

XII.

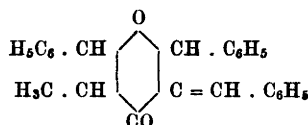
ON THE CONDENSATION OF ALDEHYDES WITH KETONES.

II.—ALDEHYDES WITH METHYLETHYLKETONE.

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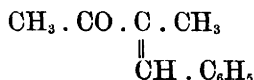
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By condensing benzaldehyde with dimethylacetylacetone Ryan and Dunlea (Proc. Royal Irish Acad., xxxii, B, p. 57) obtained a colourless crystalline compound which melted at 168-9° C., and which seemed to be the benzylidene derivative of diphenylmethyltetrahydropyrone, the reactions of the compound being best represented by the formula :—

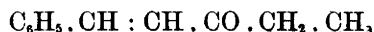


With a view to confirming the structure assigned to this compound by Ryan and Dunlea we attempted the preparation, from benzaldehyde and methylethylketone, of a compound which had been previously obtained by C. Harries and G. H. Müller [Ber. xxxv (1902), p. 968], and which the latter chemists regarded as a pyrone derivative.

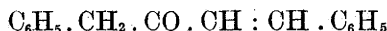
According to E. Levinstein (Inaugural Dissertation, Berlin, Jan. 29th, 1902) benzaldehyde and methylethylketone interact in the presence of dilute alkali to form γ -benzylidene-methylethylketone,



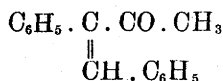
whereas from analogy with the condensation of benzaldehyde and phenylacetone in the presence of alkali—a condensation which has been studied by G. Goldschmidt and K. Krezmar [Monatsh. xxii (1901), p. 659]—we should have expected that the compound obtained by Levinstein was α -benzylidene-methylethylketone,



In the reactions which they carried out Goldschmidt and Krezmar obtained cinnamenylbenzylketone

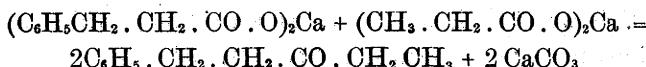


in the presence of dilute alkali, and the isomeric γ -derivative



in the presence of hydrochloric acid.

With dilute alkali as condensing agent, Harries and Müller obtained from methylethylketone and benzaldehyde a ketone, melting at 38°–39° C., previously described by Levinstein as γ -benzylidene-methylethylketone, but which Harries and Müller regarded as α -benzylidene-methylethylketone. On reduction, the ketone was converted into α -benzyl-methylethylketone, and their view of the constitution of the substance was found correct when the latter substance was also got by the dry distillation of a mixture of the calcium salts of dihydrocinnamic and propionic acids:—

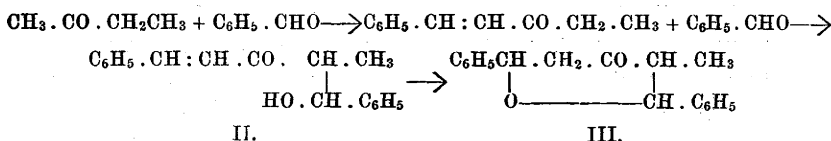


By condensing benzaldehyde with methylethylketone in the presence of hydrochloric acid, Harries and Müller prepared the isomeric ketone, γ -benzylidene-methylethylketone, which also melted at 38°–39° C.

As the result of their experiments, Harries and Müller concluded that benzaldehyde and methylethylketone in the presence of hydrochloric acid form a γ -derivative, and in the presence of dilute alkali an α -derivative.

By the further action of benzaldehyde on α -benzylidene-methylethylketone Harries and Müller prepared a colourless crystalline compound melting at 68.5° C., for which they found the empirical formula $\text{C}_{18}\text{H}_{18}\text{O}_2$, and which they regarded as a pyrone derivative.

If we assume with Harries and Müller that the compound $\text{C}_{18}\text{H}_{18}\text{O}_2$ is a pyrone derivative, its formation from benzaldehyde and methylethylketone will be represented as follows:—



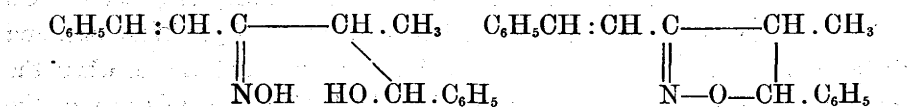
the unsaturated hydroxy-ketone (II) changing into the isomeric diphenyl-methyl-tetrahydropyrone (III) in the course of the reaction.

It seemed likely that the last compound (III) would interact with benzaldehyde to give benzylidene-diphenyl-methyltetrahydropyrone (I).

On repeating the experiments of Harries and Müller, we were unable to obtain the compound melting at 68.5°C ., and obtained instead a substance with the same empirical formula, $\text{C}_{18}\text{H}_{16}\text{O}_2$, but which melted at $81^{\circ}\text{--}83^{\circ}\text{C}$.

The compound $\text{C}_{18}\text{H}_{16}\text{O}_2$ may exist in the two structurally isomeric forms II and III. It is possible that the compound prepared by Harries and Müller may have the formula III, and that isolated by us the formula II, but since the oximes of the two substances have the same melting-point, $195^{\circ}\text{--}196^{\circ}\text{C}$., it is also possible that our substance was a purer preparation of the substance previously described by Harries and Müller.

We should expect that the oxime of a compound which has the formula II would readily change into an isoxazol



but the analysis of the hydroxylamine derivative of the compound melting at $81^{\circ}\text{--}83^{\circ}\text{C}$. showed that it was not an isoxazol, and for this reason we were at first inclined to regard the substance as a tetrahydropyrone derivative.

However, as the compound gives an orange colour with concentrated sulphuric acid, it seems more likely to be an unsaturated ketone than a tetrahydropyrone, and this view is to some extent confirmed by the behaviour of the substance on further condensation with benzaldehyde.

The compound $\text{C}_{18}\text{H}_{16}\text{O}_2$, melting at $81^{\circ}\text{--}83^{\circ}\text{C}$., condensed readily with benzaldehyde in the presence of alcoholic hydrochloric acid to form not benzylidene-diphenyl-methyl-tetrahydropyrone, $\text{C}_{28}\text{H}_{22}\text{O}_2$, which was expected, but another well crystallized compound melting at 156°C ., which has the empirical formula $\text{C}_{25}\text{H}_{20}\text{O}$.

The latter compound was also obtained by condensing benzaldehyde with α -benzylidene-methylethylketone in the presence of alcoholic hydrochloric acid.

Using the same condensing agent α -benzylidene-methylethylketone interacted with anisaldehyde and with piperonal to form analogously constituted compounds having the formulae $\text{C}_{27}\text{H}_{24}\text{O}_3$ and $\text{C}_{27}\text{H}_{20}\text{O}_3$, respectively.

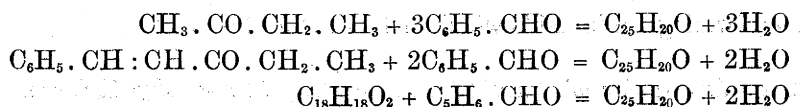
If the statement of Harries and Müller, that α -benzylidene-methylethylketone is formed from benzaldehyde and methylethylketone in the presence of alkali, and is not formed from the same components in the presence of acids, were rigidly true, we should expect that the compound $\text{C}_{25}\text{H}_{20}\text{O}$ could not be formed directly from methylethylketone and benzaldehyde in the presence of alcoholic hydrochloric acid.

Direct experiment, however, showed that the contrary is true—the

ketone and aldehyde interacting slowly at the ordinary temperature, when dissolved in alcoholic hydrochloric acid, to form the compound $C_{25}H_{20}O$.

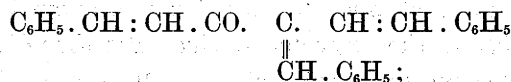
Piperonal and methylethylketone interacted under similar conditions to form an analogously constituted piperonal derivative of methylethylketone.

The preparation of the compound $C_{25}H_{20}O$ from methylethylketone, α -benzylidene-methylethylketone and the compound $C_{18}H_{18}O_2$ may be represented by the equations:—



The unsaturated nature of the compound $C_{25}H_{20}O$ was shown by the formation of a dibromide $C_{25}H_{20}OBr_2$; but we were unable to establish the presence of a keto radical in the substance, since the latter formed neither an oxime nor a phenyl-hydrazone.

Empirically the substance corresponds to a tribenzylidene derivative of methylethylketone



but as it is difficult to see how such a compound can be formed by normal reactions from benzaldehyde and methylethylketone, we shall postpone the consideration of its structure until further experimental facts have been accumulated.

EXPERIMENTAL PART.

A. Action of Benzaldehyde on Methylethylketone in the Presence of Alkali.

1. Equimolecular Quantities of Benzaldehyde and Methylethylketone.

A mixture of 130 grams of methylethylketone, and 140 grams of benzaldehyde, with a solution of 50 grams of sodium hydroxide in 1500 c.cs. of water, was shaken on a machine for eight days. The oil which separated was extracted with ether, and after evaporation of the latter the residue was distilled in a current of steam. When the benzaldehyde ceased coming over, the residue in the flask was subjected to further distillation in a current of steam, previously heated in a coil to $180^\circ C.$, while the flask from which the distillation was being conducted was heated to $180^\circ C.$ in an oil-bath.

The oil which now distilled solidified after short standing, and the solid, when recrystallized from petroleum ether, melted at 38° – $39^\circ C.$

Towards the end of the operation the distillate contained a small quantity of another compound which melted at 81° – $83^\circ C.$

α -Benzylidene-methylethylketone crystallizes from petroleum ether in large

plates which are easily soluble in alcohol, ether, benzene, or chloroform, and scarcely soluble in water.

The crystals are coloured reddish-brown on contact with concentrated sulphuric acid, in which they dissolve, forming a reddish-brown solution.

It has been shown by Harries and Müller (*loc. cit.*) that α -benzylidene-methylethylketone forms an oxime, melting at 85°–86° C., a phenylhydrazone, melting at 101° C., and that its solution in glacial acetic acid reacts with bromine, forming a dibromide which melts at 109°–110° C.

2. *Further Action of Benzaldehyde on α -Benzylidene-methylethylketone.*

A mixture of equivalent quantities of benzaldehyde and α -benzylidene-methylethylketone was shaken with a large volume of dilute aqueous alkali for about a fortnight. The oil was extracted with ether, and after evaporation of the latter, most of the unchanged α -benzylidene-methylethylketone was distilled in a current of superheated steam. When the residue, left in the flask, was recrystallized from alcohol, it melted at 81°–83° C.

It was found later that when the reaction was allowed to progress for a much longer time, and the extracted product was then distilled *in vacuo*, a better yield of the compound melting at 81°–83° C. was obtained.

A still better yield of the product was got by allowing a mixture of 8 grams of α -benzylidene-methylethylketone, and 5.3 grams of benzaldehyde with a solution of 1 gram of sodium hydroxide in 100 c.c.s. water, and 100 c.c.s. alcohol to stand for several days at the temperature of the laboratory.

The oil which separated was dissolved in warm alcohol, and when the solution was cooled the substance separated in colourless crystals which melted at 81°–83° C. After drying in a desiccator it gave on analysis the following results:—

0.2548 substance gave 0.7566 CO₂ and 0.1542 H₂O

corresponding to C 81.0, H 6.7

C₁₈H₁₈O₂ requires C 81.2, H 6.7.

The compound crystallizes from alcohol in prisms which are scarcely soluble in cold, and readily in hot, alcohol. It is very soluble in ether, chloroform, or benzene.

The crystals are coloured orange on contact with concentrated sulphuric acid, in which they dissolve to an orange-yellow solution.

By an apparently similar method Harries and Müller (*loc. cit.*) obtained a compound, the formula of which is C₁₈H₁₈O₂, but which melts at 68.5° C. From the analysis, and the properties of the compound, they regard it as a pyrone derivative. Its oxime, which they prepared, melted at 195°–196° C. As the compound prepared by us melted about fourteen degrees higher than

that got by Harries and Müller, we prepared its oxime, and found that it also melts at 195°–196° C.

An alcoholic solution of 2 grams of the condensation product melting at 81°–83° C., and 2 grams of hydroxylamine hydrochloride, was mixed with a saturated aqueous solution of 1.5 grams of sodium carbonate, and the mixture was heated to gentle boiling for several hours under a reflux condenser. The colourless, crystalline precipitate which formed was filtered, washed with water, dried, and recrystallized from chloroform and alcohol.

When dried at 110° C., it melted at 195°–196° C., and gave on analysis the following results:—

0.1229 substance gave 0.3452 CO₂ and 0.0752 H₂O
 corresponding to C 76.66, H 6.8
 C₁₈H₁₈ONOH requires C 76.87, H 6.76.

The oxime crystallizes in needles which are sparingly soluble in alcohol, and soluble in chloroform, ether, or benzene.

The *phenylhydrazone* of the compound, which melts at 81°–83° C., was prepared by dissolving 1.5 grams of the condensation-product and 1 gram of phenylhydrazine in 20 c.c.s. of absolute alcohol (warm), and letting the mixture stand with occasional warming for a few days. The phenylhydrazone was filtered and washed with alcohol. When dried it melted at 134° C., and gave on analysis the following results:—

0.1362 substance gave 9.4 c.c.s. of moist nitrogen at 19° C. and 758 m.m.p.
 corresponding to N 7.9
 C₁₈H₁₈O : N · NH · C₆H₅ requires N 7.9.

It crystallizes in short colourless needles, which slowly acquire a light-brownish colour on exposure to light.

Semi-carbazone of the compound melting at 81°–83° C.

A solution of 1.5 grams of semi-carbazide hydrochloride and an equal weight of anhydrous sodium acetate in a little water was added to an alcoholic solution of 2.6 grams of the compound melting at 81°–83° C. The mixture was allowed to stand for two days in a warm place, then heated to boiling, and filtered. After washing with water and alcohol it crystallized from a mixture of chloroform and hot alcohol in fine needles, which were filtered and washed with ether. When dried at 110° C., it melted at 195°–198° C., and gave on analysis the following results:—

0.1857 substance gave 20.2 c.c.s. of moist nitrogen at 15° C. and 757 m.m. p.
 0.1392 substance gave 0.3590 CO₂ and 0.0839 H₂O
 corresponding to C 70.3, H 6.7, N 12.7
 C₁₈H₁₈O : N · NH · CO · NH₂ requires C 70.6, H 6.5, N 12.7.

B. *Condensation of Aldehydes with Methyleneethylketone in the Presence of Acids.*1. *Action of Benzaldehyde on Methyleneethylketone in the Presence of Alcoholic Hydrochloric Acid.*

A solution of 5 c.cs. of methyleneethylketone and $17\frac{1}{2}$ c.cs. of benzaldehyde in 20 c.cs. of alcohol, which had been previously saturated with gaseous hydrochloric acid, was allowed to stand in a stoppered flask for several days. The oil which separated was dissolved in a mixture of chloroform and alcohol. The crystals which were formed were filtered and recrystallized from chloroform and alcohol. When dried at 110°C ., the substance melted at 156°C .

The same compound can be obtained by the action of benzaldehyde, in the presence of alcoholic hydrochloric acid on either α -benzylidene-methyleneethylketone or the condensation-product which melts at 81° – 83°C .

2. *Action of Benzaldehyde on α -Benzylidene-Methyleneethylketone in the Presence of Alcoholic Hydrochloric Acid.*

A solution of 2 grams of α -benzylidene-methyleneethylketone and 2.7 grams of benzaldehyde in 20 c.cs. of alcoholic hydrochloric acid rapidly turned a reddish colour, and gradually deposited an oily substance, which in the course of a few days solidified. The parent liquid was decanted, and the residue was recrystallized a couple of times from chloroform and alcohol. When dried the colourless, crystalline solid melted at 156°C .

3. *Action of Benzaldehyde on the Condensation-Product $\text{C}_{13}\text{H}_{18}\text{O}_2$ in the Presence of Alcoholic Hydrochloric Acid.*

Equimolecular quantities of the condensation-product $\text{C}_{13}\text{H}_{18}\text{O}_2$ and benzaldehyde were dissolved in alcoholic hydrochloric acid, and the solution was let stand in a stoppered flask for a few days. From the solution, which turned a reddish colour, a copious separation of crystals occurred. The solid was filtered and recrystallized from chloroform and alcohol.

After drying at 110°C . it melted at 156°C ., and gave on analysis the following results :—

0.1876 substance gave 0.6120 CO_2 and 0.1043 H_2O
 corresponding to C 89.0 H 6.2.
 $\text{C}_{25}\text{H}_{20}\text{O}$ requires C 89.2 H 6.0.

The compound crystallizes from chloroform and alcohol in short rectangular prisms, which are sparingly soluble in ether or alcohol, and readily soluble in chloroform.

The crystals are coloured a deep orange on contact with concentrated sulphuric acid, in which they dissolve, forming an orange-coloured solution.

Its alcoholic solution did not react with phenylhydrazine to form a phenylhydrazone.

Similarly attempts to prepare an oxime by the action of either hydroxylamine hydrochloride or hydroxylamine on an alcoholic solution of the compound were unsuccessful.

A chloroform solution of the substance reacted slowly with bromine to form a dibromide which, after recrystallization from ether, melted with decomposition at 145° C., and gave on analysis the following results:—

0.4340 substance treated with sodium and alcohol by Stepanow's method required 17.4 c.cs. $\frac{N}{10}$ AgNO₃ for the complete precipitation of the bromide
 corresponding to Br. 32.04
 C₂₅H₂₀OBr₂ requires Br. 32.2.

The *dibromide* crystallizes in rectangular prisms, which are sparingly soluble in alcohol or ether, and readily soluble in chloroform.

4. *Action of Anisaldehyde on α-Benzylidene-Methylethylketone in the Presence of Alcoholic Hydrochloric Acid.*

The crystalline solid, which separated when a solution of 2 grams of α-benzylidene-methylethylketone and 3.6 c.cs. of anisaldehyde in 20 c.cs. of alcoholic hydrochloric acid was allowed to stand a few days, was filtered, and then boiled with pyridine. After removal of the pyridine the residue was recrystallized a couple of times from chloroform and alcohol.

It melted at 173° C., and gave on analysis the following results:—

0.1738 substance gave 0.5194 CO₂ and 0.0974 H₂O,
 corresponding to C 81.5, H 6.2,
 C₂₇H₂₄O₃ requires C 81.77, H 6.1.

The substance forms colourless crystals, which are sparingly soluble in alcohol, benzene, or ether, and readily soluble in chloroform.

A solution of the crystals in concentrated sulphuric acid has a deep orange colour.

5. *Action of Piperonal on α-Benzylidene-Methylethylketone in the Presence of Alcoholic Hydrochloric Acid.*

On standing a few days a solution of 2 grams of α-benzylidene-methylethylketone and 3.8 grams of piperonal in 20 c.cs. of alcoholic hydrochloric acid deposited an oil, which was boiled with pyridine, and then precipitated

in a crystalline state by addition of alcohol. After a few recrystallizations from chloroform and alcohol it melted at 191°C ., and gave on analysis the following results :—

0.2592 substance gave 0.7220 CO_2 and 0.1144 H_2O ,
 corresponding to C 75.97, H 4.90,
 $\text{C}_{27}\text{H}_{20}\text{O}_5$ requires C 76.38, H 4.75.

It crystallizes from chloroform and alcohol in yellowish, hexagonal plates, which are sparingly soluble in cold or hot alcohol, and readily soluble in chloroform.

The crystals are coloured a dark red on contact with concentrated sulphuric acid, in which they dissolve, forming a cherry-red solution.

6. *Action of Piperonal on Methyleneethylketone in the Presence of Alcoholic Hydrochloric Acid.*

A solution of 8 c.cs. of methylethylketone and 32 grams of piperonal in 150 c.cs. of alcoholic hydrochloric acid rapidly turned a dark-blue colour, which gradually changed to purple. After standing a few days in a stoppered flask a tarry product separated. From the latter, by treatment with chloroform and alcohol, a bluish solid was obtained.

On mixing with dilute potash the blue colour, which was apparently due to a hydrochloric acid addition compound, or to an oxonium salt, disappeared. The substance was recrystallized several times from chloroform and alcohol. When dried at 110°C ., it melted at 212°C ., and gave on analysis the following results :—

0.1442 substance gave 0.3802 CO_2 and 0.0596 H_2O ,
 corresponding to C 71.9, H 4.6,
 $\text{C}_{28}\text{H}_{20}\text{O}_7$ requires C 71.8, H 4.3.

The substance crystallizes in long, colourless, rectangular prisms, which are very sparingly soluble in ether, benzene, or alcohol, and soluble in chloroform.

The crystals are coloured dark red on contact with concentrated sulphuric acid, in which they dissolve, forming a deep-red solution.