

CONDENSATION OF MALONANILIC ACID WITH ALDEHYDES

Part VII. Condensation with 5-Nitro-piperonal, 6-Bromopiperonal,
5-Bromovanillin and 5-Bromoveratraldehyde:
Influence of several dissimilar Groups

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THE influence of single groups like the hydroxy, methoxy, nitro, methyl and the haloid present on the ring of the aromatic aldehyde, when the aldehyde is condensed with malonic acid and with malonanilic acid, with or without pyridine, has been sufficiently obvious in the work described in the earlier papers of the two series. The general observation has been that the hydroxy, particularly in the orthoposition to the aldehyde group, is the most deterrent, the hydroxy in other positions is less so, the methyl in the para is still less, the methoxy and the nitro are only very slightly so, while the chloro and the bromo are distinctly favourable to quicker reaction and larger yields.

In the last paper, Part VI¹, condensations were described where the aldehyde had several groups that were either alike or different, and as in the aldehyde-malonic acid condensation, so, with of course differences of degree, in the aldehyde-malonanilic acid condensation, the groups that are alike have reinforced the influence of the single group, while dissimilar groups have modified the influence of one another. In the present paper the study of these condensations with malonic acid has been extended to still more complicated aldehydes, that is to aromatic aldehydes having even a larger number of groups, *e.g.*, to 6-nitro-piperonal and 6-bromopiperonal, and to 5-bromovanillin and 5-bromoveratraldehyde. It must be stated that here the situation is no longer as simple or as clear as before and that the generalisation holds but without uniformity; the features are already too complex to permit the results to be easily predictable or understandable.

We may take piperonal for instance, Piperonal-malonic acid condensations, conducted in the presence of a trace ($=0.15$ or about $1/6$ mol.) of pyridine, have been among the most successful of the series (Vahidy and Pandya, 1935²): these are understandable as the two hydroxy groups are

far away from the aldehyde and are completely replaced by methylenedioxy group. With malonanilic acid, the condensation gave two different products, one in the absence and the other in the presence of pyridine-trace, *viz.*, 70.7% of the piperonylidene-malonanilic acid and 90% of the 3:4-methylenedioxcinnamanilide respectively (Ittyerah and Pandya¹). The 6-nitro- and the 6-bromo-piperonal give results where the maximum yields are still comparable. 6-Nitropiperonal gives, in the absence of pyridine, 78.9% yield, made up of 30.9% acid and 48% cinnamanilide, while, with the pyridine-trace, it gives 76.9% of the cinnamanilide alone. The maximum is thus distinctly below the 90%, again showing that the nitro group is not so very favourable in the pyridine-trace condensation as it is in the Perkin's condensations.³ It may also be noted that the maximum yield with the pyridine-trace needed eight hours' heating on waterbath: with decreased heating (*e.g.*, five hours) the yield was less, *viz.*, 74.6%, composed of 16.9% acid and 57.7% cinnamanilide. A stronger base like piperidine in traces induced resinification (which happened so much in the condensation of dinitrobenzaldehyde⁴), from which only 16% (3.2% acid and 12.8% cinnamanilide) could be isolated.

The influence of the bromine group is clear in 6-bromopiperonal, where bromine occupies the same position that the nitro group did. The more powerful effect is seen in the maximum yield of 90.9% of the cinnamanilide obtained with a trace of piperidine: the pyridine trace gave a little less yield than the nitroderivative, however, namely, 63%, made up of 40% acid and 25% cinnamanilide. With glacial acetic acid, there was no decarboxylation, but the yield was 78.3% of the acid. A strange part here was that in the absence of any of the condensing reagents mentioned above, no product was obtained, much of the aldehyde being recovered unchanged or sublimed.

The efficiency of bromine-group was expected to show itself very decisively in the bromine derivatives of vanillin and veratraldehyde, which both were prepared from vanillin. As protocatechuicaldehyde gave little condensation-product with malonanilic acid¹, vanillin with one hydroxy group methylated gave 19.0% acid and 59.5% cinnamanilide, respectively in the absence and presence of pyridine¹, and veratraldehyde with no hydroxy group gave 36.7% acid and 91.8% anilide respectively,¹ higher yields still were looked forward to from their bromo-derivatives. But 5-bromovanillin and 5-bromoveratraldehyde did not sustain this expectation.

5-Bromovanillin gave no reaction when there was no condensing reagent: and gave no acid product, whatever condensing agent was used. With

piperidine-trace it gave 28·7%, with glacial acetic acid (Haydruck's method⁵) also 28·7%, with pyridine-trace 57·5%, with pyridine-piperidine at room temperature (three weeks, Vorsatz' method⁶) also 55·7% of the cinnamanilide, while when heated with the pyridine-piperidine mixture it only gave tar. The bromo-derivative here gave less than vanillin while the expected acid did not make its appearance at all.

5-Bromoveratraldehyde has however done almost the reverse: it gave a slightly higher yield of the acid in the absence of any condensing agent, *viz.*, 49·2%, compared with 36·7% from the unbrominated aldehyde, but with pyridine or piperidine it simply went into resin from which nothing useful could be isolated.

Possibly 6-bromovanillin and 6-bromoveratraldehyde might show better results: at least they could compare better with 6-bromopiperonal.

The products described above and in the Experimental are all new. Identical or very similar conditions of condensations have been tried. Greater modifications are being tried in order to avoid resin-formation if possible.

Of these four aldehydes, only two 6-nitro-piperonal and 6-bromopiperonal have so far been condensed with malonic acid, when they gave 93 and 81% yields respectively (unpublished, Miss R. Pandya), in the presence of a trace of pyridine.

Experimental

Condensation with 6-Nitropiperonal

6-Nitropiperonal was prepared by the method described by Pandya and Verghese.⁷ The usual procedure of the experiments was similar to what has been described earlier, with occasional differences that have been mentioned.

With no Condensing Agent.—The 6-nitropiperonal and malonanilic acid were heated together (1 : 1 mol.) on a water-bath for five hours. The acid and the anilide both were obtained here in yields of 30·9 and 48% respectively. The 6-nitro-3:4-methylenedioxy-cinnamanilide came out in pale yellow needles melting at 198°. Found N = 8·92%, the cinnamanilide $C_{16}H_{12}O_5N_2$ requires 8·97%. It was recrystallised from acetone and alcohol. The acid recrystallised from alcohol came out in long pale yellow needle crystals, melting at 238°. Found N = 8·24%, 6-nitro-3:4-methylenedioxy-benzylidenemalonanilic acid $C_{17}H_{12}O_7N_2$ requires 7·86%. It also gave a bright yellow silver salt which gave. (Found Ag = 24·06%, the

salt $C_{17}H_{11}O_7N_2$. Ag requires 23.3%.) Ray and co-workers⁸ describe the acid but give 230° (dec.) as the melting point of it, which must be less pure.

With a Trace of Pyridine.—With the usual trace of pyridine and five hours' heating on water-bath, the same two products, but now in a different ratio, came out: the acid was less 16.9%, and the anilide 57.7%, making the total yield 74.6%. Heating on the waterbath for eight hours changed the whole product into the cinnamanilide, which was a little higher 76.9%. Higher temperature, such as 110–115° induced resinification and reduced the yield.

With Piperidine trace.—The mixture became dark even at the ordinary temperature, while heating gave much tar and little product (about 5% acid and 13% anilide).

Condensation with 6-Bromopiperonal

The 6-bromo-piperonal was prepared from piperonal by the method of Parijs.⁹ It melted at 129°; yield = 45%.

Without a Condensing Agent.—There was no reaction, even when the temperature was raised to 120°.

*With Glacial Acetic Acid*⁵.—1.2 g. 6-bromopiperonal, 0.9 g. malonanilic acid and 1 c.c. glacial acetic acid were heated together on a water-bath. The sodium carbonate gave a sodium salt that was insoluble even when digested with hydrochloric or sulphuric acid. Ammonium carbonate was therefore used which gave a 78.3% yield of the 6-bromo-piperonylidene-malonanilic acid, melting at 226° (dec.). Though the acid came out from alcohol in pale yellow needles, it turned deep yellow just before melting. (Found: N = 3.56%, the acid $C_{17}H_{12}O_5$ NBr requires 3.59%. Found Br = 20.91, 20.33%, the acid requires 20.51%.)

With a Trace of Piperidine.—Heated on waterbath for five hours and extracted with alcohol, gave the 6-bromo-3:4-methylenedioxcinnamanilide, melting after recrystallisations from alcohol at 191°. (Found N = 4.18%, $C_{16}H_{12}O_3$ NBr requires 4.05%. Found Br = 23.32%, the anilide requires 23.12%. Yield = 90.9%.)

With a Trace of Pyridine.—It gave total yield of 65% made up of 40% acid and 25% anilide.

Condensation with 5-Bromovanillin.—

The 5-bromovanillin was prepared from vanillin by the method of Dakin¹⁰: m.p. 164°, yield 90%.

Without any Condensing Reagent.—No reaction happened at 100°. At 125° the whole mass became liquid, after which the temperature was gradually lowered. There was no reaction however.

With Pyridine.—Five hours on waterbath gave no acid, but only the 5-bromo-4-hydroxy-3-methoxy-cinnamanilide in shining colourless crystals melting at 200–201°. Yield 57·5% (Found N = 4·11%, the cinnamanilide $C_{16}H_{14}O_2NBr$ requires 4·02%.) It dissolved in soda or potash solutions giving yellow solutions. It dissolved in concentrated sulphuric acid also giving a yellow colour, which on heating changed first to green then to dark.

With a Trace of Piperidine.—Much tarry matter from which about 28·7% of the cinnamanilide was recovered.

With Pyridine-Piperidine Mixture.—The product was tarry, even after four hours' heating Vorsatz's method⁶ gave 57·5 of the cinnamanilide. 0·6 g. 5-bromovanillin, 0·9 g. malonanilic acid, 1·4 g. pyridine and 2 drops piperidine were mixed and kept at room temperature (20–25°) for three weeks, when a solid cake was obtained. This was treated with ammonium carbonate solution but it had no action. The residue was the cinnamanilide (yield = 57·5%).

*With Glacial Acetic Acid*⁵.—Eight hours on waterbath, when the mass became yellow and green. Only 28·7% of the anilide was obtained.

Condensation with 5-Bromoveratraldehyde.

This aldehyde was prepared from bromovanillin by ordinary methylation by means of dimethyl sulphate and potassium hydroxide. It came out in 82·6 yield, melting at 62°.

Without any Condensing Agent.—2·5 g. 5-bromoveratraldehyde and 1·8 g. malonanilic acid were heated in a flask on waterbath for five hours. After fusion and effervescence, the colour changed from straw yellow to pale green. Sodium carbonate solution dissolved it, leaving some unacted aldehyde. The alkali extract lost its colour when washed with ether. The sticky mass set on cooling and when recrystallised from alcohol, came out as colourless crystals melting at 198° (dec.). Yield = 49·2%. (Found N = 3·56%, the 5-bromoveratrylidenemalonanilic acid $C_{18}H_{16}O_5NBr$ requires 3·44%.) With longer time at lower temperature, twelve hours at 90° only 39·3% of the acid was isolated.

With a Trace of Pyridine.—Five hours on waterbath or with a higher temperature, a nonacid viscous mass was obtained from which nothing could be separated. So also with a pyridine-piperidine mixture on three hours' heating nothing could be separated.

Summary

Malonanilic acid have been condensed under different conditions, with 6-nitro-piperonal, 6-bromopiperonal, 5-bormovanillin and 5-bromoveratraldehyde. The reactions with the first two give yields that may be more or less expected. The last two give some unexpected features, particularly 5-bromoveratraldehyde from which the expected cinnamanilide has not yet been isolated or obtained. All the products described in the paper are new.

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