

# THE CONDENSATION OF ALDEHYDES WITH AMIDES

## Part VII. The Condensation of Piperonal

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THE condensations of several aromatic aldehydes with about five of the common acid amides have already been reported with certain peculiarities of each. Thus the condensations of salicylaldehyde (Sodhi<sup>1</sup>) showed the great effect of a trace of pyridine in the condensations, as not only did it give larger yields than what were obtained by other methods, but so far the yields from salicylaldehyde have been the highest produced from any other aldehyde, being often almost quantitative. The condensations of *m*-hydroxy-benzaldehyde (Mehra<sup>2</sup>) with the same amides present a sharp contrast, as the organic base did not materially increase—it even caused some resin-formation—and the yields were uniformly poor and were actually nil with formamide and acetamide. In the case of *p*-hydroxy-benzaldehyde (Manzur<sup>3</sup>), the yields again increased, being very nearly as good as those obtained from salicylaldehyde, pyridine again playing some part, though not as great, in increasing the yields. All the products from these three sources were, however, quite similar, chemically and physically: physically they looked like 'organic glass', did not always give a good melting-point, though they analysed well, had a very limited solubility in the ordinary organic solvents and were more or less coloured. Chemically they were all of the benzylidene-mono-amide type, instantly decolorising Baeyer's reagent and bromine in solution, and giving characteristic colorations with concentrated sulphuric, and, often, with concentrated hydrochloric acid.

When next the methyl ethers of the three aldehydes were submitted to condensations with the same amides, there was a considerable difference, both in the nature and in the quantity of the condensation-products. Formamide did not condense with any of the three, and the other amides gave in all cases products that were saturated, that were of the benzylidene-*bis*-amide type, which crystallised and melted well, and the yields of which were either unaffected or unfavourably affected, by the presence of an organic base. The yields, though not bad, never exceeded 60% of theory (Mehra<sup>4</sup>).

It became a matter of interest to find out how piperonal would behave, because it is also a derivative of a dehydroxy-aldehyde, but with the two hydroxy groups replaced by one methylene-dioxy group instead of the two methoxy groups.

The condensations of piperonal with amides have not been met with in literature, and in this paper are presented the results of the condensations of piperonal with eight different amides. The products obtained are in a line with those obtained from the three methoxy-benzaldehydes, *i.e.*, they are all of the benzylidene-*bis*-amide type, all well-crystallisable high-melting substances, almost all colourless, and came out best when piperonal and the amide were heated alone, without pyridine. Here also formamide did not condense, though a variety of different conditions were tried. The yields were on the whole good: the lowest was 38% (with propionamide) and the highest 77% (with heptamide).

In the first condensation, different conditions have been tried, while in the case of the succeeding ones only the more promising conditions have been applied.

On the whole the aldehyde-amide condensations offer certain interesting but obvious contrasts in results as well as in the influence of the substituent groups with the aldehyde-malonic acid condensations that have been already reported in several parts.<sup>5</sup>

### *Experimental*

#### *Condensation with Benzamide—*

(i) *Without any Condensing Agent.*—(i) 1.5 g. piperonal pure and 1.21 g. benzamide (1/100th mol. each) were taken in a round-bottomed flask of about 50 c.c. capacity, well mixed and heated on the water-bath for three hours without a condenser. The whole mass melted to a chocolate-coloured liquid and some water-vapours were given out. It was then allowed to cool overnight; the solid mass was washed next morning with alcohol to remove the unreacted aldehyde and amide, and the white residue left was found to melt at 214° C. to a brownish liquid. This melting-point, which was so much higher than that of the amide or of the aldehyde, indicated that it was a condensation-product. On recrystallisation from alcohol, the m.p. rose to 221°. The yield was poor.

(ii) The same experiment was repeated but the heating was continued a little longer (five hours); the crude product melted at 215° and the yield was 1.4 g. The product had solidified during the heating.

(iii) The heating temperature was now 110–20° (oil-bath). The crude product was much cleaner, melted at 220°, melted after recrystallisation at 222°, and weighed 1.5 g.

(iv) The oil-bath temperature was kept at 130–40° C., but this made the product reddish, gave a lower melting-point 216° (crude) and decreased the yield to 1.2 g.

(v) The molecular proportions were now 1:2 mol., *i.e.*, 1.5 g. of the aldehyde and 2.42 g. of the amide were used. The heating at water-bath temperature was continued for five hours. The yield was poor, only 1.1 g. Much of the benzamide remained unacted.

(vi) The same quantities were heated on the oil-bath at 125–30° for six hours, and the yield increased to 2.4 g., which is 64.17% of the theoretical. This was the best yield obtained.

(ii) *In the Presence of Various Condensing Agents.*—1.5 g. of piperonal, 1.21 g. of benzamide and 0.1 c.c. of pyridine (1:1:0.12 mol.) were heated on the water-bath for five hours. The reacting mass did not resolidify during the heating, but was found solid next morning. The crude product was very impure (m.p. 203°) and the yield only 0.4 g.

When fused sodium acetate was tried (according to the method of Cebrian,<sup>6,7</sup> and Titherley and Marples) in 1:1:1 mol. proportions, under the same conditions as above, the product was very much coloured, melted (crude) at 205°, (purified) at 221°, but weighed only 0.1 g.

Acetic acid was tried as the condensing agent (according to the method of Noyes<sup>8</sup>), the substances being in the proportion of 1:1:0.2 mol., the heating being for five hours on water-bath. The yield was 0.8 g.

The condensation-product after purification came out as colourless micro-crystals, needle-shaped, and melting at 222°. It was also soluble in acetone from which it could also be crystallised, though alcohol is a much more suitable solvent. It is only slightly soluble in the ordinary organic solvents like benzene, ether and chloroform. It did not decolorise Baeyer's reagent nor bromine in chloroform. It gave a yellow coloration with concentrated sulphuric acid, which on a gradual addition of water produced a violet ring, and the whole solution became deep brown on shaking.

Nitrogen, found 7.34%, 7.48%; piperonyl-*bis*-benzamide, C<sub>22</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub> requires 7.48%: the corresponding monoamide requires 5.53%.

About 1 g. of the bisamide and about 15 c.c. of 2 N sulphuric acid were refluxed in a flask for about one hour. The solution was filtered hot

and gave on cooling, crystals of benzamide, identified by the melting-point. Piperonal was identifiable by its characteristic fragrant smell.

*Condensation with Acetamide—*

3 g. piperonal and 2.4 g. acetamide (1 : 2 mol.) were heated as usual on a water-bath for five hours. The reacting mass melted to a chocolate-coloured liquid but solidified to a cake after 3.5 hours' heating. The usual treatment gave a white crystalline product: m.p. 229° (crude), 235° (recrystallised). The yield was poor.

The same experiment was repeated at 120° (oil-bath), and produced an yield of 0.8 g.

As a good deal of acetamide had sublimed away during these two experiments, in the third experiment an air-condenser was attached to the flask in which the two were being heated, and the heating was carried on for six hours at 120–25° (oil-bath). The crude product melted at 234°: yield 2.1 g. or 42% of theory.

When, in another experiment, the heating was for only 30 minutes and by means of a low free flame, the reacting mass resinified and was mixed with a lot of tarry matter, from which nothing useful could be extracted. Higher temperatures are clearly detrimental.

The product crystallised out from hot alcohol in white long silky needles, melting at 237–38°. It was more soluble in hot alcohol than the corresponding benzamide condensation-product. All the other properties of this were identical with those of the latter, only with strong sulphuric acid it gave a deep colour after some time, and on the addition of water, it gave a violet ring which changed to a violet solution on shaking.

Nitrogen found 11.17%; piperonyl-*bis*-acetamide  $C_{12}H_{14}O_4N_2$  requires 11.20%: the mono-compound requires 7.33%.

*Condensation with Propionamide—*

1.5 g. piperonal and 0.73 g. of propionamide (1 : 1 mol.) were heated on water-bath as before for four hours. The mixture first melted and then set to a hard mass. The white product taken out of it as usual melted at 223°. The yield was very poor.

The reacting proportions were then changed to 1 : 2 mol. 1.5 g. piperonal and 1.46 g. propionamide were heated on a water-bath for ten hours. The product weighed 1.0 g., melting at 225° (recrystallised from hot alcohol).

The same amounts as in the second experiment were heated at 120–25° (oil-bath), but the product taken out weighed 1.0 g. only: this was the highest yield, equal to 36% of theory.

In another experiment the same amounts were heated in the same way, but for 10 hours: the yield did not improve, as it was 0.9 g. Its colour also was an indication of impurity.

The product was easier to recrystallise from hot alcohol than the two earlier products: white silky needles, m.p. 225°. Its other properties were similar to those of the two preceding compounds: only with strong sulphuric acid it gave a pale yellow colour which changed to green on standing. On the addition of water, the usual violet ring was formed at the inter-surface of the two liquids, but this on shaking coloured the whole solution violet, and then immediately black.

Nitrogen, found: 10.12%; piperonyl-*bis*-propionamide  $C_{14}H_{18}O_4N_2$  requires 10.07%: the mono-amide requires 6.83 %.

#### *Condensation with Formamide—*

(i) 3.0 g. piperonal and 1.8 g. formamide (1:2 mol.) were heated in a flask fitted with an air-condenser for five hours over a water-bath. The mixture remained in the liquid condition all through. At the end, it was cooled and added to a large quantity of water, when only piperonal separated out.

(ii) The same quantities were taken, but the heating was done for ten hours on an oil-bath at 130°. The mixture remained a liquid, and when a test portion was taken out and poured into water, only piperonal was obtained. The remaining portion was then heated again for another five hours at 150°. The mass had however resinified and nothing could be separated from it.

(iii) 1.5 g. piperonal, 0.9 g. formamide and 0.1 c.c. pyridine (1:2:0.12 mol.) were heated together at 130° for five hours. At the end, most of the piperonal was recovered when the mixture was poured into water.

It was evident that neither temperature nor pyridine induced the condensation in this case.

#### *Condensation with Phenylacetamide—*

(i) 1.5 g. piperonal and 2.7 g. phenylacetamide were heated together for five hours on a water-bath (1:2 moles.). After about two hours the molten mass set to a hard mass. Washed with alcohol at the end, the yield was poor, the crude product melted at 219°, and the purified one at 234°.

(ii) The heating was done at 120–25° in an oil-bath for five hours. The crude product melted at 220° and weighed 2.0 g. (about 50% yield).

(iii) The temperature was now 125–30°, all other conditions being the same as in (ii). The product weighed 2.2 g. or 54.7% yield, and melted at 220°.

When taken out from hot alcohol, piperonyl-*bis*-phenylacetamide came out in very small colourless needles, melting at 224°. It was less soluble in the organic solvents than the products obtained from acetamide and propionamide: it was very little soluble in benzene, ether, etc.

It had no effect on Baeyer's reagent or on bromine in carbon tetrachloride. It gave a yellow colour with concentrated sulphuric acid, which deepened on standing and changed to brown: on the addition of water a violet ring was formed at the interface of the two liquids, while the solution became deep brown when shaken.

Nitrogen, found = 7.19%: piperonyl-*bis*-phenylacetamide  $C_{24}H_{22}O_4N_2$  requires 6.97%, the mono-formula would require 5.24%.

#### Condensation with Cinnamamide—

The cinnamamide (prepared in the laboratory from cinnamic acid, and melting at 147°) 2.94 g. and piperonal 1.5 g. (1 : 2 mol.) were heated together at 120° (oil-bath) for six hours. The product was extracted with alcohol. The crude piperonyl-*bis*cinnamamide melted at 238°. When crystallised several times from alcohol, and then three times from pyridine it melted finally at 248°. It weighed 3.5 g., *i.e.*, was 81.9% of theory. The white silky needles gave a deep yellow colouration with concentrated sulphuric acid.

Nitrogen, found: 6.65%, the *bis*-cinnamamide  $C_{26}H_{22}O_4N_2$  requires 6.57%.

#### Condensation with *n*-Butyramide—

1.5 g. piperonal was heated with 1.74 g. *n*-butyramide in an oil-bath at 115–20° for seven hours. The reacting mass had solidified after about 3.5 hours and the heating was stopped after another 3.5 hours. The product taken out in the usual way came out in white needle crystals (hot alcohol) melting at 208°. Yield = 1.7 g. or 55.6% of the theoretical. It also gave a yellow coloration with strong sulphuric acid.

Nitrogen, found : 9.40%; the piperonyl-*bis*-butyramide  $C_{16}H_{22}O_4N_2$  requires 9.15%.

*Condensation with n-Heptamide—*

0.75 g. piperonal and 1.29 g. *n*-heptamide (1:2 mol.) were heated at 115–20° for seven hours. The mass which was liquid for three hours set in to a solid afterwards. The product, long white crystals (hot alcohol) melted at 163° and weighed 1.5 g. The yield was thus = 76.9% of theory.

Nitrogen, found : 7.67%: the piperonyl-*bis*-heptamide requires 7.18%.

*Summary*

Piperonal condenses best when heated without any other condensing reagent, with seven of the common amides, giving characteristic piperonyl-*bis*amides. It does not condense with formamide.

## REFERENCES

1. Sodhi and Pandya .. *Proc. Ind. Acad. Sci. (A)*, 1938, 7, 361.
2. Mehra and Pandya .. *Ibid.*, 1939, 10, 279.
3. Manzur and Pandya .. *Ibid.*, 1939, 10, 282.
4. Mehra and Pandya .. *Ibid.*, p. 285.
5. Pandya and colleagues *J. I. C. S.*, 1934, 11, 823; *Proc. Ind. Acad. Sci. (A)*, 1935, 1, 440, and other parts.
6. Cebrian .. *Ber.*, 1898, 30, 1592.
7. Titherley and Marples *J. C. S.*, 1908, 93, 1933.
8. Noyes .. *J. Am. C. S.*, 1933, 55, 3493.