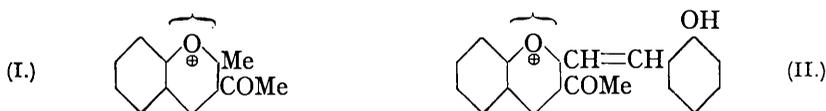


105. The Acid Condensation of Salicylaldehyde with Acetylacetone, Ethyl Acetoacetate, and Pyruvic Acid.

By R. J. W. LE FÈVRE.

(a) BY saturating a mixture of salicylaldehyde and acetylacetone with dry hydrogen chloride, Chatterji and Ghosh (J., 1918, **113**, 446) prepared a substance which they described as the chloride of (I)—this view, for reasons already outlined (J., 1933, 1197), seems



unlikely. By the method of the Indian authors an impure chloride has now been obtained from which a *perchlorate* can be produced identical with that formed in one step from salicylaldehyde (2 mols.) and acetylacetone (1 mol.) in ethereal hydrogen chloride-perchloric acid. The yield is a maximum when the reactants are in the proportion stated, and this fact, with the analytical results, shows that the salt of Chatterji and Ghosh was in reality the chloride of (II).

Salicylideneacetylacetone (Knoevenagel and Arnot, *Ber.*, 1904, **37**, 4496), subjected to the latter process, yields a *perchlorate* which is different from the above and is therefore probably the perchlorate of (I).

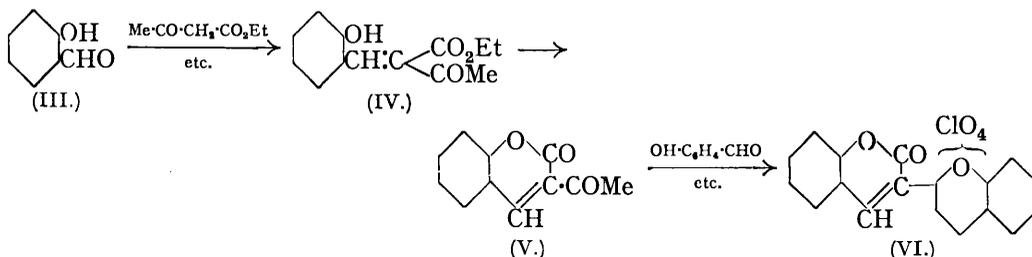
The direction of ring closure found for salicylidenebenzoylacetone (J., 1933, 1197) and the results now recorded for salicylideneacetylacetone are paralleled exactly by the interactions of *o*-aminobenzaldehyde with the appropriate diketones, *except* that, even in the presence of a considerable excess of salicylaldehyde, the substituted quinolines can be isolated with the 2-methyl group unattacked (Stark and Hoffmann, *Ber.*, 1909, **42**, 715):



Such resemblance, although common, is not general; *e.g.*, application of Friedländer's conditions to ethyl acetoacetate and ethyl benzoylacetate affords 3-carbethoxy-2-methylquinoline and 3-carbethoxy-2-phenylquinoline respectively (Friedländer and Göhring, *Ber.*, 1883, **16**, 1835)—results which do not correspond to those obtained from salicylaldehyde and these ketonic esters in the present work.

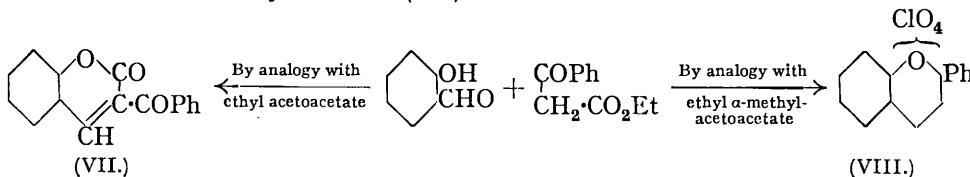
(b) Both De (*J. Indian Chem. Soc.*, 1927, **23**, 137) and Löwenbein and Katz (*Ber.*, 1926, **59**, 1377) have noted that, when direct formation of the pyrylium perchlorate is attempted from salicylaldehyde and β -ketonic esters by application of the ethereal hydrogen chloride-perchloric acid technique, ketonic scission of the ester apparently precedes condensation and the ultimate results are the same as those obtained from salicylaldehyde and the corresponding ketone (*e.g.*, ethyl α -methylacetoacetate gives the same pyrylium salt as does methyl ethyl ketone).

De (*loc. cit.*), however, failed to identify the product from ethyl acetoacetate and salicylaldehyde under these conditions. This reaction has now been re-examined, and a highly insoluble substance obtained, m. p. 300–305°, which is neither 2-*o*-hydroxystyrylbenzopyrylium perchlorate, m. p. 196° (Buck and Heilbron, *J.*, 1922, **121**, 1198), nor its 3-carbethoxy-derivative. A possible course (III \rightarrow IV \rightarrow V \rightarrow VI) of the reaction was suggested by the fact that even under the action of piperidine salicylaldehyde and



ethyl acetoacetate condense, with loss of the elements of alcohol *but without decarboxylation*, to give 3-acetylcoumarin (V) (Knoevenagel, *Ber.*, 1898, **31**, 732). In accordance with this suggestion, 3-acetylcoumarin readily interacts with salicylaldehyde, etc., to produce a *perchlorate* indistinguishable from the substance formed directly from ethyl acetoacetate. Parallel results are obtained from 2-naphthol-1-aldehyde and ethyl acetoacetate (see experimental).

It appears likely that decarboxylation as described by Löwenbein and Katz (*loc. cit.*) only occurs when the α -carbon atom of the β -ketonic ester is not part of an intact methylene group, for, in contrast with the formation of 2-phenyl-3-methylbenzopyrylium perchlorate from ethyl α -methylbenzoylacetate observed by these authors, it is now found that ethyl benzoylacetate behaves essentially similarly to its acetyl analogue and under the standard treatment does not give 2-phenylbenzopyrylium perchlorate (VIII) but instead is largely transformed into 3-benzoylcoumarin (VII) :



Replacement of salicylaldehyde by 2-naphthol-1-aldehyde causes production of 3-benzoylnaphthacoumarin in an analogous manner.

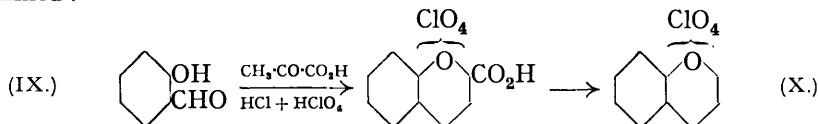
(c) The two methods available for the preparation of salts of benzopyrylium, namely, the cyclisation of *o*-coumaraldehyde by mineral acids and the direct condensation of salicylaldehyde with acetaldehyde under the influence of 70% sulphuric acid (Decker and von Fellenberg, *Annalen*, 1907, **356**, 298; 1909, **364**, 21), are not suited to large-scale

operation: the chief disadvantage of the latter method is the formation of a black resin, often in 90% yield.

o-Acetoxybenzaldehyde and *o*-acetoxybenzaldehyde diacetate readily give 2-phenylbenzopyrylium perchlorate under the standard conditions, but with acetaldehyde, its oxime, or its diacetate, or with acetal, the main product is the bakelite-like resin.

Coumarin, under the reduction conditions which transform xanthone into the ψ -base of the xanthylum salts, is recovered without change.

Since benzaldehyde and pyruvic acid form cinnamoylformic acid by treatment with dry hydrogen chloride (Claisen and Claparède, *Ber.*, 1881, **14**, 2472), the following sequence was examined:



2-Carboxybenzopyrylium perchlorate (IX) was prepared in moderate yield, but the yield of the salt (X) obtained by its decarboxylation was not better (calculated on the salicylaldehyde) than that obtained by the procedure described in this vol., p. 42.

EXPERIMENTAL.

Repetition of Chatterji and Ghosh's Experiment.—Acetylacetone (2 g.) and salicylaldehyde (2.5 g.) were dissolved in the minimum quantity of methyl alcohol and saturated with dry hydrogen chloride for 3 hours (temperature not above 0°). The mixture became dark red. After remaining for 2 days at the ordinary temperature, the crystals were collected and washed with alcohol. The total product was nearly all extracted by hot acetic acid, and perchloric acid (70%, 15 c.c.) was added to the filtered clear solution. On cooling, a brown-black powder (ca. 0.5 g.) was obtained, m. p. 115—125° (raised by admixture with the substance, m. p. 135—140°, described below) (Found: C, 60.0; H, 4.2. Calc. for C₁₉H₁₅O₇Cl: C, 58.4; H, 3.8%).

Direct Formation of 3-Acetyl-2-o-hydroxystyrylbenzopyrylium Perchlorate (as II).—A mixture of salicylaldehyde (1.2 g.) and acetylacetone (1.0 g.) in anhydrous ether (40 c.c.) containing perchloric acid (70%, 4 c.c.) began to develop a red colour spontaneously; it was saturated with dry hydrogen chloride and left for 2 days. Filtration and ether-washing then afforded 1.1 g. of a red-black powder, m. p. 130—135° (raised by admixture with the following product, m. p. 135—140°).

When 2 mols. of salicylaldehyde (2.4 g.) were treated as described above, the yield was increased to 2.1 g.; the perchlorate was again dark red and amorphous and did not crystallise satisfactorily from any solvent. The best specimen had m. p. 135—140° (Found: C, 59.1; H, 4.1. C₁₉H₁₅O₇Cl requires C, 58.4; H, 3.8%).

3-Acetyl-2-methylbenzopyrylium Perchlorate (as I) (?).—Salicylideneacetylacetone (Knoevenagel and Arnot, *loc. cit.*) (2 g.) was dissolved in anhydrous ether (50 c.c.) and saturated with hydrogen chloride (ice-cooling). Perchloric acid (70%, 5 c.c.) was then added, and the mixture kept for 24 hours. The small golden-brown needles (ca. 0.5 g.) formed had m. p. 145—150° and depressed the m. p. of the perchlorate previously mentioned (Found: C, 51.0; H, 4.0. C₁₂H₁₁O₆Cl requires C, 50.2; H, 3.8%).

3-Acetyl- and 3-Benzoyl-quinaldine.—In the preparation of these bases described by Stark (*Ber.*, 1907, **40**, 3427; 1909, **42**, 717) it is better, after the prescribed 48 hours' boiling under reflux, to add an excess of water, wash the oil formed by decantation (it can be solidified by cooling), extract it with much light petroleum, and evaporate the resulting solution (dried with sodium sulphate) until crystallisation begins. The constitution allotted to the condensation product from benzoylacetone depended merely upon the results of a potash fusion. Alkaline hypiodite solution is apparently without action upon the substance, whereas, in contrast, 3-acetylquinaldine readily gives rise to iodoform, in complete agreement with the formulation of Stark.

Condensation of Ethyl Acetoacetate with Salicylaldehyde.—A solution of ethyl acetoacetate (1.3 g.) and salicylaldehyde (1.3 g.) in ether (40 c.c.) containing perchloric acid (70%, 4 c.c.) was saturated with hydrogen chloride. After 2 days, the bronze-red needles were collected and washed with ether (yield, 1.6 g.; m. p. 285—290°).

Repetition of the above procedure with 2 mols. of salicylaldehyde (2.6 g.) gave the same perchlorate (3.4 g.) in a slightly purer condition, m. p. 299—305° (Found : C, 57.9; H, 3.0%). It was sparingly soluble in all the common solvents, but formed orange plates, m. p. 300—305°, from hot nitrobenzene.

Synthesis of the previous salt. (a) Equivalent quantities of salicylaldehyde (1.3 g.) and ethyl acetoacetate were mixed and treated with two drops of piperidine. Crystallisation began almost at once; after 3 days the mass was pressed on porous tile and crystallised from slightly diluted alcohol. It formed pearly plates of 3-acetylcoumarin (2.4 g.), m. p. 116—117° (Found : C, 70.3; H, 4.25. Calc. : C, 70.2; H, 4.2%).

(b) 3-Acetylcoumarin (1.4 g.) was mixed with salicylaldehyde (1 g.), anhydrous ether (30 c.c.), and perchloric acid (70%, 4 c.c.) and saturated with hydrogen chloride. After several days the orange perchlorate (VI) was collected (4.3 g., m. p. 260—280°) and recrystallised from acetic acid-nitrobenzene; m. p. 300—305° (not depressed by admixture with the salt obtained directly from salicylaldehyde and ethyl acetoacetate above) (Found : C, 57.6; H, 2.9. $C_{18}H_{11}O_7Cl$ requires C, 57.6; H, 2.9%).

Condensation of 2-Naphthol-1-aldehyde and Ethyl Acetoacetate.—A mixture of the aldehyde (2 equivs.) and the ester (1 equiv.), treated as in the above cases, formed an orange powder, which could be crystallised from much nitrobenzene and had m. p. over 300° (Found : C, 65.8; H, 3.3. $C_{26}H_{15}O_7Cl$ requires C, 65.7; H, 3.16%). This substance was synthesised from 3-acetylnaphthacoumarin (from ethyl acetoacetate and 2-naphthol-1-aldehyde in the presence of a few drops of piperidine) and an equivalent amount of the naphtholaldehyde by the general method.

Condensation of Salicylaldehyde and Ethyl Benzoylacetate.—The keto-ester (1.9 g.), with salicylaldehyde (1.2 g.) and ethereal perchloric acid as before, was left saturated with hydrogen chloride for 3 days; much of the ether had then evaporated. The solid residue, after pressing on porous tile and several crystallisations from alcohol, had m. p. 129—130° (alone or mixed with authentic 3-benzoylcoumarin prepared as described by Knoevenagel and Arnot, *Ber.*, 1904, 37, 4497).

Analogous treatment of a mixture of 2-naphthol-1-aldehyde and ethyl benzoylacetate similarly afforded 3-benzoylnaphthacoumarin, m. p. 207—208° after recrystallisation from acetic acid (Found : C, 79.8; H, 4.1. Calc. for $C_{20}H_{12}O_3$: C, 80.0; H, 4.0%).

Formation of 2-Phenylbenzopyrylium Perchlorate.—Mixtures of acetophenone (0.01 g.-mol.) and *o*-acetoxybenzaldehyde (prepared by the method of Rivals, *Compt. rend.*, 1897, 124, 369) or its diacetate (Perkin, *Annalen*, 1868, 146, 371) (0.01 g.-mol. in each case) were dissolved in dry ether (40 c.c.) and saturated with hydrogen chloride. After 24 hours the yellow-orange plates were filtered off and crystallised from acetic acid; m. p. 179° (alone or mixed with an authentic specimen) (Found : C, 58.6; H, 3.7%). *o*-Methoxybenzaldehyde was recovered unchanged from a mixture of the above type after 2 days.

Condensation of Salicylaldehyde with Pyruvic Acid.—(a) *Acid conditions.* A mixture of salicylaldehyde (1.2 g.) and pyruvic acid (0.9 g.), dissolved in either acetic acid (15 c.c.) or anhydrous ether (25 c.c.), was saturated with hydrogen chloride at 0°. The development of a deep red colour was slower in the former solvent than in the latter, but after 4 days' standing at the ordinary temperature both solutions yielded on filtration and washing, etc., about 0.3 g. of a yellow-green crystalline powder, m. p. 230—235° (decomp. with efferv.) (Found : C, 44.2; H, 3.1. $C_{10}H_7O_7Cl$ requires C, 43.7; H, 2.6%). 2-Carboxybenzopyrylium perchlorate is sparingly soluble in hot or cold water, giving a pink solution, but dissolves in sodium carbonate or dilute sodium hydroxide solution with production of a yellow-brown coloration.

Attempted decarboxylation. The perchlorate (1 g.), dissolved in glycerol (40 c.c.), was heated at 200—210° until the evolution of carbon dioxide ceased. Dilution of the bright red solution with water and the addition of much aqueous perchloric acid produced a brown precipitate (0.1 g., m. p. 230—240°), which gave approximately the correct analysis for *benzopyrylium perchlorate monohydrate* (Found : C, 43.9; H, 3.8. $C_9H_7O_5Cl \cdot H_2O$ requires C, 43.5; H, 3.6%).

(b) *Alkaline conditions.* A mixture of pyruvic acid (12 g.) and salicylaldehyde (12 g.) was added to 10% caustic soda solution (800 c.c.) and kept for 3 weeks. Acidification then liberated only salicylaldehyde (9 g.).

Condensation of Pyruvic Acid with Piperonal.—A mixture of pyruvic acid (9 g.), piperonal (14 g.), and 10% sodium hydroxide solution (600 c.c.), *i.e.*, a slight molecular excess of pyruvic acid, was left at the ordinary temperature for 12 days. The resulting yellow solution was filtered, extracted with benzene, and acidified with dilute sulphuric acid. The precipitate

crystallised from dilute alcohol in yellow needles, m. p. 161—162° (after preliminary darkening) (Found : C, 60.1; H, 3.7. $C_{11}H_8O_3$ requires C, 60.0; H, 3.6%).

The experiments on the condensation of ethyl acetoacetate with salicylaldehyde were begun in collaboration with Mr. J. Pearson, M.Sc.

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