

# THE CONDENSATION OF ALDEHYDES WITH AMIDES.

## Part I. The Condensation of Salicylaldehyde.

BY KANTILAL C. PANDYA AND TEJPAL SINGH SODHI.

(From the Department of Chemistry, St. John's College, Agra.)

Received January 3, 1938.

THE condensations of aldehydes with acid amides have been studied by a very large number of workers and the literature is extensive. Often the condensation is brought about by merely heating the aldehyde with the amide alone: in other cases condensing agents of several kinds have been used, such as, hydrogen chloride, potassium hydroxide, potassium carbonate, diethylamine, triethylamine, sulphuric acid dilute, anhydrous sodium acetate with, or without, acetic anhydride. Frequently, the condensation has been carried out without a solvent. Reich<sup>1</sup> alone has used pyridine, but he has employed 1 to 1.5 mols. of pyridine for every mol. of the aldehyde and has generally carried out the condensations in sealed tubes by heating at high temperatures, about 180° C., and for 12 hours or so.

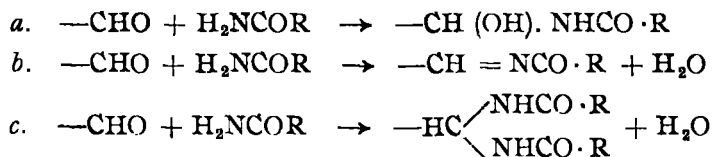
The observation made in this Laboratory, of the rôle of organic bases, and particularly of pyridine, as catalysts in promoting condensations of a different type, *viz.*, of the aldehydes with malonic acid, and yielding an exceedingly simple and successful method, of synthesising  $\alpha\beta$ -unsaturated acids,<sup>2</sup> prompted the inquiry whether the aldehyde-amide condensations also would be susceptible to similar catalytic influences. The perusal of the condensations of salicylaldehyde, which have all been conducted so far by means of heating with anhydrous sodium acetate only, and the fact that this was the aldehyde the study of whose condensation with malonic acid first led to the observation of the catalytic effect of pyridine,<sup>3</sup> made the choice of salicylaldehyde, as the first aldehyde to be studied in this series, altogether inevitable.

In order to make comparisons fair in respect of procedure and of yields, the earlier condensations have been repeated, *viz.*, the condensations of the aldehyde with benzamide, formamide and acetamide, achieved by heating with anhydrous sodium acetate by Cebrian<sup>4</sup> first, and later on by Titherley and Marples.<sup>5</sup> The latter authors have, however, confined themselves to only the first condensation, namely with benzamide, but have identified

the condensation-product correctly as salicylidene-benzamide. Our observations entirely confirm this structure in the case of this product as well as in the cases of the products obtained from other amides, which were identical in properties with those obtained by Cebrian with the same method. The condensations of salicylaldehyde were then repeated by the new method, namely, by heating in the presence of traces of pyridine, piperidine and lutidine respectively. The products were the same as before, namely, salicylidene-benzamide, salicylidene-formamide and salicylidene-acetamide. Propionamide and phenylacetamide were also tried for the first time, and they fell in a line with the other amides, giving salicylidene-propionamide and salicylidene-phenylacetamide, which are thus prepared for the first time.

The organic bases employed are thus as effective as sodium acetate: nay, they are even more, in several distinct ways. It was possible to carry out the reaction at a lower temperature than 160–70° C., so often employed with sodium acetate, resinification was thus reduced or altogether avoided, and the alkyldene-amides were uniformly cleaner, purer and in larger yields (*vide* tables). Moreover, the organic base was a true catalyst, as in every case condensation would occur even when the aldehyde and the amide were heated alone without the base or without any condensing reagent, but proceeded to a lesser extent during the same period of heating, or required much longer heating to give comparably good yields, as were obtained in the presence of a trace of the base.

With respect to the course of the reaction, Titherley and Marples<sup>5</sup> suggest three different possibilities:



where R is the alkyl or aryl radical in the acid amide. *a* is the simple aldol condensation, giving aldol-like products (Einhorn and others<sup>6</sup>). *b* is the straightforward condensation, eliminating water and giving, as in the present case, salicylidene-amides, or similar products. The *c* requires two molecules of the amide for every one of the aldehyde and gives the -bisamide, like benzylidene-bisbenzamide, and so on.<sup>7,1</sup> Similar products have also been obtained in our Laboratory, *viz.*, cinnamylidene-bisamides, by Mehra.<sup>8</sup> (The last paper will soon be published.)

The product in any condensation may, therefore, be any one of the above three types, or may be even a mixture of two or more. In the present case the structure is, beyond doubt, the one obtained exclusively by *b*.

Apart from the arguments given by Titherley and Marples,<sup>5</sup> a number of observations confirm the conclusion. The evolution of copious water-vapours rules out *a*. All our products instantly decolorise Baeyer's reagent in the cold, indicating unsaturation, and the reaction takes place between one molecule of the aldehyde and one of the amide, which rule out *c*. Further confirmation is given by analysis.

The salicylidene-amides are, at the end of the reaction in the flask, yellow or brown, transparent and often hard, looking very much like "organic glass". Their behaviour with solvents is peculiar, and it was difficult or impossible to crystallise them from any solvent. They gave a pink coloration with concentrated sulphuric acid, as noted by earlier workers.

Titherley and Marples<sup>5</sup> have separated the crude salicylidene-benzamide obtained by them into two isomers, the  $\alpha$ - and  $\beta$ -forms, as they are called. This observation is confirmed, and the two forms have been obtained as described, not only from the condensation carried out in the presence of anhydrous sodium acetate, but also from the products obtained from the condensations carried out in the presence of a trace of pyridine or of piperidine. The  $\alpha$ -form alone was, however, obtained when the condensation took place in the presence of a trace of lutidine as well as when it took place without the presence of any reagent whatever.

Salicylidene-formamide was more easily recrystallised than the others. It was also obtained in quantitative yields when lutidine was employed and also gave the sharpest melting-point in the series ( $98^{\circ}$  C.), and yet the crude product, left in a sample-tube, was found, after a few months, to have changed into a dark red resin.

#### EXPERIMENTAL.

##### Condensation of salicylaldehyde with benzamide.—

(i) *In the presence of anhydrous sodium acetate.*—Salicylaldehyde 10 g., benzamide 10 g. and sodium acetate anhydrous 6 g. (1 : 1 : 1 mol.) were mixed (Cebrian<sup>4</sup>) in a 250 c.c. open flask and heated on an oil-bath at  $140^{\circ}$  C. for five hours. At  $110^{\circ}$  C. copious vapours of steam came out and at  $120$ – $25^{\circ}$  C. the reacting mass became one clear liquid. No condenser was used. After five hours' heating, the flask was allowed to be cool and was filled up with 200 c.c. of water. The next morning the solid was taken out, crushed in a mortar with plenty of cold water, dried and weighed. Yield 14.2 g., or 77% of theory. Its properties were as described by Titherley and Marples<sup>5</sup> and it could be separated by means of acetone into the soluble or the  $\alpha$ -form

and the insoluble or  $\beta$ -form. On heating, the  $\alpha$ -form did not melt but started to decompose at 195–96° C. (Ti. and Mar. give 190°). The  $\beta$ -form started to decompose at 198–205° C. (Ti. and Mar. give 200°). In amount the  $\alpha$ -form was about twice that of the  $\beta$ -. A mixed melting-point showed no change, the decomposition starting at 195–96°.

(ii) *With a trace of pyridine.*—Salicylaldehyde 3 g., benzamide 3 g. and pyridine 0.285 g. (1 : 1 : 0.15 mol.) were heated in the same way in an open flask without a condenser, at 130–40° C., for three to four hours, and the flask was left to cool by itself overnight. Next morning the product was taken out with cold water, washed and dried. The dried product was not brown as in the preceding experiment but was yellow and weighed after purification 5.3 g., the yield being thus 96.4% of theory. It was identical with the product obtained by Cebrian's method and could be resolved in the same way into the  $\alpha$ - and the  $\beta$ -form.

(iii) *With a trace of piperidine.*—The experiment (ii) was repeated with 0.315 g. of piperidine instead of pyridine. The product and the yield were exactly the same, 5.3 g. or 96.4%.

(iv) *With a trace of lutidine.*—With 0.390 g. of lutidine, the yield, though still very good, was a little less, namely 4.4 g. or 80%. The product was brownish, dissolved completely in acetone and was thus the  $\alpha$ -form, without any admixture of the  $\beta$ -.

(v) *Without any reagent.*—Under the same conditions, but without any base or without sodium acetate, the product again was the  $\alpha$ -form alone. The yield on five hours' heating was 5 g. or 91% of theory, and was thus higher than was obtained by Cebrian's method above.

The acetone-soluble salicylidene-benzamide was found to contain N = 5.9%. Calc. N = 6.2%.

TABLE I.

Heated with	Proportions	Time	Temperature	Product	
				Wt. %	Yield Colour
Sodium acetate anhydrous	1 : 1 : 1 mol.	5 hrs.	140° C.	77	Brown ; pale yellow (pure)
Pyridine ..	1 : 1 : 0.15 ..	3-4 ..	130-40°	96.4	Yellow
Piperidine ..	" ..	" ..	"	96.4	"
Lutidine ..	" ..	" ..	"	80.0	Brown, $\alpha$ - only
Alone ..	1 : 1 : 0.0 ..	5 ..	"	91.0	Yellow, $\alpha$ - only

**Condensation with formamide.—**

(i) *With sodium acetate anhydrous.*—Salicylaldehyde 12 g., formamide 4 g. and anhydrous sodium acetate 6 g. were heated on the water-bath (according to Cebrian<sup>4</sup>) for five hours in an open flask; water vapour soon came off and the whole mass turned liquid. Treated as before, it gave a brown powder, weighing 5 g. (yield = 34 %), and melting at 90–1° C. After recrystallization from alcohol, the melting point rose to 98° C. (Cebrian gives 98°). It was lemon-yellow in colour, and resembled in properties, etc., the salicylidene-formamide described by previous workers.

(ii) *With a trace of pyridine.*—Salicylaldehyde 3 g., formamide 1 g. and pyridine 0.285 g. (1 : 1 : 0.15 mol.) were heated on a water-bath for eight hours, left overnight and the salicylidene-formamide extracted as usual. Yield 3.1 g. or 87% of theory. The heating had to be longer than usual, otherwise a viscous mass was formed and the yield was diminished.

(iii) *With a trace of piperidine.*—0.315 g. of piperidine was used instead of pyridine. Even after 8 hours' heating, the product was a dark brown viscous mass, which gave only 1.3 g. or 36.5% yield. The condensation was repeated with twice the molecular proportions of formamide, in order to replace the formamide lost on heating, but the result was not affected.

(iv) *With a trace of lutidine.*—With 0.390 g. of lutidine as the base, and with 8–10 hours' heating, the yield improved to 3.5 g. or 100%.

(v) *Without any reagent.*—Several experiments were made with changes in the period of heating. With 18 hours' heating the yield became 2.8 g. or about 81% of theory.

On analysis salicylidene-formamide gave N = 9.5 %. Calc. N = 9.5%.

TABLE II.

With	Proportions Molar	Temp.	Time of heating	Yield %	Colour
Sodium acetate anhydrous ..	1 : 1 : 1	100°	5 hours	34	Brown
Pyridine ..	1 : 1 : 0.15	„	8 hours	87	Lemon-yellow
Piperidine ..	„	„	„	36	Brown
Piperidine ..	1 : 2 : 0.15	„	„	36	„
Lutidine ..	1 : 1 : 0.15	„	8–10 hours	100	Yellow
Nothing ..	1 : 1 : 0.0	„	18 hours	81	„

**Condensation of salicylaldehyde with acetamide.—**

(i) *With sodium acetate anhydrous.*—Cebrian's experiment was repeated. 10 g. of the aldehyde, 5 g. acetamide and 6 g. anhydrous sodium acetate, heated at 140° C. for 4 hours, gave with the usual treatment 12.4 g. of salicylidene-acetamide (yield = 90 %). It was brown and amorphous, and after repeated purifications became lighter in colour; it did not melt but decomposed between 160° and 170° C. (Cebrian says 'turns brown and decomposes at 150° C.').

(ii) *With a trace of pyridine.*—Salicylaldehyde 3 g., acetamide 1.5 g. and pyridine 0.19 g., were heated for four hours at 130–40° C. The salicylidene-acetamide obtained weighed 3.8 g. (yield = 98 %).

(iii) *With a trace of piperidine.*—The same amounts of the aldehyde and the amide with 0.21 g. of piperidine, gave 3.5 g. or 93% yield.

(iv) *With a trace of lutidine.*—With 0.260 g. of lutidine and heating for 4–5 hours at 130–40° C., the yield was 3.5 g. or 98%.

(v) *Without any reagent.*—Heating alone at 140° C. for 5 hours gave a yield of 3.5 g. (93%).

Salicylidene-acetamide was found to contain N = 8.98%. Calc. N = 8.5 %.

TABLE III.

With	Proportions Molar	Temp.	Time	Yield %	Colour
Sodium acetate anhydrous ..	1 : 1 : 1	140°	4 hours	91	Yellow-brown
Pyridine ..	1 : 1 : 0.10	130–40°	„	98	Bright yellow
Piperidine ..	„	„	„	93	Dirty „
Lutidine ..	„	„	4–5 „	98	Yellow
No reagent ..	1 : 1 : 0.0	140°	5 hours	93	Brownish yellow

**Condensation of salicylaldehyde with propionamide.—**

(i) *With sodium acetate anhydrous.*—3 g. salicylaldehyde, 1.8 g. propionamide and 3 g. sodium acetate anhydrous were heated at 140° C. for 4 hours. Salicylidene-propionamide came out as a brown yellow amorphous powder, weighing 4.1 g., but containing some resinous matter, which was removed by means of pyridine, in which it did not dissolve. The filtered pyridine solution gave a bright yellow solid which was sparingly soluble in hot alcohol, but insoluble in most of the ordinary solvents. It resembled

the other products described above in almost all respects. The repeatedly purified solid did not melt but started to decompose at 190–95° C. After purification, the yield was 3.2 g. or 73%.

(ii) *With a trace of pyridine.*—Salicylaldehyde 1.2 g., propionamide, 0.7 g. and pyridine 0.12 g. on heating at 130–40° C. for 3–4 hours gave a bright yellow product, which was identical, weighing 1.5 g. = 88.2% of theory.

(iii) *With a trace of piperidine.*—With 0.13 g. of piperidine the same amounts of the aldehyde and the amide gave, under the same conditions, 1.3 g. or 76.4 % yield.

(iv) *With no reagent.*—Under the same conditions, the yield was 1.2 g. or 70.5%.

The salicylidene-propionamide gave on analysis:—C = 67.48 %, H = 6.21% and N = 7.6%. Calc. C = 67.7%, H = 6.2% and N = 7.9%.

TABLE IV.

With	Proportions Molar	Temp.	Time	Yield %	Colour
Sodium acetate anhydrous ..	1 : 1 : 1	140°	4 hours	73	Yellow
Pyridine ..	1 : 1 : 0.15	130–40°	3–4 hours	88.2	Bright yellow
Piperidine ..	..	..	..	76.4	..
No reagent ..	1 : 1 : 0.0	130–40°	..	70.4	..

#### Condensation of salicylaldehyde with phenylacetamide.—

Phenylacetamide was prepared (m.p. 154–55° C.) in a good yield and in a very pure condition by treating phenylacetic acid with thionyl chloride and then treating the acid chloride in the usual way with strong ammonia.

(i) *With anhydrous sodium acetate.*—Salicylaldehyde 2.4 g., phenylacetamide 2.7 g. and sodium acetate anhydrous 1.6 g. were heated for 4 hours at 140° C. and the salicylidene-phenylacetamide mixed up with some resin was taken out as usual. On purification the yield was found to be about 65 %.

(ii) *With a trace of pyridine.*—The same amounts of the aldehyde and the amide were heated with 0.285 g. of pyridine at 140°. As usual the water-vapours were given off and the whole mass became a liquid, which soon began to set again to a solid, indicating a quicker reaction. After 2–3 hours' heating, salicylidene-phenylacetamide was taken out as a lemon-yellow

powder. It resembled in properties the other members described above. After purification it melted at 110–14° C. The yield was 4.1 g. or 8.57%.

(iii) *With a trace of piperidine.*—0.315 g. of piperidine was used in place of pyridine, and the yield under the same conditions was 3.5 g. or 73%.

(iv) *With a trace of lutidine.*—With 0.390 g. of lutidine, the yield came up to 3.1 g. or about 65% after 5 hours' heating.

(v) *With no reagent.*—Heated alone for 4 hours, the two gave an yield of 2.8 g. or 58%.

The salicylidene-phenylacetamide gave on analysis:—Found: C = 75.23 %, H = 5.9 % and N = 5.8 %. Calc. C = 75.3 %, H = 5.3 % and N = 5.8 %.

TABLE V.

With	Proportions Molar	Time	Yield %	Colour
Sodium acetate anhydrous ..	1 : 1 : 1	4 hours	65	Brown
Pyridine ..	1 : 1 : 0.15	2–3 hours	85.7	Lemon yellow
Piperidine ..	..	..	73	..
Lutidine ..	..	4–5 hours	65	..
No reagent ..	1 : 1 : 0.0	4 hours	58	Brownish yellow

The heating was throughout at 140° C.

### SUMMARY.

The condensation of salicylaldehyde with five different amides has been studied, using anhydrous sodium acetate, a trace of an organic base as a catalyst or using no reagent whatsoever.

A comparison is made of the yields obtained, and it is found that the catalytic influence of a base promotes the reaction better, and gives a purer product than was obtained by the usual sodium acetate method.

### REFERENCES.

1. Reich, *Monatsch*, 1904, 25, 933, 967.
2. Azhar Ali, Kurien and Pandya, *Proc. Ind. Acad. Sci.*, 1935, 1, 440, etc.
3. Kurien and Pandya, *J. Ind. Chem. Soc.*, 1934, 9, 824.
4. Cebrian, *Ber.*, 1898, 30, 1592.
5. Titherley and Marples, *J.C.S.*, 1908, 93, 1933.
6. Einhorn and Ladisch, *Ann.*, 343, 265; Jacobson, *ibid.*, 157, 245, and so on.
7. Hofmann and Victor Meyer, *Ber.*, 25, 212, etc. Also Noyes, *J. Am. C. S.*, 1933, 55, 3493.
8. Mehra and Pandya, *Proc. Ind. Sci. Cong.*, 1938, Part III, Abstracts, 61.