

CONDENSATION OF MALONANILIC ACID WITH ALDEHYDES

Part V. With *o*- and *p*-Chlorobenzaldehydes and *m*-Bromobenzaldehyde: the Influence of the Halogens

BY KANTILAL C. PANDYA AND (MISS) RASHMI BALA PANDYA
(Chemistry Department, St. John's College, Agra)

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IN Part I of this series¹ the use of a trace of pyridine or piperidine, found so interesting in aldehyde-malonic acid condensations,² was extended to aldehyde-malonanilic acid condensations and was found to give, on the whole, very much larger yields than those obtained by the pyridine-piperidine-mixture method. In Part II³ it was shown that the condensation-reaction is very much influenced by two factors, *viz.*, the presence or the absence of pyridine and by the nature of the group present on the ring of the aromatic aldehyde, and also according to its position with regard to the aldehyde group. This latter observation was further corroborated in Parts III⁴ and IV,⁵ wherein the influence of the hydroxy,⁴ the nitro⁵ and the methyl groups⁶ was described. In the present paper are described the observations indicating the influence of the halogens, chlorine and bromine, when present on the ring with the aldehyde.

The whole subject of aldehyde-malonic acid condensation is thus capable of being investigated and reviewed under three distinct heads :—

- i. The influence of the presence or absence of pyridine.
- ii. The influence of the various groups and their positions on the aromatic ring of the aldehyde.
- iii. The influence of the groups on the acid molecule, *i.e.*, the groups combined with the reactive methylene.

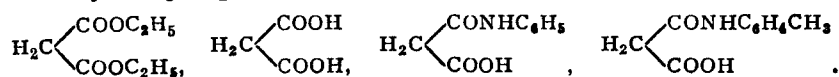
Regarding i, it may be stated that, as observed by earlier workers also, condensation does take place in the entire absence of pyridine or any other condensing reagent. But it is exceedingly slow: quantitative yields, however, are obtainable under carefully controlled conditions⁷: the product, in the case of malonic acid, is generally the dibasic acid derivative of malonic acid, and, in the case of malonanilic acid, the corresponding derivative of that acid. The use of a trace of pyridine, in both the condensations,

not only speeds up the condensation, but gives excellent yields, of high purity, often in quantitative proportions, and further causes decarboxylation, the product in each case having lost one molecule of carbon dioxide. The malonic acid and malonanilic acid condensations are in this respect very similar.

Regarding ii also the two condensations appear to be comparable. The influence of groups is seen when results and yields are compared with those obtained with unsubstituted benzaldehyde and malonic or malonanilic acid. The hydroxy group, particularly in the ortho-position to the aldehyde group, exerts the most depressing effect in both the condensations, but yields very greatly improve when the hydroxy group is in the *m*- or the *p*-position. There is a further improvement in the case of the methyl (only the *p*-methyl investigated so far⁶) and the methoxy groups; the latter group, when in the *m*- and *p*-positions, give, in the presence of pyridine, over 90% yields. The nitro group gives quantitative yields when in *m*- and *p*-positions, while the yield is still very high, but definitely less, about 70%, when it occupies the ortho-position.

The chloro- and the bromo-groups had given a very striking increase in the aldehyde-malonic acid condensation⁷ as well as in the Perkin's condensation-method⁸: in the aldehyde-malonanilic acid condensation the same effect is seen, though without the same uniformity, the yields from the *p*-chlorobenzaldehyde falling even a little below that obtained from benzaldehyde. The highest yield about 99% is obtained from *m*-bromobenzaldehyde; *vide* Table.

Regarding iii, the observation might have been, but was not quite, expected. It was first made when the malonic ester behaved differently from the malonic acid, ethyl malonate giving, under identical conditions, either no yields with certain aldehydes, or giving very poor yields after a very long time.^{7,9} The malonanilic acid, as stated, gives comparable good yields: occasionally the action is quite rapid. When the $-\text{CO.NHC}_6\text{H}_5$ group is further altered to $\text{CO NHC}_6\text{H}_4\text{CH}_3$, the yields show an all-round improvement, as shown by the condensations of *o*-, *m*- and *p*-malon-toluidic acids (still unpublished, Ittyerah). Thus there is a perceptible difference in the reactivity of the methylene group itself according to what its distant neighbours are:



Experimental

Condensation of p-Chlorobenzaldehyde in the presence of a trace of Pyridine: p-Chlorobenzylidene-malonanilic acid and p-Chlorocinnamanilide.

1.4 g. Malonanilic acid, 1.8 g. *p*-chlorobenzaldehyde and 0.14 c.c. pyridine (1 : 1 : 0.16 mol.) were heated together in a flask on water-bath. The mixture became a homogeneous liquid in about ten minutes and effervescence started after another ten minutes. The heating was continued for four hours. On cooling a dirty yellow solid was seen, which did not liquefy when the flask was again heated on the water-bath on the next day. Treatment with sodium carbonate solution removed only a part of the product. The remaining cinnamanilide, separated by filtration, was washed, first with water and then with ether to remove any unreacted aldehyde : at the end of this, it came out as a colourless solid weighing 1.8 g. and melting at 172°. On recrystallisations from alcohol, it came out in long colourless needles. After being air-dried for some hours, they melted at 180°. (Yield about 70%.) It decolourised Baeyer's reagent.

The *p*-chlorobenzylidene-malonanilic acid was recovered from the sodium carbonate extract by acidification, when it came down as a white solid, melting between 180–90°. Recrystallisation from dilute alcohol or benzene made it melt sharp at 190°. (Yield about 6%.)

Condensation in the absence of any condensing agent.

0.9 g. Malonanilic acid and 0.7 g. *p*-chlorobenzaldehyde were heated as before on the water-bath for eight hours, when a green solid was left on cooling. It was extracted with 10% sodium carbonate solution when the bulk of it went into solution leaving only a small amount of a greenish blue powder. This was filtered off and dried : on melting it became colourless, or it melted to a colourless liquid. On purification by alcohol it became colourless and melted at 180°, being identical with the cinnamanilide described above. (Yield 8%.)

The sodium carbonate extract, when acidified, also gave a light blue coloured solid melting at 190–200°. A second treatment with a quantity of sodium carbonate solution, followed by acidification, gave a colourless solid, which on the usual crystallisation melted at 192°. Though colourless when freshly crystallised, it became bluish on exposure to air in a moist condition : it also became blue just before melting and the hot melt was also bluish. The melting was accompanied with effervescence. (Yield = 66%.)

p-Chlorocinnamanilide : Found Cl = 13.63%; C₁₅H₁₂ONCl requires 13.79%.

p-Chlorobenzylidenemalonanilic acid : Found : Cl = 11.28%, C₁₆H₁₂O₃NCl requires 11.77%. Molecular weight, Found = 304.3; required 307.5.

Condensation with o-Chlorobenzaldehyde : o-Chlorobenzylidene-malonanilic acid and o-Chlorocinnamanilide. In the presence of a trace of Pyridine.—1.79 g. malonanilic acid, 1.40 g. *o*-chlorobenzaldehyde and 0.14 c.c. pyridine were heated as usual on a water-bath for four hours. There was considerable effervescence and a solid began to be formed within the first hour. The anilide and the acid were separated as before. The yields were, the acid = 13%, and the cinnamanilide = 70%. In another condensation piperidine replaced pyridine, when on three hours' heating nearly the same yields were obtained: acid = 6.6%, and the anilide = 70%.

Without any Catalyst.—2.7 g. Malonanilic acid and 1.4 g. *o*-chlorobenzaldehyde were heated together on a water-bath: a solid with a greenish tinge started coming out within the first hour and the action appeared to have been completed in three hours in all, when the heating was stopped. Only a small amount of cinnamanilide (about 2–4%) was obtained, while the acid came out in nearly theoretical yield.

Crude *o*-chlorobenzylidenemalonanilic acid was fairly pure, melting at about 220°: after recrystallisation from alcohol the melting-point remained unchanged at 225°. Found: Cl = 11.99%, required 11.77%. Found: Molecular weight by titration = 300.6, required = 301.5.

The crude *o*-chlorocinnamanilide melted over a long range, 150–70°. Recrystallisation from different solvents and refluxing the alcoholic solution with animal charcoal, filtering and cooling gave the first crop melting at 176° (recrystallised from ethyl acetate, m.p. 176–77°). A second crop came out from alcohol, which, after repeated recrystallisations from alcohol, melted at 149–50°, which rose to 153–54° when the crystallisations were repeated with hot ethyl acetate. It was clear that both were cinnamanilides: analysis gave Cl, in the higher melting, found = 13.68%, in the lower melting, found = 13.98% : required = 13.79%.

Moreover, when a small quantity of the *o*-chlorobenzylidenemalonanilic acid was carefully decarboxylated by a gentle heating for a short time just above the melting point, effervescence took place, the melted liquid turned yellow first and then green, a small part undergoing decomposition. After removing the decomposed portion, the clear residue was found to be a mixture of the two, separable into the two forms already obtained and identifiable with them by the mixed-melting-point method.

Condensation with m-Bromobenzaldehyde: m-Bromobenzylidene-malonanilic acid and m-Bromocinnamanilide. In the presence of a trace of pyridine.—0.92 g. *m*-Bromobenzaldehyde, 0.9 g. malonanilic acid and 0.07 c.c. pyridine were heated together on a water-bath. Effervescence was observed, but no

solid came out when the heating was stopped after four hours. It was left overnight and treated in the usual way next morning, though the solid product was not washed with ether as it was completely soluble in ether. After washing with water it was taken on a porous plate and dried. The crude cinnamanilide melted at $112-20^{\circ}$: recrystallised from alcohol, the m.p. rose to $128-29^{\circ}$. Yield = 87%, with only a trace of the acid. In another and more careful experiment, the product came out as a highly viscous liquid which on keeping in water became solid. No acid was obtained from the sodium carbonate washing and extract, but the yield of the cinnamanilide was over 99%.

In the absence of any condensing agent.—1.79 g. malonanilic acid and 1.85 g. *m*-bromobenzaldehyde were heated together on water-bath for eight hours. After four hours a green solid had started coming out. Treatment with sodium carbonate dissolved the main portion of the product, though without effervescence. About 10% (the cinnamanilide) was left undissolved, which was repeatedly treated with sodium carbonate solution and finally separated. On recrystallisation, however, it melted at a very much higher temperature, namely at 162° , instead of at $128-29^{\circ}$. The filtrate containing the sodium salt was shaken up with ether to remove any aldehyde still remaining, and acidified, when the bromobenzylidenemalonanilic acid came down as a green precipitate. On recrystallisation from alcohol, it melted at $186-88^{\circ}$. (Yield = 72%.) The pure acid came out in colourless needles.

The lower-melting cinnamanilide gave: Found Br = 26.30: $C_{15}H_{12}ONBr$ requires 26.49%. The higher-melting was too little for analysis and no more of the bromobenzaldehyde was obtainable. The *m*-bromobenzylidenemalonanilic acid: Found Br = 22.9%: $C_{16}H_{12}O_3NBr$ requires 23.1%.

Summary

The condensation of malonanilic acid with *o*- and *p*-chloro- and *m*-bromobenzaldehydes is described. The reaction is fairly rapid and gives very good yields. The products, in the absence of any catalyst and in the presence of a trace of pyridine, are in a line with those obtained from other aromatic aldehydes. The production of isomeric *o*-chlorocinnamanilides, and probably of two isomeric *m*-bromocinnamanilides, in these condensations is rather remarkable. The influence of the halogen, chlorine and bromine groups, in the positions mentioned, is as uniform as was noticed in the aldehyde-malonic acid condensations.

TABLE

The heating was throughout on water-bath, though the hours of heating were not always identical : usually five hours, about one to two for the nitro and much more for the hydroxy.

Aldehyde	Yields % with a trace of base			Without any		
	Anilide	Acid	Total	Acid	Anilide	Total
Benzaldehyde	89.7	0	89.7	86.0	0	86.0
<i>o</i> -Hydroxy-	37.8	0	37.8	30.2	0	30.2
<i>m</i> - "	79.6	0	79.6	52.0	0	52.0
<i>p</i> - "	79.6	0	79.6	18.0	0	18.0
<i>p</i> -Methyl-	71.7	0	71.7			
Piperonal	56.2	3.7	59.9			
<i>o</i> -Methoxy-	84.6	0	84.6	26.7	46.1	73.8
<i>m</i> - "	92.3	0	92.3	26.7	53.8	80.5
<i>p</i> - "	92.3	0	92.3	47.0	23.0	70.0
<i>o</i> -Nitro-	70.9	0	70.9	32.1	37.7	69.8
<i>m</i> - "	67.0	0	67.0	30.2	70.7	100
<i>p</i> - "	74.6	0	74.6	77.2	22.4	99.6
<i>p</i> -Chloro-	70.0	6	76	66.3	8	74.3
<i>o</i> - "	70	13	83	90	0	90
<i>m</i> -Bromo-	99	0	99	72.3	10	82.3

REFERENCES

1. Mehra and Pandya .. *Proc. Ind. Acad. Sci.*, 1938, 7, 369.
2. Pandya and collaborators .. *J. Ind. Chem. Soc.*, 1934, 2, 823 ;
Proc. Ind. Acad. Sci., 1935, 1, 440,
and subsequent numbers.
3. Ittyerah and Pandya .. *Ibid.*, 1941, 13, 119.
4. ————— .. *Ibid.*, 1941, 13, 122.
5. ————— .. *Ibid.*, 1941, 13, 461.
6. Mehra and Pandya .. *Ibid.*, 1939, 9, 510.
7. Pandya and Miss Pandya .. *Ibid.*, 1941, 13, 112.
8. Lock and Bayer .. *Ber.*, 1939, 72, 1064.
9. Kurien, Pandya and Peter .. *Proc. Ind. Acad. Sci.*, 1935, 1, 775.