchanged material, and a lower aqueous layer (9 g.). The second fraction (44 g.) distilled at 110—115°/40 mm. and after redistillation was found to consist of *αγ-methylenedioxy-β-acetyl-β-methylpropane*, b. p. 109°/29 mm., $n_D^{20°}$ 1·4495, $d_{20°}^{20°}$ 1·082, $[R_L]_D$ 35·69 (calc., 35·43) (Found: C, 58·5; H, 8·5. $C_7H_{12}O_3$ requires C, 58·3; H, 8·3%).

2 : 4-*Dinitrophenylhydrazone of αγ-Methylenedioxy-β-acetyl-β-methylpropane.*—αγ-Methylenedioxy-β-acetyl-β-methylpropane (5 g.) was refluxed with 2 : 4-dinitrophenylhydrazine (7·5 g.), methyl alcohol (125 c.c.), and concentrated hydrochloric acid (1 c.c.) until a homogeneous solution was obtained. On cooling, orange-yellow rectangular prisms were precipitated which after recrystallising from methyl alcohol melted at 155—157° (Found: C, 48·0; H, 4·9; N, 17·4. $C_{13}H_{16}O_6N_4$ requires C, 48·1; H, 4·9; N, 17·3%).

Semicarbazone of αγ-Methylenedioxy-β-acetyl-β-methylpropane.—A boiling solution of αγ-methylenedioxy-β-acetyl-β-methylpropane (1·8 g.), semicarbazide hydrochloride (1·8 g.), and methyl alcohol (20 c.c.) was saturated with anhydrous potassium carbonate; water (20 c.c.) was added slowly and the solution left overnight at 0°. The white plates (1·4 g.) that had separated were recrystallised from methyl alcohol; m. p. 174—176° (Found: C, 48·6, 48·3; H, 7·7, 7·5; N, 20·1, 19·0. $C_8H_{15}O_3N_3$ requires C, 47·8; H, 7·5; N, 20·9%).

Ketazine of αγ-Methylenedioxy-β-acetyl-β-methylpropane.—Hydrazine sulphate (10 g.) and potassium carbonate (20 g.), dissolved in 50% aqueous methyl alcohol (120 c.c.), were added, with sufficient water (50 c.c.) to bring about complete solution, to αγ-methylenedioxy-β-acetyl-β-methylpropane (10 g.) dissolved in methyl alcohol (50 c.c.). This liquid was refluxed for 2 hours and left for several weeks at 0°. Lemon-yellow needles (2 g.) separated, m. p. 88—90° after recrystallisation from methyl alcohol (Found: C, 59·1; H, 8·8; N, 9·9. The hydrazone $C_7H_{14}O_2N_2$ requires C, 53·1; H, 8·8; N, 17·7%. The *ketazine* $C_{14}H_{24}O_4N_2$ requires C, 59·3; H, 8·4; N, 9·8%).

Hydrolysis of αγ-Methylenedioxy-β-acetyl-β-methylpropane.—The compound (5·0804 g.) was refluxed with 2*N*-hydrochloric acid (200 c.c.) and phloroglucinol (7·00 g.) for 5 hours; a brick-red precipitate of the formaldehyde-phloroglucide $C_7H_6O_3$ was then obtained. After washing with water (500 c.c.) and drying at 130°, this precipitate weighed 4·786 g., whereas complete hydrolysis would yield 4·869 g. of phloroglucide (or 98·3% hydrolysis). To the filtrate from the phloroglucide was added 2 : 4-dinitrophenylhydrazine (9·0 g.), dissolved in 50% hydrochloric acid, and after being left overnight the crystalline precipitate was dried and weighed (5·01 g.); mixed with the 2 : 4-dinitrophenylhydrazone of γ-keto-β-hydroxymethyl-β-methylbutyl alcohol, it gave no depression of melting point (m. p. 160—162°).

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