

THE CONDENSATION OF ALDEHYDES WITH AMIDES

Part X. The Condensation of *m*- and *p*-Nitrobenzaldehydes and 2:4-Dinitrobenzaldehyde

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THE condensations of *o*-nitrobenzaldehyde with seven different aliphatic and aromatic acid amides have been already reported (Ittyerah and Pandya¹). In the present paper are given the condensations of *m*- and *p*-nitrobenzaldehydes with the same amides. The reactions proceed well, the products are in all cases the saturated nitrobenzylidene-bisamides, formed by the reaction of one molecule of the aldehyde with two of the amide. The optimum temperature is 130–40°; higher temperatures produced resinification and lower temperatures reduced yields leaving some of the materials unacted. Heating longer than eight hours also caused resinification.

Pyridine or any other base, used even in traces, did not increase the yield generally under the condition that were attempted. This experience in the case of the *o*-nitrobenzaldehyde condensations¹ discouraged attempts in the present case.

The yields in the case of the *m*- and *p*-nitrobenzaldehydes were distinctly higher than in the case of the *o*-isomer: in fact the *p*-isomer reacted most quickly, usually two hours were sufficient to give the same yield as was obtained from the others after longer heating. The *o*- takes the longest time and gives comparatively the smallest yields: the *m*- is quicker and gives also better yields: the *p*- may be put down as the quickest, giving excellent yields.

All the condensation-products are white needle crystals, except the products of the *p*-nitrobenzaldehyde-acetamide and -formamide condensations respectively.

The condensation-products of the three nitro-benzaldehydes differ from the products of the condensations of the three hydroxy-benzaldehydes, not only in chemical character, but also in their inability to give any colouration with concentrated sulphuric acid in the cold.^{2, 3, 4} They certainly dissolve in the cold concentrated acid, but give no colour, unless kept at

room temperature for about twenty-four hours, when only a pale yellow colour develops, which may be due to decomposition. Decomposition and charring take place when the acid solution is warmed.

Refluxed with dilute sulphuric acid, hydrolysis takes place and the aldehyde and the amide are obtained.

So also attempts to nitrate products like benzylidenebisacetamide with a mixture of nitric and sulphuric acids were unsuccessful, decomposition taking place instead.

Only two of the products reported in this paper have been previously made, namely *m*-nitrobenzylidene-bis-acetamide and the corresponding -bisbenzamide, by Glazer and Frisch (1928).⁵ The melting-points of their products, as reported are, however, very much lower than those of our products. The rest are new.

The comparative yields of the condensation-products of the three nitrobenzaldehydes can be seen in the table at the end. It may be noted that phenylacetamide gives almost theoretical yields with the *m*- and the *p*-nitrobenzaldehydes, while the *n*-heptamide gives the same good yield with all the three.

While the yields in the case of these mono-nitrobenzaldehyde-amide condensations have been so good, it is remarkable that the 2:4-dinitrobenzaldehyde altogether failed to condense with either acetamide or with benzamide, although a very large variety of conditions were tried. The difficulties met with in the condensation of this aldehyde with malonic acid have already been recorded in another place.⁶

Experimental

Condensation of m-nitrobenzaldehyde.

Condensation with Formamide: m-Nitrobenzylidenebisformamide.—The reaction was extraordinarily quick, good yields being obtained only on ten minutes' heating of the two on water-bath. Longer heating (eight hours) gave resins from which only a small amount could be isolated. When taken in 1:2 mole. proportion (4 g. and 2.4 g.) a solid was formed in ten minutes, which was digested with water and washed with ether; the residue, on recrystallisation from alcohol; melted at 168°. The yield was 59.5% (3.5 g.) but was raised to 67% when the ratio of the two was 1:3 mol. The bisformamide was soluble in acetone, moderately soluble in alcohol and insoluble in ether. [Found: Nitrogen, 18.47%; $C_9H_9O_4N_3$ requires 18.83%. Molecular weight, (Rast) 221.3, calc. 223.]

Condensation with Acetamide *m*-Nitrobenzylidenebisacetamide.—2 g. aldehyde and 1.6 g. amide (1:2 mol.) were heated as usual: the mass remained a clear straw-coloured liquid for the first six hours, but afterwards small white crystals began to make their appearance. Heating was stopped after eight hours. The yield was 0.8 g. or 24%. The same experiment was repeated with a trace of pyridine, but the yield did not alter. Another lot heated at 140° for four hours showed vigorous reaction, copious water-vapours being given off and solid formation of the product taking place more quickly. The yield was 3 g. or 60%. It was soluble in alcohol, less in cold alcohol, still less in chloroform and insoluble in ether. The recrystallized needles melted at 255–56°. Glazer and Frisch⁵ (1928), have reported 236–37°. (Found: Nitrogen, 16.98, 16.88%; $C_{11}H_{13}O_4N_3$ requires 16.73%.)

Condensation with Propionamide: *m*-Nitrobenzylidenebispropionamide.—As in the preceding case, the reaction was very slow on water-bath, crystals started to show themselves at the end of six hours. After eight hours' heating, the product, taken out as usual, weighed only 17% of theory. Pyridine did not alter the yield when used in a trace, but heating at 130–40° for four hours accelerated the reaction and produced an yield of 67.3%.

Recrystallised from hot alcohol, the bispropionamide melted at 220–21°. Its solubility in organic solvents was similar. [Found: Nitrogen, 15.36, 15.23%; $C_{13}H_{17}O_4N_3$ requires 15.06%. Mol. Wt. (Rast), 270.6: calc. 279.]

Condensation with n-butyramide: *n*-Nitrobenzylidenebis-*n*-butyramide.—As the *n*-butyramide was found to sublime in a large amount during the course of the heating, a small amount of glacial acetic acid was also added to the reaction-mixture. 0.75 g. *m*-nitrobenzaldehyde, 0.9 g. *n*-butyramide and 0.5 g. glacial acetic acid were mixed and heated at 105–10° for six hours. The whole melted quickly and after about two hours the formation of a solid was noticed. The product taken out as usual weighed 1.3 g. 84.6%. m.p. 194°. (Found: Nitrogen, 13.96%; the bisbutyramide $C_{15}H_{21}O_4N_3$ requires 13.68%.)

Condensation with n-Heptamide: *m*-Nitrobenzylidenebis-*n*-heptamide.—0.75 g. aldehyde and 1.3 g. amide were heated alone at 105–10° for six hours. The product weighed 1.9 g. yield 97%, m.p. 149°. (Found: Nitrogen, 10.87%; the bisheptamide $C_{21}H_{33}O_4N_3$ requires 10.74%.)

Condensation with Benzamide: *m*-Nitrobenzylidenebisbenzamide.—Heated 3.0 g. aldehyde and 4.9 g. amide at 130–40° for four hours. After cooling, the mass was extracted with methyl alcohol and the bisbenzamide recrystallized from an acetone-alcohol mixture. M.P. 228–30° (224°, according to Glazer and Frisch⁵). Yield = 6 g. or 80.5%. [Found: Nitrogen, 11.42%;

the bisbenzamide $C_{21}H_{17}O_4N_3$ requires 11·20%. Mol. Wt. (Rast) 365·4: calc. 375.]

Condensation with Phenylacetamide: m-Nitrobenzylidenebis-phenylacetamide.—Heated as above, the mixture quickly softened but soon set to a hard mass which was, at the end, digested with hot water, then washed with a little ether, and recrystallised from hot alcohol. Yield = 5·2 g. (from 2 g. aldehyde and 3·6 g. amide), *i.e.*, 97·4%. m.p. 214–16°. [Found: Nitrogen, 10·60, 10·51%; the bisphenylacetamide $C_{23}H_{21}O_4N_3$ requires 10·42%, Mol. Wt. (Rast), 410·2, calc. 403.)

Condensation of p-Nitrobenzaldehyde.

Condensation with Formamide: p-Nitrobenzylidenebisformamide.—Heating under different conditions was tried, at 60–70°, on the water-bath and at 120–30° temperatures and from four to ten hours. A very large number of experiments were made, all of which gave a dark red or orange amorphous powder, insoluble in almost all the usual solvents, except acetone. Purification was very difficult, the product generally obtained melting at 210–20°. The nitrogen content was found to be about 1–2% low. Molecular weight (Rast) was found to be 736 and 747, the calculated value is only 223. The product is apparently a polymer, or a mixture of several polymers.

1·0 g. aldehyde and 0·6 g. formamide were mixed and dry hydrogen chloride was passed in it for two hours. Heat was evolved during this operation. The solid was then extracted with water and then ether, and finally recrystallised from alcohol. The colourless needles melted at 194°. Yield = 1·0 g. or 67·7%. (Found: Nitrogen, 18·66%; the bisformamide $C_9H_9N_4O_3$ requires 18·83%).

Condensation with Acetamide: p-Nitrobenzylidenebisacetamide.—No condensation was found to take place when the two were heated together on water-bath for even ten hours. 1·0 g. aldehyde and 0·9 g. formamide were heated together at 120–30° for four hours. The mixture first melted to a light yellow liquid and crystals began to appear after some time. Cooling and extracting in the usual way gave 0·9 g. of the bisamide, 54·2% yield. Recrystallised from dilute acetone, the pale yellow needle crystals melted at 272°. The solubility and chemical character were similar to those of the other products. Heating for more than four hours did not improve the yield and made the product dark-coloured and difficult to crystallise (Found: Nitrogen, 16·4, 15·58%; the bisacetamide $C_{11}H_{13}O_4N_3$ requires 16·73%.]

Condensation with Propionamide: p-Nitrobenzylidenebispropionamide.—3 g. of each were mixed and heated at 130–40° for two hours; at the end of which the whole had become a solid crystalline mass. (Note.—longer heating might possibly improve the yield.) The bisamide was treated with water and then with dilute alcohol: the yield was 3 g. or 54·1%, m.p. 252°. Long silky needles. (Found: Nitrogen 14·86, 15·05%; the bispropionamide $C_{13}H_{17}O_4N_3$ requires 15·06%.)

Condensation with n-Butyramide: p-Nitrobenzylidenebis-n-butyramide.—0·75 g. aldehyde and 0·9 g. amide were heated together at 110°. The mixture first fused and solid-formation was noticed after three hours. There was also some sublimation, the sublimate having formed on the inner wall of the condenser. The solid in the flask was a high-melting substance. The sublimate was washed down with a little glacial acetic acid and the heating continued for three hours more (total about six hours). The product was treated with water and filtered: the residue was washed with ether and crystallised from alcohol. Yield=1·1 g., 71·7%, m.p. 224°. (Found: Nitrogen, 13·72%; the bisbutyramide $C_{15}H_{21}O_4N_3$ requires 13·68%.)

Condensation with n-Heptamide: p-Nitrobenzylidenebis-n-heptamide.—0·7 g. aldehyde and 1·3 g. amide were heated together at 105–10° for six hours. Crystal-formation was noticed after about one hour's heating. At the end the product was extracted with a little cold alcohol, and the residue crystallised from alcohol. Yield=1·9 g., 97·4%, m.p. 170°. (Found: Nitrogen, 10·97%; the bisheptamide $C_{21}H_{33}O_4N_3$ requires 10·74%.)

Condensation with Benzamide: p-Nitrobenzylidenebisbenzamide.—3 g. aldehyde and 4·8 g. benzamide were heated at 130–40°: the reaction appeared to be complete in two hours. The product recrystallised from acetone-alcohol melted at 258–59°. Yield=6 g., 80·5%. [Found: Nitrogen, 11·53, 11·27%; the bisbenzamide $C_{21}H_{17}O_4N_3$ requires 11·20%. Mol. Wt. (Rast) 371, calc. 375.]

Condensation with Phenylacetamide: p-Nitrobenzylidenebis-phenylacetamide.—2 g. aldehyde and 3·6 g. amide were heated together at 130–40° for two hours and the reaction product was extracted first with hot water and then with dilute alcohol. Yield=5·2 g., 97·5%. Recrystallised from acetone alcohol it melted at 248°. [Found: Nitrogen, 10·59, 10·60%; the bis-phenylacetamide requires $C_{23}H_{21}O_4N_3$, 10·42%. Mol. Wt. (Rast) 415, calc. 403.]

Condensation of 2:4-Dinitrobenzaldehyde.

Condensation with Benzamide.—All attempts failed. About fifteen experiments were made, using water-bath, 130–40°, traces respectively of

pyridine, piperidine, lutidine, and triethanolamine, pyridine in molecular proportions, concentrated sulphuric acid, alcohol and dry hydrogen chloride, glacial acetic acid, acetic acid and acetic anhydride, acetic acid and dry hydrogen chloride and anhydrous zinc chloride.

With Acetamide.—No condensation took place when heated alone, or with traces as well as molecular proportions of lutidine, pyridine and piperidine respectively.

Many other conditions involving changes in temperature up to 160° and in heating hours, from four to fifteen, were also tried, but without success.

Summary

Condensations of *m*- and *p*-nitrobenzaldehyde with seven different amides are reported, most of the products being new. The *p*-isomer seems to undergo condensation in the shortest time, the *m*-being intermediate. The *p*- also gives the best yields. There is a clear indication of the influence of the particular position occupied by the nitro-group on the ring of the aldehyde molecule. The influence of the different groups associated with the amido group in RCONH₂ is even more obvious. The 2:4-dinitrobenzaldehyde, on the other hand, does not appear to condense.

TABLE

Yields of Nitrobenzylidenebisamides, highest % Obtained

Amide	<i>o</i> -	<i>m</i> -	<i>p</i> -
Formamide ..	40	67.7	67.7
Acetamide ..	48.2	60	54.5
Propionamide ..	48.7†	67.3	54.1
<i>n</i> -Butyramide ..	65.1	84.6	71.7
<i>n</i> -Heptamide ..	97.1	97.1	97.4
Benzamide ..	54	80.5	80.5
Phenylacetamide ..	46.9	97.4	97.4

REFERENCES

1. Ittyerah and Pandya .. *Proc. Ind. Acad. Sci.*, 1942, **15**, 6.
2. Pandya and Sodhi .. *Ibid.*, 1938, **7**, 361.
3. Mehra and Pandya .. *Ibid.*, 1939, **10**, 279.
4. Mansur and Pandya .. *Ibid.*, 1939, **10**, 282.
5. Glazer and Frisch .. *Arch. Pharm.*, 1928, **266**, 103; *Br. Chem. Ab.*, A, 1928, 652.
6. Ittyerah, Pandya and Miss Pandya .. *Journ. Uni. Bom.*, 1941, **X**, Part 3, 78.

† obtained with a trace of pyridine.

Most of the *p*-compounds were obtained within about half the time taken by the *o*- and the *m*- analogues.