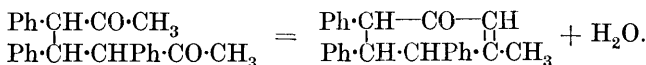


CCXCV.—*The Condensation of Benzyl Methyl Ketone
with Salicylaldehyde.*

By ROBERT DICKINSON.

THE condensation of benzyl methyl ketone with benzaldehyde was studied by Goldschmiedt and Knöpfer (*Monatsh.*, 1897, **18**, 437; 1898, **19**, 406) and Goldschmiedt and Krczmar (*ibid.*, 1901,

22, 659). With dilute aqueous sodium hydroxide as condensing agent, the product obtained was a mixture of styryl benzyl ketone and 2 : 3 : 6-triphenyltetrahydro-4-pyrone, together with a very small quantity of $\alpha\gamma\epsilon$ -triphenylacetyl- $\beta\delta$ -diphenylpentane. With dry hydrogen chloride as condensing agent, δ -chloro- $\gamma\delta$ -diphenylbutan- β -one was obtained which readily lost hydrogen chloride to give $\gamma\delta$ -diphenyl- $\Delta\gamma$ -buten- β -one, isomeric with styryl benzyl ketone; when an excess of the ketone was used, the product contained a yellow substance which was regarded as 4 : 5 : 6-triphenyl-3-methyl- Δ^2 -cyclohexenone, formed according to the equation :



Goldschmiedt and Krczmar (*ibid.*, p. 749) obtained the homologues of styryl benzyl ketone and 2 : 3 : 6-triphenyltetrahydro-4-pyrone from *p*-tolualdehyde, whilst anisaldehyde and piperonal gave the corresponding styryl ketones only. They state that the condensation of benzyl methyl ketone with salicylaldehyde, 2-methoxybenzaldehyde, cinnamaldehyde, and cuminaldehyde was attempted, but only viscous oils or resinous masses were obtained.

The condensation of benzyl methyl ketone with salicylaldehyde has now been fully investigated, two types of condensing agent—amines and sodium hydroxide—being used.

(1) With piperidine or diethylamine, a substance, $\text{C}_{16}\text{H}_{14}\text{O}_2$, was obtained formed according to the equation :

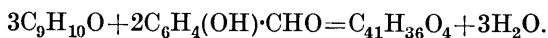


Since the compound is an unsaturated phenolic ketone, the only possible structural formulæ are $\text{HO}\cdot\text{C}_6\text{H}_4\cdot\text{CH}:\text{CH}\cdot\text{CO}\cdot\text{CH}_2\text{Ph}$ (I) and $\text{HO}\cdot\text{C}_6\text{H}_4\cdot\text{CH}:\text{CPh}\cdot\text{CO}\cdot\text{CH}_3$ (II). The compound is regarded as 2-hydroxystyryl benzyl ketone (I), since its methyl ether is not identical with the compound obtained by condensing 2-methoxybenzaldehyde with benzyl methyl ketone in presence of hydrogen chloride. The latter compound is almost certainly the methyl ether of (II), since condensation in presence of acid always takes place preferentially at a methylene group. The possibility of the two methoxy-compounds being *cis-trans*-isomerides has not been overlooked, but it is considered unlikely in view of other work carried out in these laboratories (compare McGookin and Heilbron, *J.*, 1924, **125**, 2099; McGookin and Sinclair, *J.*, 1925, **127**, 2539).

(2) In the condensation by means of aqueous-alcoholic alkali, remarkable results were obtained. Although many variations in the experimental conditions were tried, no trace of the normal product (I) was detected. Five compounds together with traces of others were isolated, but the investigation of these was hampered

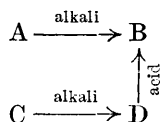
by the difficulty of separating them, and more particularly by the small amounts of pure material eventually obtained, much resinous matter being present. Further, only small quantities of material could be condensed at a time, otherwise a more than proportional increase in the formation of resinous by-products occurred.

The five substances all gave analytical values agreeing with the formula $C_{41}H_{36}O_4$:

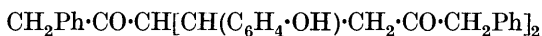


Other pairs of aldehydes and ketones have been found to condense in the same ratio, but in the cases previously studied only 2 mols. of water were lost (compare Kostanecki and co-workers, *Ber.*, 1896, 29, 1488, 1495, 1891, 2245, 2248).

The five isomerides are designated A, B, C, D, and E. Whereas the last is yellow and dissolves readily in cold aqueous alkali to a deep red solution, from which it is precipitated unchanged on acidification, the other four substances are colourless, insoluble in cold aqueous alkali, and show interesting relationships to one another as will be seen from the following : Treatment of A with concentrated alcoholic potassium hydroxide gives a pale yellow solution which slowly becomes brownish-red. Addition of water produces no precipitate, but on acidification a yellow solid separates which is readily soluble in aqueous alkali. Crystallisation of this solid from alcohol or benzene produces B. B also reacts with alcoholic potash to give a red solution, but is recovered unchanged on dilution and acidification. C can be converted into D under precisely the same conditions. D, on being boiled in alcoholic solution with a few drops of concentrated hydrochloric acid for $\frac{1}{2}$ hour, is converted into B. The series of changes is shown in the diagram :



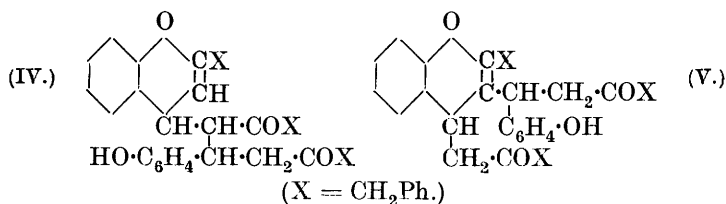
From these intimate relationships it follows that these substances must be very similar in structure. Probably they are stereoisomerides, similar cases having been noted by Kostanecki (*loc. cit.*) and Conant and Cutter (*J. Amer. Chem. Soc.*, 1926, 48, 1016). They are probably derived from the unisolated intermediate compound, $\alpha\gamma\epsilon$ -triphenylacetyl- $\beta\delta$ -di-*o*-hydroxyphenylpentane,



(III), by loss of one molecule of water.

From the insolubility of the compounds in aqueous alkali, it may reasonably be inferred that at least one of the phenolic hydroxyl groups has been utilised in this secondary reaction, giving rise to pyran derivatives of the type (IV) or (V). These formulations are

supported to some extent by the fact that A readily yields a disemicarbazone.



Insolubility in alkali does not prove the absence of hydroxyl, for 2-hydroxybenzylidenediacetophenone is likewise insoluble (Cornelson and Kostanecki, *Ber.*, 1896, **29**, 240; Feuerstein and Kostanecki, *ibid.*, 1898, **31**, 710).

On methylation, A, B, and D give rise to dimethyl ethers, those of the former two, m. p. 135°, being identical. The dimethyl derivative of D melts at 138°, and at an intermediate temperature when mixed with the ether of A or B. This does not necessarily imply that they are identical, especially in view of the fact that repeated crystallisation of the lower-melting compound failed to alter the melting point. These ethers are not direct derivatives of (III), formed by the opening of the pyran ring in presence of alkali, but apparently correspond to enolic forms of (IV) or (V).

In E, which differs entirely from the other products, it is suggested that both phenolic hydroxyl groups are present. Owing to the difficulty of isolating this substance in appreciable quantity, experimental data in favour of any special structure could not be obtained.

EXPERIMENTAL.

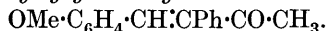
2-Hydroxystyryl Benzyl Ketone.—A solution of benzyl methyl ketone (26.8 g.) and salicylaldehyde (24.4 g.) in absolute alcohol (40 c.c.) became orange-red on addition of piperidine (20 drops). A week later, more of the base (15 drops) was added to the syrupy liquid, from which, after a few days, bulky clusters of yellow needles slowly separated; these were periodically filtered off. The last crops contained an impurity, which coloured the solid pink and could not be removed by crystallisation or by treatment with charcoal. The residue was a dark red, viscous syrup. The product was twice crystallised from alcohol, giving clusters of long, colourless, silky needles (yield, 23 g.), m. p. 181°, which were insoluble in water but formed an orange solution in dilute aqueous sodium hydroxide. Exposed to light, the crystals rapidly became olive-green on the surface (Found: C, 80.5; H, 5.8. $\text{C}_{16}\text{H}_{14}\text{O}_2$ requires C, 80.7; H, 5.9%). The same compound was obtained when diethylamine was used instead of piperidine, but the yield was less satisfactory.

The *semicarbazone*, obtained in the usual manner, formed clusters

of short, colourless needles, m. p. 205—206° (Found: N, 14.2. $C_{17}H_{17}O_2N_3$ requires N, 14.2%). The *carbomethoxy*-derivative separated from alcohol in colourless needles, m. p. 64—65°.

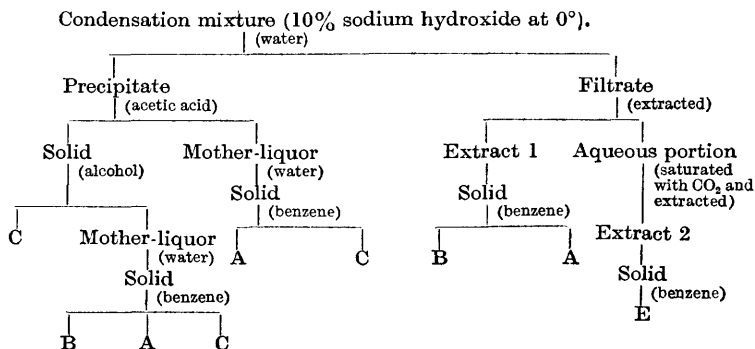
2-Methoxystyryl Benzyl Ketone.—2-Hydroxystyryl benzyl ketone was treated alternately with small quantities of methyl sulphate and 8% potassium hydroxide solution, at 30—40°, and continuously shaken, until addition of the alkali failed to produce a yellow colour. The separated solid crystallised from aqueous alcohol in long, lustrous, faintly yellow needles, m. p. 79° (Found: C, 80.4; H, 6.4. $C_{17}H_{16}O_2$ requires C, 80.9; H, 6.4%).

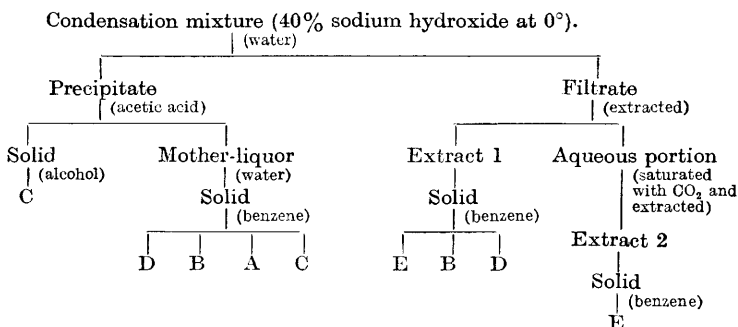
α-Phenyl-2-Methoxystyryl Methyl Ketone.



—A solution of 2-methoxybenzaldehyde (5 g.) and benzyl methyl ketone (5 g.) in absolute alcohol (40 c.c.) was cooled in ice-water and saturated with a slow stream of dry hydrogen chloride. After several hours, the reddish-brown liquid was poured into water (300 c.c.) and rendered faintly alkaline. The precipitated semi-solid, yellow mass was taken up in ether, and after drying, the bulk of the solvent was removed. The crystalline deposit was twice crystallised from alcohol, being obtained in colourless rhombs which, when viewed in bulk, showed a faint pink colour; m. p. 145° (yield, 3.5 g.) (Found: C, 81.1; H, 6.1. $C_{17}H_{16}O_2$ requires C, 80.9; H, 6.4%).

Condensation of Benzyl Methyl Ketone and Salicylaldehyde by Means of Sodium Hydroxide.—The condensation was usually carried out with equal tenth-molecular quantities of the reactants. Various temperatures were employed and the concentration of the alkali (of which at least 2 mols. were always used) was varied from 2% to 40%. The type of condensation most fully studied was as follows: A solution of benzyl methyl ketone (13.4 g.) and salicylaldehyde (12.2 g.) in alcohol (50 c.c.) was cooled in ice-water, and 10% sodium hydroxide solution (80 c.c.) slowly added. The pale red





solution became ruby-red after remaining for 3 days in the ice chest. The method of working is best followed from the accompanying charts, of which the following is a brief description. The condensation mixture was poured into water (1000 c.c.) and kept until the colloidal precipitate had coagulated. The resulting yellow solid was crystallised from glacial acetic acid, and the separated crystals (product C) were recrystallised from alcohol. The acetic acid mother-liquor was diluted with water, and the precipitate fractionally crystallised from benzene. The original aqueous filtrate was extracted with ether, saturated with carbon dioxide, and again extracted. After being washed and dried, the ethereal solutions were concentrated and the solid separating in each case was fractionally crystallised from benzene.

Condensation by means of hot 40% sodium hydroxide solution yielded a product which gave no precipitate on dilution and contained no substance A. Condensation by 2% sodium hydroxide at room temperature gave none of the products recognised above, but in this case no material has yet been obtained in sufficient quantity for investigation.

Substance A, which was the main product of most of the condensations studied, separated from benzene, carbon disulphide, or carbon tetrachloride as a white, micro-crystalline powder, m. p. 185° (decomp.). It is insoluble in water or cold aqueous alkali, moderately easily soluble in benzene, and readily soluble in alcohol. It does not noticeably react with bromine (Found: C, 83.4; H, 6.4. $C_{41}H_{36}O_4$ requires C, 83.1; H, 6.1%).

The *disemicarbazone*, prepared by the usual method, separated from alcohol in colourless plates, softening with decomposition at 230°. Analysis showed the compound to be impure, but recrystallisation was not attempted owing to lack of material (Found: N, 10.4. The mono- and the di-semicarbazone require N, 6.5 and 11.9% respectively).

The *dimethyl ether* was obtained by keeping a solution of A (1 g.) in acetone (50 c.c.) with an excess of 40% potassium hydroxide solution until the red colour was fully developed and then treating it slowly at 40—50° with methyl sulphate until the colour was discharged. The product was precipitated by water and crystallised twice from alcohol, from which it separated in colourless needles, m. p. 135° [Found: C, 83.4; H, 6.6; OMe, 8.9. $C_{41}H_{34}O_2(OMe)_2$ requires C, 83.2; H, 6.5; OMe, 10.0%].

Substance B crystallised from benzene in rosettes of minute, colourless needles and from alcohol in colourless rhombs, m. p. 228° (decomp.) (Found: C, 83.3; H, 6.1%).

Conversion of A into B.—A solution of A (1 g.) in alcohol (40 c.c.) was treated with 60% potassium hydroxide solution (5 c.c.) and kept at room temperature for 3 hours, its colour changing from yellow to red. The diluted solution was acidified, and the precipitated solid crystallised from alcohol. Its identity with B was proved by a mixed melting-point determination.

Substance B, treated in the same way, was recovered unchanged. Its alkaline solution, on methylation, gave a product identical with that obtained from A.

Substance C crystallised from benzene or alcohol in colourless needles, m. p. 186° (Found: C, 83.1; H, 6.2%). The m. p. of a mixture with A showed a considerable depression.

Substance D separated from benzene as a white, micro-crystalline powder, m. p. 209° (decomp.), containing 1 mol. of benzene of crystallisation. It was always found accompanying A, and its resemblance to the latter rendered separation of the two difficult (Found: C, 84.2; H, 6.3. $C_{41}H_{36}O_4 \cdot C_6H_6$ requires C, 84.2; H, 6.2%). Its *dimethyl ether* separated from alcohol in the same crystalline form as that from A and B, but melted at 138° (Found: C, 82.7; H, 6.6; OMe, 9.1%).

Conversion of C into D.—This was carried out in the same manner as that of A into B, except that the product was crystallised from benzene.

Conversion of D into B.—An alcoholic solution of D was treated with a few drops of concentrated hydrochloric acid, and the whole gently boiled under reflux for $\frac{1}{2}$ hour; after cooling, the product was diluted with water. The dried solid was crystallised first from benzene and then from alcohol. It was identified with B both by its crystalline form and by the m. p. of a mixture of the two. Under the same conditions, A, B and C remained unchanged.

Substance E separated from benzene as a canary-yellow, micro-crystalline powder, m. p. 239° (decomp.). It was insoluble in water, but dissolved readily in cold aqueous sodium hydroxide, to a deep

red solution. In the condensation mixture, it was always accompanied by other yellow compounds, but the amounts of these were too minute for investigation (Found : C, 83.1 ; H, 5.9%).

In conclusion, I wish to express my gratitude to the Advisory Council of the Department of Scientific and Industrial Research for a maintenance grant, and to the Lancashire Education Committee for the renewal of a scholarship during the tenure of which this research was carried out. My thanks are also due to Professor I. M. Heilbron, D.S.O., D.Sc., whose advice and encouragement have been of great value, and to Mr. E. Formby, M.Sc., for much assistance in the preliminary work.

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