

THE CONDENSATION OF ALDEHYDES WITH MALONIC ACID IN THE PRESENCE OF ORGANIC BASES.

Part III. The Condensation of Salicylaldehyde with Ethyl Malonate.

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IN Part I¹ the condensation of various aldehydes with malonic acid in the presence of pyridine alone has been studied. It was found that, while, in the case of several aromatic aldehydes, the condensation took place easily and with theoretical yields, in the presence of pyridine in molecular proportion, by modifying the methods of Staudinger and Florence,² all the methods broke down in the case of aromatic hydroxy-aldehydes like salicylaldehyde and vanillin. But by employing pyridine in traces, not only these hydroxy-aldehydes but many other aldehydes as well allowed condensation to take place. Thus pyridine in traces is quite comparable with Knoevanagel's famous reagent piperidine in traces.³

Many other organic bases have now been studied and have been found to have a similar, though not an equal, efficiency in promoting these condensations. Thus salicylaldehyde could be condensed, in the presence of many other organic bases in traces, with malonic acid, as shown in Part II.⁴

Knoevanagel⁵ also condensed salicylaldehyde with malonic ester by simply leaving the two together for several days with a trace of piperidine. In the present paper it has been shown that here also pyridine and several other organic bases could take the place of piperidine.

On repeating Knoevanagel's experiment it was seen that it required five days at room temperature to give a 55% yield with piperidine. The product was solid coumarin-carboxylic ester. With this as a rough guide, experiments were started with pyridine. It was soon found that different

¹ Kurien, Pandya and Surange, *Journ. Ind. Chem. Soc.*, 1934, 11, 823.

² Florence, *Bull. Soc. Chem.*, 1927, 41, 440.

³ Knoevanagel, *Ber.*, 1898, 31, 2596.

⁴ Azhar Ali Khan, Kurien and Pandya, *Proc. Ind. Acad. Sci.*, 1935, 1, 440.

⁵ Knoevanagel, *Ber.*, 1898, 31, 2593; D.R.P. 97734.

conditions were required. When piperidine was used, a solid appeared in the flask within a few hours, but with pyridine no solid formation could be observed, and no condensation could be detected, even after as many as ten days. Investigations, made at different temperatures, showed some action and a low yield at temperatures of or above 100° C. (Table I.) Higher temperatures diminished the yield. The time of heating was then changed from 5 hours, when it was seen that the yield increased with time up to 18 hours of heating on the water-bath. Longer hours had either an adverse or no effect. (Table II.) The amount of pyridine used above was 0.15 mol. Other proportions, varying from 0.02 to 1 mol. were tried and the results were in a line with those obtained with malonic acid (Part II). The highest yield was obtainable only when pyridine was between 0.15 to 0.5 mol. Above or below that range, the yields were poor. (Table III.)

The best yield was 58 %, obtainable when 0.15 mol. of pyridine was added to the mixture of the aldehyde and the ester, the whole kept on water-bath for 18 hours (6 hours a day for 3 days), and then left at room-temperature for 3 days (*vide* Experimental).

Condensations with other bases were carried out under exactly the same conditions, the bases taken being:—quinoline, iso-quinoline, lutidine, α -naphthoquinoline, quinaldine, cinchonidine, dimethylaniline and diethylaniline.

Salicylaldehyde, reported to be so very reluctant to give these condensations,⁶ with pyridine-piperidine mixture, does actually give good yields, with a large variety of organic bases, on undergoing condensation with malonic acid as well as with ethyl malonate. It is also to be noted that while malonic acid does not enter into condensation with the base present in full molecular proportion (Part I), but breaks down into acetic acid and carbon dioxide immediately (Part II), the ester—probably on account of greater stability—does condense with salicylaldehyde, though giving no more than 18 % of the theoretical yield of the coumarin-carboxylate.

Experimental.

In all experiments 4 grams of Merck's or Schiller-Kahlbaum's pure ethyl malonate (freshly distilled, b.p. 197–199° C.) and 3 grams of Merck's pure salicylaldehyde were used. The organic bases also were purified as far as practicable.

Piperidine.—Knoevanagel's experiment was repeated as under. The aldehyde and the ester were taken as above, with 0.3 c.c. (0.15 mol.) of

⁶ Dutt, *Journ. Ind. Chem. Soc.*, 1925, 1, 298.

piperidine added and properly mixed. The flask was kept at room-temperature (20–23° C.) for five days, being frequently shaken. At the end of the time, the solid formed was separated, washed with alcohol and recrystallised from hot alcohol, when pale yellow crystals, m.p. 94–95° C. were obtained. (Knoevanagel, ethyl coumarin-carboxylate, 94–95° C.)

Pyridine.—Merck's pure pyridine, left over pure caustic potash for a few weeks, distilled (113–114.5° C.), was substituted in the same proportion. No solid was observed and no yield obtained even after 10 days. Heating on water-bath for 5 hours at various temperatures, 40°, 60°, 80° and 100° C. successively, also produced no sign of reaction. On raising the temperature further to 110° C., 0.5 gram (8 %) yield was obtained. In another experiment, the temperature was raised straight away, on an oil-bath, to 120° C. and maintained for six hours. The product, left overnight, was thrown on crushed ice, when a little solid separated. It was identified by its melting-point. Yield 1 gram or 17 %. Another lot was kept gently boiling by a naked flame for 4 hours, but in this case the yield diminished (8 %). (*Vide* Table I.)

TABLE I.
Pyridine 0.3 c.c. or 0.15 mol.

Temperature	Time of heating	Yield gram	Percentage
Room 20–23°	10 days	0	0
40°	5 hours	0	0
60°	5 „	0	0
80°	5 „	0	0
100°	5 „	0	0
110°	5 „	0.5	8%
120°	5 „	1	17%
Boiled on free flame	4 „	0.5	8%

Heating for different periods of time at 100° and 110° C. was then tried. It was found that longer hours at the water-bath temperatures gave a better yield, up to 55 %. In all cases the yields appreciably improved by keeping the mixture at room-temperature for about 3 days after the conclusion of

the heating. *Vide* Table II. Eighteen hours on water-bath seemed to be the most favourable condition.

TABLE II.
Pyridine the same.

Temperature	Time of heating	Yield gram	Percentage
110°	10 hours	2	35
100°	5 "	0	0
"	12 "	1	17
"	18 "	3.2	58
"	24 "	3	55

The effect of altering the proportion of pyridine was then studied and the results are to be found in Table III. The lowest yield of 9 % was obtained with 0.02 mol. of pyridine, which increased up to 58 %, when the

TABLE III.
Temperature of the boiling-water-bath, time 18 hours.

Pyridine quantity	Mol. proportion	Yield gram	Percentage
2 drops	0.02	0.5	9
4 "	0.04	1.0	18
6 "	0.06	1.0	18
8 "	0.08	1.0	18
10 "	0.1	1.2	22
0.3 c.c.	0.15	3.0	55
0.6 "	0.3	3.0	55
1.0 "	0.5	3.0	55
2.0 "	2.0	1.0	18

base was increased up to 0.5 mol. With a full molecular proportion, however, the yield went down to about 18 % only.

Other Bases.—The other bases were tried under the conditions of maximum yield with pyridine. As these had a range of 0.15–0.5 mol. of pyridine, it is possible that the other bases might give a better yield by slight changes in proportions used. Table IV gives some of the results. The highest yields obtained so far were 58 % with pyridine as well as with cinchonidine.

TABLE IV.

Base	Amount	Mol.	Yield gram	Percentage
Piperidine	0.3 c.c.	0.15	3	55
Pyridine	0.3 „	0.15	3.2	58
„	1.0 „	0.5	3	55
Quinoline	0.3 „	0.1	2.5	45
„	1.0 „	0.33	1.5	28
Iso-quinoline ..	0.3 „	0.1	2.5	45
Lutidine	0.3 „	0.12	2.7	49
„	1.0 „	0.4	2.3	40
α -Naphthoquinoline ..	0.3 „	0.05	2.5	45
Quinaldine	0.3 „	0.1	2.0	35
Cinchonidine ..	0.3 gram.	0.04	1.2	20
„	1.0 „	0.14	3.2	58

The last result was obtained by Mr. Ram Kumar Bountra, who also repeated some of the other condensations.