THE CONDENSATION OF ALDEHYDES WITH AMIDES

Part IX. The Condensation of *o*-Nitrobenzaldehyde

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IN Part VII of this series (Pandya and Varghese[1]), it has been pointed out that the aldehyde-amide condensations have three interesting features, *viz.*, (i) the influence of a trace of pyridine, (ii) the nature of the condensation-product and (iii) the yield. These seem to be vitally related to the group that happens to be present on the ring of the aromatic aldheyde: as for example, the influence of the free hydroxy, or phenolic, group appears to be very different from that of the methoxy and the methylene-dioxy groups. It may be added that cinnamaldehyde also seems to fall in with the latter class (Mehra and Pandya[2]). In order to find out whether a distinct group like the nitro has any modifying influence, a comparison has also been made (in Part VIII, Pandya and Varghese[3]) of the condensations of the same eight amides with piperonal and with 6-nitropiperonal. In respect of (i) and (ii) above, there was little difference, but in respect of (iii) as well as of the speed of the reaction, the difference was noticeable. It is also clear that different amides also make a great difference among themselves, and this, therefore, may be put down as another important factor governing the reaction as well as the final yield. In fact, peculiar results have been obtained with formamide and have been referred to already.

In order to judge the real influence of the nitro group, it is necessary to select nitrobenzaldehydes, where there are no other interfering groups (as in 6-nitropiperonal) and where also there is only one single nitro group. The results of this study are presented in this and the succeeding paper.

The aldehyde-amide condensation, under different conditions, has been very extensively studied, and of *o*-nitrobenzaldehyde itself condensations with three different amides, formamide, acetamide and benzamide, are mentioned in the literature. Formamide has been condensed by the simple action of gaseous hydrogen chloride passed through a mixture of the amide and the aldehyde, which resulted in the formation of *o*-nitrobenzal-bisformamide (Riedel[4]). More recently, Glazer and Frisch[5] mention having prepared

o-nitrobenzylidene-diacetamide and -dibenzamide by condensing the aldehyde and the amide in alcoholic solution by mere addition of a little hydrochloric acid. For the present study seven different amides have been condensed with *o*-nitrobenzaldehyde, under a variety of conditions. Pyridine trace appeared to be innocuous, doing neither good nor harm, except occasionally when it produced a little resin. The product in all cases was of the bisamide type. In the majority of cases the yield was about 50 %, but heptamide gave almost theoretical yield.

The nitrobenzylidene-bis-formamide obtained by our method was identical with Riedel's, whose experiment was repeated and the two products were compared by their single and mixed melting-points. The *o*-nitrobenzylidene-bisacetamide prepared by our method melted at a slightly higher temperature than that given by Glazer and Frisch. But there was a considerable disparity between the melting-points of the bisbenzamide obtained by us and the dibenzamide reported by the same two workers. Thus our product melted at 251–52° and their product is reported to melt at as low a temperature as 217–18°. We have not so far succeeded in repeating their experiment but analysis as well as molecular weight determination are in favour of the purity and identity of our product.

The products obtained by the condensations with propionamide, *n*-butyramide, *n*-heptamide and phenylacetamide are new.

Experimental

Condensation with Formamide.—(i) 2 g. aldehyde and 1·2 g. formamide were mixed in a flask and 0·08 c.c. of pyridine added (1 : 2 : 0·15 mol.) and the whole was heated on a water-bath at 50–60° for five hours. The mass was then extracted with water to remove formamide and then with ether to remove aldehyde that may have remained. A pale brown product remained, which when recrystallised from dilute acetone came out as pale yellow micro-crystals (needles) melting at 162°, and thus showing that they were not yet pure. Yield about 40%.

(ii) 1 g. aldehyde and 0·6 g. formamide were heated on the water-bath at 60–70° for eight hours. The mass soon became a straw-coloured liquid and bubbling was also noticed. Small, very pale yellow crystals gradually separated. At the end they were thoroughly washed first with cold water and then with ether: after recrystallisation from aqueous alcohol, the bis-formamide came out in white needle crystals, m.p. 177°. Yield about 40%.

(iii) Riedel's experiment was repeated, and 0·5 g. of the aldehyde and 0·3 g. of formamide were mixed and a stream of dry hydrogen chloride

passed: the mass soon melted to a clear liquid as heat was evolved: after about ten minutes solidification took place; the gas was passed for about one hour, the product was taken out as before and recrystallised from hot water. The yield was about 40%, and the m.p. 177°. The mixed melting-point of this product with that obtained in exp. (ii) was also 177°.

The temperature of the water-bath gave a brown colour to the product. That the reaction was quick was shown by another experiment in which the aldehyde and the amide in proper proportions were just heated together till they became a homogeneous liquid. The two were then left together at room temperature for three weeks. About 33% yield was obtained from this.

Condensation with Acetamide.—Acetamide did not condense so easily, not even at full water-bath temperature. But condensation took place when heated for six hours at 130–40°, with a trace of pyridine or without it; the yields in each case being about 48%.

o-Nitrobenzylidene-bisacetamide came out in white silky needles (from hot alcohol) and melted at 235°. Glazer and Frisch[5] give 231–32°. Nitrogen, found 16·49%; the nitrobenzylidene-bisacetamide $C_{11}H_{13}O_4N_3$ requires 16·73%.

Condensation with Propionamide: o-Nitrobenzylidene-bispropionamide.—(i) 2 g. aldehyde and 2 g. propionamide were heated alone on water-bath for seven hours. The mass treated as usual gave no product. There was no action.

(ii) The same were heated at 130–40° for four hours. During this time copious evolution of water-vapour took place and at the end white crystals began to make their appearance in the hot liquid. After cooling, extracting as usual and recrystallising from hot alcohol, the bispropionamide came out in white lustrous long needles, which softened at 218° and melted at 223–25°. Yield 37·9%.

(iii) The same experiment, repeated, but the heating extended to eight hours, made the reacting mass set to a white solid in the flask. The yield was 1·7 g. or 46%.

(iv) The same experiment with a trace of pyridine and the heating being four and eight hours respectively in two different lots, gave an identical yield of 1·8 g. or 48·7%.

(v) When a trace of piperidine was tried, even at water-bath temperature, and in eight hours heating, the mass had become dark red resin which defied all attempts at purification. Probably still lower temperatures might have been more suitable,

The *o*-nitrobenzylidine-bispropionamide is fairly soluble in alcohol and acetone, but not in ether: it melts at 223–25°. (Found: N, 14·80; the bispropionamide $C_{13}H_{17}O_4N_3$ requires 15·05%.)

Condensation with n-*Butyramide*: o-*Nitro-benzylidene-bis*-n-*butyramide.*—As this amide sublimes very much when heated with the aldehyde, a small amount of glacial acetic acid was added to prevent its escape from the reacting mass. Thus, 0·75 g. aldehyde, 0·9 g. *n*-butyramide and 0·5 c.c. of glacial acetic acid were mixed and heated at 110° for six hours. The white solid left was treated with water, washed with ether and recrystallised from alcohol. The bisbutyramide came out in long white needles, melting at 181°. It weighed 1·0 g. or the yield was = 65·1%. It did not decolourise Baeyer's reagent, nor bromine water. (Found: N, 13·81; $C_{15}H_{21}O_4N_3$ requires 13·68%.)

Condensation with Heptamide: o-Nitrobenzylidene-bisheptamide.—0·75 g. of the aldehyde and 1·3 g. of heptamide were heated together for six hours at 105–10°. The mass first melted to a clear liquid and began to solidify after three hours. At the end of the heating, the white solid was extracted with a little cold alcohol to remove the unchanged reactants and the residue was recrystallised from alcohol: the white needles melted at 135° and weighed 1·9 g. (Found: N, 10·93; the bisheptamide $C_{21}H_{33}O_4N_3$ requires 10·74%.) Yield = 97·1%.

Condensation with Benzamide: o-Nitrobenzylidene-bisbenzamide.—There was very little reaction at the water-bath temperature. 4 g. aldehyde and 6·5 g. amide (1 : 2 mol.) were heated together on an oil-bath at 130–40° for four hours. The molten mass soon set to a white solid, after giving out water vapours. On cooling it was extracted with methyl alcohol, and the residue recrystallised from acetone plus alcohol. White needles, melting at 251–52°. Yield = 5·4 g. or 54%.

When heated with a trace of pyridine in the same way, the mass was extracted with acidulated water and then with methyl alcohol. Yield = 52%. The crystals were insoluble in ether and methyl alcohol: and fairly soluble in acetone and ethyl alcohol. (Found: N, 11·43; the bisamide $C_{21}H_{17}O_4N_3$ requires 11·65%. Molecular weight, Rast: 370·8; Expected 375.)

Condensation with Phenylacetamide: o-Nitrobenzylidene-bisphenylacetamide.—2 g. aldehyde and 3·6 g. the amide (1 :2 mol.) were heated at 130–40° for four hours. Water vapours were given out and the mass set to a solid, which was washed first with water and then with ether. Recrystallised from alcohol, the product came out in long white needles, m.p. 229–30°. It was sparingly soluble in the usual organic solvents. Yield = 2 g. or 37·5%. In

another experiment the heating was continued for eight hours, when the yield improved to 2·5 g. or 46·9%.

When the condensation was carried out in the presence of a trace of pyridine, the yield, with four hours' heating, was the same, *viz.*, 2 g. (Found: N, 10·55; the bisamide $C_{23}H_{21}O_4N_3$ requires, 10·42%; Found: Mol. weight, 406·5; calc. 403.)

Summary

o-Nitrobenzaldehyde has been condensed with seven different amides, by heating them together by themselves or with a trace of pyridine. Pyridine is found to be neither helpful nor harmful in these cases. The condensation-product in every case has been of the benzylidene*bis*amide type. The yields were quite fair, ranging from 40 to 65%, and were nearly quantitative in the case of heptamide.

REFERENCES

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3. Pandya and Varghese .. *Ibid.*, 1941, **14**, 25.
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5. Glazer and Frisch .. *Arch. Pharm.*, 1928, **266**, 103; *Br. Chem. Ab.*, A, 1928, 652.