

CONDENSATION OF MALONANILIC ACID WITH ALDEHYDES

Part IV. With *o*-, *m*- and *p*-Methoxybenzaldehydes: The Influence of a Hydroxy-group

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IN the condensations of malonic acid with aromatic aldehydes in the presence of a trace of an organic base, attention has already been drawn to the retarding or restricting influence of the hydroxy-group, which, when present on the ring, lowered the yield of the corresponding cinnamic acid derivative.¹ It has also been observed that the yields became quantitative when the hydroxy-group was replaced by the methoxy-² or the methylene-dioxy-group.³ A similar observation is now made regarding condensations with malonanilic acid: in Part II of the present series,⁴ the yields obtained from the reactions of malonanilic acid on *o*-, *m*- and *p*-hydroxybenzaldehydes were on the whole significantly low. Of the nine condensations studied, one gave only 18% yield, three gave approximately 33%, one gave 51%, two gave slightly above 60% and only two gave about 80%. The nitrobenzaldehydes on the other hand gave remarkably better yields, some times reaching up to the theoretical (Part III).⁵ The present paper describes the condensations with the corresponding methoxybenzaldehydes, which show, as expected, a rise in the yields up to about 92% of the theoretical.

As in so many well-known cases, and also as in the malonic acid condensations, the hydroxy-group represses the activity and the reaction of the aldehyde-group to the greatest extent, as indicated by the yields of the reaction-products, when it is in the ortho-position to the aldehyde.⁶

As in Parts I, II and III,^{7, 4, 5} the condensations have been carried out in three different conditions, (i) by Robinson's method as adopted by Ray and collaborators,⁸ *i.e.*, the pyridine-piperidine method; (ii) by our pyridine-trace method, and (iii) in the absence of any base. The results are in conformity with those obtained earlier, *i.e.*, the highest yields are obtained with the trace-method; and secondly, the products are exclusively or mainly the corresponding cinnamanilide, when a base is used, and are exclusively or mainly the corresponding benzylidene-malonanilic acid, when no base is present: in other words, the presence of even a trace of an organic base favours decarboxylation as well as the condensation reaction.

In the case of the methoxybenzaldehydes the condensations have been studied under a greater variety of conditions than usual, different temperatures and periods of heating being employed and different organic bases being also used. Triethanolamine has been used for the first time in these condensations, but the result it gave has not been encouraging.

The condensation of malonanilic acid with *p*-methoxybenzaldehyde (pyridine-piperidine) has already been carried out by Ahluwalia, Haq and Ray,⁸ who mention the products but do not state the yields. The condensation by their method is repeated for purposes of comparison of the yields, which are lower than those obtained by the trace-method (*vide* also 7). The *m*- and *o*-methoxybenzaldehydes are condensed with malonanilic acid for the first time and the products are new.

Experimental

Condensation with p-Methoxybenzaldehyde.

Without any Base. (*p*-Methoxybenzylidene-malonanilic acid and *p*-Methoxycinnamanilide).—1.4 g. of the aldehyde and 1.8 g. of malonanilic acid (1:1 mol.) were mixed and heated in a flask on a water-bath. The whole soon melted to a brown liquid, gradually turned green, and solidified in about 1.5 hours. Heating was continued for 5 hours in all. The flask was then cooled, the product extracted with 10% sodium carbonate solution, and the unreacted aldehyde separated. The alkaline extract, when acidified with concentrated hydrochloric acid, gave a pale green solid, which, on recrystallisation from aqueous alcohol, came out as white needles, melting at 212°. (*p*-Methoxybenzylidenemalonanilic acid, m. 213° dec. Ray and workers,⁸ *loc. cit.*)

The acid gave a silver salt, melting with decomposition at 200°. (Ag, Found: 26.67%; C₁₇H₁₃O₄NAg requires 26.79%.) Yield, 1.8 g., *i.e.*, 60% of theory.

In another experiment, the heating was continued for eight hours, which gave the acid as well as some of the decarboxylated cinnamanilide, the total yield being slightly higher (about 70%, made up of 47% acid and 23% anilide).

With Pyridine-Piperidine Mixture.—0.7 g. aldehyde, 0.9 g. malonanilic acid, 2 g. pyridine and 2 drops of piperidine (1:1:5:trace) were heated together at 50–60° for one hour, the product allowed to cool, acidulated water added, and the whole kept for some time. The water was then decanted off, the residue was treated with sodium carbonate solution, and the acid and the anilide were separated as above. The acid weighed 0.7 g. (47% of theory) and the anilide 0.4 g. (30.8% of theory), the total yield being about 77.8%.

p-Methoxy-dibromocinnamanilide.—The cinnamanilide (m.p. 140°) decolorised both Baeyer's reagent and bromine water. A saturated solution of this in alcohol was made and treated with bromine (two atoms) in alcohol or water: the mixture was thoroughly shaken and kept for about four hours, when a white solid had separated out, which was filtered off and recrystallised from dilute alcohol. It came out in white needles, melting at 180°. (Bromine, Found: 39.08%; C₁₆H₁₄O₂NBr₂ requires 38.83%.)

With a Trace of One Base.—Condensations were carried out with a trace of pyridine at different temperatures and for different periods of time. Condensations were also conducted with traces of piperidine, lutidine and triethanolamine respectively: the best yields were found when piperidine in a trace was used. The results are all given in a table below (Table I).

TABLE I

Base	Temperature	Time of heating	Yields %		
			Acid	Anilide	Total
None	Water-bath	5 hours	60	0	60
"	"	8 hours	47	23	70
Pyridine-piperidine ..	50°-60°	1 hour	47	30.8	77.8
Pyridine-trace	Room	1 week	0	0	0
	60°-70°	12 hours	26.7	23	49.7
	Water-bath	5 "	20	46	66
	"	8 "	0	61.5	61.5
	110°-20°	1.5 "	0	77	77
Piperidine-trace	Room	1 week	20	8	28
"	Water-bath	5 hrs. or 8	0	92.3	92.3
	110°-20°	1.5 "	0	92.3	92.3
Lutidine-trace	Water-bath	5 "	0	69.2	69.2
	"	8 "	0	84.6	84.6
Triethanolamine-trace ..	"	8 "	13.3	38.4	51.7

Condensation with m-Methoxybenzaldehyde.

Without any Base. (*m*-Methoxybenzylidene-malonanilic Acid and *m*-Methoxy-cinnamanilide).—1.4 g. of the aldehyde and 1.8 g. of the malonanilic acid (1:1 mol.) were heated together on a water-bath for five hours. The reactants soon melted to a clear liquid, a slight effervescence was noticed and

there was a copious evolution of water vapour. After three hours the liquid began to set to a solid green mass. At the end it was extracted as usual. The acid, recrystallised from aqueous alcohol, came out as colourless needles, melting at 182° (dec.), and decolorising Baeyer's reagent and bromine water. (N, Found : 4.86%; $C_{17}H_{14}O_4N$ requires 4.73%.) The acid gave a silver salt, which starts decomposing at 210° and completely decomposes with frothing at 220° (Ag, Found : 26.72%; $C_{17}H_{13}O_4NAg$ requires 26.79%). The *m*-methoxy-cinnamanilide, recrystallised (dilute alcohol), melted at 107° and also decolorised Baeyer's reagent and bromine water (N, Found : 5.3%; $C_{16}H_{14}O_2N$ requires 5.5%). The yields of the acid and the anilide were 1.2 and 0.8 g. respectively. On longer heating the acid diminished, and the anilide increased, the total also being slightly greater. (*Vide* Table II.)

With Bases.—Condensations were carried out as above in the presence of pyridine-piperidine mixture (Ray's method) and of a trace of pyridine, piperidine, lutidine and triethanolamine respectively. The highest yields were obtained with a trace of pyridine. The detailed results are set in Table II below:—

TABLE II

Base	Temperature	Time of heating	Yields %		
			Acid	Anilide	Total
None	Water-bath	5 hours	40	30.8	70.8
		8 "	26.7	53.8	80.5
Pyridine-piperidine ..	60°-70°	1 hour	40	23	63
Pyridine-trace ..	Water-bath	5 hours	0	77.5	77.5
		8 "	0	92.3	92.3
		2 "	0	77.5	77.5
Lutidine-trace ..	Water-bath	8 "	0	38.4	38.4
Triethanolamine-trace ..	"	8 "	13.3	30.8	44.1

Condensation with o-Methoxybenzaldehyde.

Without a Base. (*o*-Methoxybenzylidene-malonanilic Acid and *o*-Methoxy-cinnamanilide).—Condensations were carried out as before. A greenish solid product came out which by the usual treatment gave (i) the acid, colourless flat crystals, melting at 228°, which was the acid (N, Found : 4.86%; $C_{17}H_{14}O_4N$ requires 4.73%); (ii) the anilide came out as colourless needles, melting at 164° (N, Found : 5.72%; $C_{16}H_{14}O_2N$ requires 5.55%). Both the

products were crystallised from dilute alcohol, and decolorised bromine water as well as Baeyer's reagent. As can be seen from Table III below, the total yield was good, 70%, which increased to about 74% on longer heating.

With Base.—With pyridine-piperidine, the yield was about the same, 63%, in one hour's heating, but on account of the shorter time of heating, the acid was about twice as much as the anilide.

A trace of pyridine or of piperidine gave still better yields, up to about 85%, though requiring longer heating-time. Lutidine and triethanolamine, in a trace, gave lesser yields even with full eight hours' heating.

TABLE III

Base	Temperature	Time of heating	Yields %		
			Acid	Anilide	Total
None	Water-bath	5 hours	47	23	70
	„	8 „	26.7	46.1	73.8
Pyridine-piperidine ..	60–70°	1 hour	40	23	63
Pyridine-trace	60–70°	12 hours	6.8	61.5	68.3
	Water-bath	8 „	0	84.6	84.6
	110–20°	2.5 „	0	77	77
Piperidine-trace	Water-bath	8 „	0	77	77
	110–20°	2.5 „	0	84.6	84.6
Lutidine-trace	Water-bath	8 „	0	38.4	38.4
Triethanolamine-trace ..	„	8 „	13.3	38.4	51.7

The following table (Table IV) gives consolidated figures of the maximum yields, of the acids, of the anilides and of the total, obtained respectively from the three hydroxy-benzaldehydes and the three methylated benzaldehydes. (The former figures are taken from the results already published⁴.)

In every case the maximum yield of the acid was obtained when no base or any other condensing agent was used, and so also the highest anilide-yield was obtained when only pyridine, or sometimes piperidine was used in a trace. Except in the case of *m*-hydroxybenzylidene-malonanilic acid, the yields are decidedly superior when the hydroxy-group is changed to the methoxy.

TABLE IV

Aldehyde	Acid	Anilide	Total
<i>o</i> -Hydroxy-benzaldehyde	0·0	37·8	37·8
<i>o</i> -Methoxy- „	47·0	84·6	84·6
<i>m</i> -Hydroxy- „	51·8	79·6	79·6
<i>m</i> -Methoxy- „	40·0	92·3	92·3
<i>p</i> -Hydroxy- „	18·0	79·6	79·6
<i>p</i> -Methoxy- „	60·0	92·3	92·3

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