

THE CONDENSATION OF ALDEHYDES WITH MALONIC ACID

Part XV. Condensation of 5-Bromosalicylaldehyde and of 3: 5-Dibromosalicylaldehyde: Influence of Dissimilar Groups

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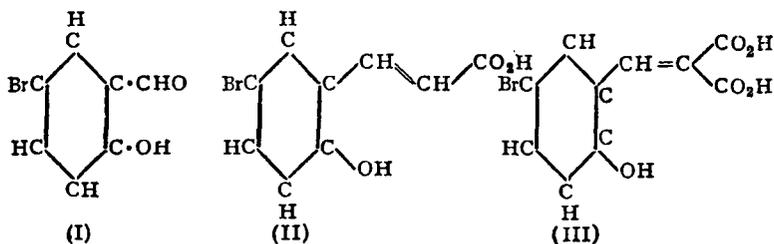
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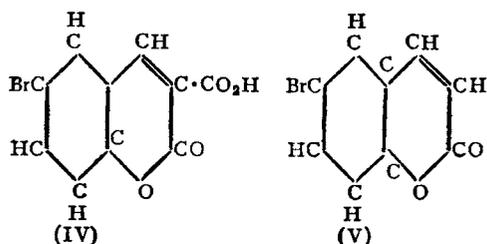
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IN Part XIV¹ it was shown that the presence of two nitro-groups on the aromatic ring, as in 2:4-dinitrobenzaldehyde, made the condensation with malonic acid extremely slack and it was only after many attempts that the yield of 50% of the theoretical was obtained. It is possible that two nitro-groups in different positions from the above might have behaved differently.

In Part XIII,² it has been shown that the influence of a chloro- or a bromo-group present on the aromatic ring of the aldehyde affected the reaction very favourably, as regards both the speed and the final yield, which includes its purity also. In Part I³ it was shown that salicylaldehyde gave about 51% yield only with a small trace of pyridine: the question may be asked, if a chloro- or a bromo-group were placed on the aromatic ring in salicylaldehyde, would the yield be increased? The investigations described in this paper give data for an answer in the affirmative.

Two bromo-salicylaldehydes have been condensed here with malonic acid, in the presence as well as in the absence of pyridine-traces. Three different products have been obtained from each of the aldehydes, while a fourth was obtained from each by Perkin's method. On the whole the yields in the aldehyde-malonic acid condensations have been much higher than those obtained by Perkin's method, and are also greater than the 51% obtained from the simple salicylaldehyde-malonic acid condensation, though in no case full theoretical yields are obtained as in the condensations with the chloro- and bromo-benzaldehydes.²

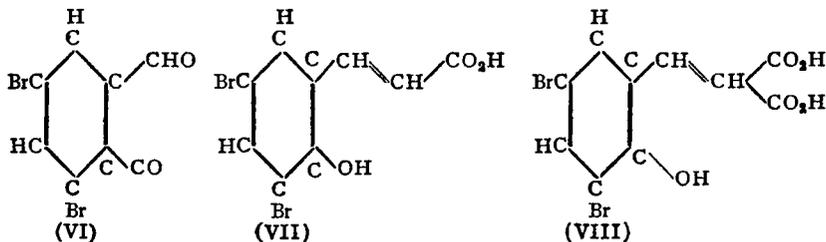


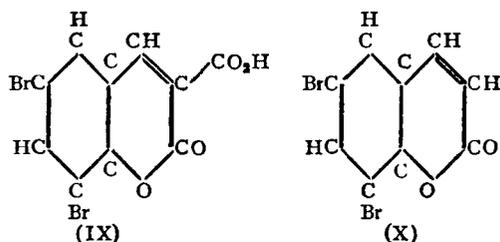


The 5-bromosalicylaldehyde (I) took some time to condense with malonic acid in the presence of pyridine, difficulties being caused by the sublimability of the aldehyde below the water-bath temperature. The sublimated amount was repeatedly scraped off and added to the reacting mass or was washed down with a drop or two more of pyridine. After prolonged heating 5-bromo-orthocoumaric acid (II) was obtained, but the yield was between 50 and 58%. 5-Bromosalicylidene-malonic acid (III) was also formed and was discovered in the filtrate of the bromo-orthocoumaric acid. It was only about 20–25% of the theoretical, but the total yield of the two would be about 78%, which is better than that from the ordinary salicylaldehyde.

As the decarboxylating action of pyridine is well known it was expected that the condensation in the entire absence of pyridine might give more of the dibasic 5-bromosalicylidene-malonic acid (III). However, the main bulk of this condensation was 6-bromo-coumarincarboxylic acid (IV), which melted at 200° and which came out in yields of 92·5%. It was accompanied by another still higher melting product, m.p. 241°, which was too little to be properly investigated. It however melted with effervescence. This was not 6-bromocoumarin (V), which was obtained by following Perkin's method and which melted at 164°.

Condensations with the 3:5-dibromosalicylaldehyde (VI) were a little less difficult, as the sublimation was much less and could be controlled more easily. Perkin's method gave the expected 6:8-dibromocoumarin (X), m.p. 176°. When pyridine was present three products were obtained, two of which were the expected 3:5-dibromo-orthocoumaric acid (VII) and the 3:5-dibromosalicylidene-malonic acid (VIII), melting at 187–189° and 158°, or





157–159°, respectively. These have been identified, but the third, melting at 327° or above, was all used up in purification and qualitative tests. It did not appear to have either a hydroxy or an aldehyde or a carboxylic group and had to be left over for the time. Condensation in the absence of pyridine gave as before 6:8-dibromocoumarincarboxylic acid (IX), in yields of about 74%.

Experimental

*Preparation of 5-Bromosalicylaldehyde.*⁴—5 Grams salicylaldehyde were dissolved in 9.6 c.c. (10 g.) of glacial acetic acid. The flask was placed in freezing-mixture and a solution of bromine 1.8 c.c. (6.6 g.) in glacial acetic acid was added drop by drop with constant stirring. The 5-bromosalicylaldehyde was at once precipitated and washed and dried. The weight of the crude product on drying was 6.5 g., i.e., 82.5% of theory. Recrystallised from dilute alcohol, it melted at 105° (the expected m.p. was 104–105°⁴).

*Condensation by Perkin's method: the Preparation of 6-Bromocoumarin.*⁵—2 G. 5-bromosalicylaldehyde, 4 g. freshly fused sodium acetate and 6 c.c. acetic anhydride were mixed and heated in a flask for five hours at 180–190°. It set to a solid mass at the end of 4.5 hours. The mass was repeatedly extracted with hot water until it gave no colour with ferric chloride. It was then repeatedly washed with ether until that also ceased giving colour with ferric chloride. The white mass left behind melted at 155–165°. It was dissolved in hot caustic soda and reprecipitated by dilute hydrochloric acid. Recrystallised from absolute ethyl alcohol it melted at 164°. (160°, Simonis⁴). The yield was 1 g. or 50%.

Condensation with Malonic Acid with a Trace of Pyridine.—5-Bromosalicylaldehyde 3 g., malonic acid 2.1 g. and 8 drops of pyridine were heated on an oil-bath at 95° for two hours and then at 100–105° for nearly 18 hours. About 8 drops more of pyridine had to be added during the course of this heating. There was much effervescence and the mixture liquefied in the first hour. The sublimed aldehyde was frequently scraped and thrown back into the flask or returned to the mixture by a drop or so of pyridine. After two hours the liquid became quite clear, effervescence had stopped and the

temperature was raised to 100–105°. Gradually the clear liquid became viscous and then set to a solid. The flask was cooled overnight and the contents were extracted with sodium bicarbonate (10%) solution. On acidifying the extract a white precipitate was obtained, which was filtered and washed with water. It melted at 145–148°. Crystallised from ethyl acetate and benzene, it melted at 150–152°. The yield was 50–55%.

It melted without effervescence, gave no colour with ferric chloride but decolorised Baeyer's reagent. Bromine found 32·5%, *bromo-orthocoumaric acid* $C_9H_7O_3Br$ requires 32·9%.

The filtrate was concentrated and on cooling deposited crystals which were removed and the mother-liquor on shaking up with ether and distilling off the ether gave more crystals. These melted at 170°, and on recrystallisation from ethyl acetate and benzene it melted at 175°. It melted with effervescence, gave no colour with ferric chloride and decolorised Baeyer's reagent immediately. A small portion of it was kept in an oil-bath at 180°: it melted and the effervescence continued for some time. After about 15 minutes it was taken out and, on cooling and reheating, melted at 148–150°. When mixed with the bromo-orthocoumaric acid, m.p. 150–152°, the melting-point did not change at all. Bromine found 27·57, 27·58%: *5-bromosalicylidene-malonic acid* $C_{10}H_7O_5Br$ requires 27·87%. Equivalent weight, found by titration with potassium hydroxide, 148·3; required = 143·5. The yield was about 24%, the total yield being about 78%.

Condensation without any Reagent: *6-Bromo-Coumarincarboxylic Acid* (IV)—3 G. 5-bromosalicylaldehyde and 2·1 g. malonic acid were mixed up and heated on the water-bath for 9 hours and then for 8 hours on an oil-bath at 100–105°. The sublimed aldehyde was scraped and added on from time to time. There was plenty of effervescence and after about two hours an opalescent liquid was formed. The mixture never became a clear transparent liquid. One hour after it had solidified again, the temperature was raised up by a change of the bath. The product at the end was extracted with ether to remove the unreacted aldehyde. A grey solid remained undissolved which was filtered off. In the crude condition it melted at 195–200° and weighed 3·7 g. Recrystallised from hot benzene, the melting-point rose only slightly to 200°. It was soluble in hot water and acetone as well, and insoluble in ether.

This experiment was repeated several times, and it was found that only six hours' heating on a water-bath was sufficient to give the same yield, *i.e.*, 92·5%, of the first solid, m.p. 200°, which was the *6-bromocoumarincarboxylic acid*: Bromine, found = 29·43, 29·44%, the acid $C_{10}H_5O_4Br$ requires 29·74%. It melted without effervescence and gave no colour with ferric chloride. It decolorised alkaline permanganate.

When the ethereal extract was treated with sodium dicarbonate solution, it gave much effervescence: excess was then added and the two layers separated. On acidification, the lower layer gave a solid white substance, m.p. 237° (dec.) (y. = 0.3 g.).

This high-melting substance melted at 241° on further purification, but melted with effervescence. It was not in sufficient amount for a clear identification.

*3-5-Dibromosalicylaldehyde.*⁶—5 g. salicylaldehyde were taken in a flask and to this were added 17.5 g. of bromine (a little more than 2 mol. proportion) drop by drop and with vigorous shaking. The flask was kept at room temperature for two days with occasional shakes: on the third day the whole mass had set to a solid and was taken out with about 500 c.c. or more of water. This was washed free of the excess of bromine. Recrystallised from dilute alcohol it melted at 82–84° (m.p. 83°)⁶. Yield about 87% of the theoretical.

*Condensation by Perkin's method: 6-8-Dibromocoumarin.*⁷—1.4 G. dibromosalicylaldehyde, 2 g. fused sodium acetate and 3 g. acetic anhydride were mixed and heated in the usual way, 170–180°, when the whole mass solidified at the end of three hours. The cold mass was washed with plenty of water, the residue was dried and washed with ether repeatedly till the washing gave no colour with ferric chloride. The residue was dried and recrystallised from rectified spirit. It melted at 176°. Yield about 33%. (6:8-Dibromocoumarin melts at 174–176°).⁷

Condensation in the Presence of Pyridine: 3:5-Dibromo-salicylidenemalonic Acid and 3:5-Dibromo-orthocoumaric Acid.—Very many condensations had to be tried to get conditions of good yield, as three different substances were found to occur in the product of this single reaction. Higher temperatures than 100° gave better yields of a substance which seemed to melt at about 300°, but has not been identified. Two other products 3:5-dibromosalicylidenemalonic acid (VIII) and 3:5-dibromo-orthocoumaric acid (VII) were also formed, but the amounts of their yields varied greatly with the temperature and the manner of heating. On the other hand ordinary water-bath heating for several hours even gave poor yields and much of the original aldehyde was found remaining unaffected but mixed up with resin.

2.8 G. dibromosalicylaldehyde, 1.4 g. malonic acid and 6 to 8 drops of pyridine were mixed in a flask and the whole was heated on an oil-bath at 110° for 4 hours. There was much effervescence and the mixture changed into a thick viscous mass, a little aldehyde that had sublimed was washed in with a drop or two of pyridine. The temperature was gradually raised to 125°,

and then the whole was left to itself overnight. The next day the temperature was raised up to 135°, and after one hour quickly to 160°. A solid mixed with much viscous matter appeared to have been formed and the heating was stopped. To the cold flask ether was added when much dissolved, leaving behind a solid which in the crude condition melted at 260°–270°. It was found insoluble in most of the usual organic solvents. Pyridine however dissolved it readily but gave crystals that were very impure and sticky. After a recrystallisation from pyridine-benzene, the substance was washed with dilute hydrochloric acid which removed some of its colour. The substance was then washed with alcohol, then with alcohol plus hydrochloric acid and finally with water to remove the acid. It was finally washed with alcohol and ether. It was now white in colour, and on heating began to get black at 290° and decomposed finally with effervescence at 295–300°. It was again treated with pyridine and benzene, and a little alcohol was added: after two days clear white crystals came out which on drying melted at 323–327°, becoming dark at 310°. It was insoluble in sodium bicarbonate solution and gave no effervescence with it. In fact it gave no indications of the presence of a hydroxy or an aldehyde or a carboxyl group, though it showed bromine.

From the ether-extract the two acids were separated. Addition of sodium bicarbonate solution to it gave effervescence, so excess was added and it was allowed to remain for a couple of hours when white crystals of a sodium salt came out. These were filtered off, treated with hydrochloric acid and with water. The solid obtained after recrystallisation melted at 185–187° without effervescence. This was *dibromo-orthocoumaric acid*, soluble in ether, alcohol, etc., but insoluble in benzene (hot or cold). Found Bromine = 49·38%, the acid $C_9H_6O_3Br_2$ requires 49·68%. The best yield = 31%.

The filtrate contained the soluble sodium salt of the dibromosalicylicidenemalonic acid, which was decomposed by dilute hydrochloric acid. It melted with effervescence at 140–150°, but on recrystallisation from alcohol, it melted at 157–159°. Heated alone on a naked flame for some time it gave off carbon dioxide and was changed into the monobasic acid, m.p. 187–189°. Heating with pyridine also brought about the same change. Found Bromine = 43·28%, the acid $C_{10}H_6O_5Br_2$ requires 43·71%. The best yield = 22%.

Condensation in the Absence of any Condensing Reagent: 3:5-4:6-Dibromo-coumarincarboxylic Acid (IX).—3:5—Dibromosalicylaldehyde 1·4 g. and malonic acid 0·7 g. were mixed and heated together for 5 hours on a water-bath and then for one hour in an oil-bath at 130°. In another experiment the heating was at 130° at the beginning but was then lowered to 110–120° after the whole mass had melted, the total amount being six hours. The

product in both cases was the same and the yield also was the same about 76%. The product was extracted with ether, when the dibromocoumarin-carboxylic acid was left undissolved. It was recrystallised from alcohol and melted at 224–226°. The ethereal extract was a mixture of the same acid with some of the unreacted aldehyde. Found Bromine = 45.72%, the acid $C_{10}H_4O_4Br_2$ requires 45.97%. It appeared to be dimorphous; crystallised from alcohol, it came out in white needles, and from benzene it came out in cubes.

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Summary

5-Bromosalicylaldehyde and 3:5-dibromosalicylaldehyde have both been condensed with malonic acid in the presence of pyridine as well as in its entire absence, and the yields are on the whole greater than were obtained from the condensation of salicylaldehyde with malonic acid in the presence of pyridine, the highest being 92.5%. Perkin's reaction gave different products altogether and in much smaller yields.

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