

CONDENSATION OF ALDEHYDES WITH AMIDES

Part XVII. Of 5-Chloro- and 3: 5-Dichlorosalicylaldehydes

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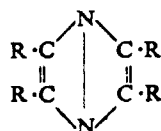
Received January 6, 1948

IN Part I of this series⁷ have been described studies on the condensations of several amides with salicylaldehyde under different conditions. It has been shown that under all the conditions examined only one product was formed, namely, salicylidene-monoamide, and that, of all these conditions, the one using $\frac{1}{8}$ th of a molecule of pyridine at water-bath temperature gave the highest yield, which at times was nearly quantitative. Later work showed that condensations with *m*-hydroxy-¹⁰ and *p*-hydroxy-¹¹ benzaldehydes gave also similar -monoamide products, but when there were groups on the aromatic ring like methyl,^{9, 15} methoxy,¹² methylenedioxy,¹³ nitro,¹⁴ chloro,¹⁶ -CH:CH.CHO,⁸ -CH₂CH₂.CHO¹⁷ and so on, the product was invariably the -bisamide type. Benzaldehyde¹⁶ and *n*-heptaldehyde¹⁸ also gave -bis-amides. It has also been found that in most of these cases the presence of pyridine was not always favourable; in some cases it led to resinification; higher yields came out generally when the aldehyde and the amide were heated alone, preferably, in some cases, at 100–110°.

The condensations of two different chloro-derivatives of salicylaldehyde, 5-chloro- and 3: 5-di-chloro-salicylaldehydes, with about eight amides, under two or three different conditions, are described here. They present a good contrast with those of salicylaldehyde itself.⁷

The monochloro- derivative gave -monoamides but only with three amides, with *n*-heptamide, with benzamide and with benzene-sulphonamide, and gave -bisamides with all the others including benzamide also, which last thus gave both the products. In the case of the dichlorosalicylaldehyde, it gave the *bis*-products with all except with benzene-sulphonamide. Urea gave the two usual products according as the condensation was carried out above or below the melting-point of urea.⁴ Formamide was peculiar as it often has been found to be; it gave corresponding pyrazine-derivatives*

* Bülow³ has earlier established the formation of tetraphenylpyrazine from the condensation at high temperatures of benzaldehyde with formamide¹⁹; a related product has also been obtained in this laboratory from the condensation of cinnamaldehyde with formamide.¹



[R = C₆H₅ (Bülow³); and = C₆H₃(OH)Cl and = C₆H₃(OH)Cl₂ in the present paper]

(tetra-monochloro-hydroxyphenyl-pyrazine and tetra-dichlorohydroxyphenyl-pyrazine) in both cases, but with a little of the *-bisformamide* also in the case of the 3:5-dichlorosalicylaldehyde.

There was also considerable disparity in the yields. Excepting in two cases, in the condensations with formamide and with urea, the yields obtained from the condensations of the dichlorosalicylaldehyde were all higher, sometimes very much higher, than those obtained from the condensations of the monochlorosalicylaldehyde; in two cases (propionamide- and benzenesulphonamide-dichloro-salicyl aldehyde condensations) the yields were very nearly theoretical.

The mono- and the bis-amides were distinguished not only by analysis but also by the usual properties associated with each of the derivatives, particularly by the reactions with Baeyer's reagent and the coloration with cold concentrated sulphuric acid.

Urea has been found to give very useful and important condensation-products by reacting with aldehydes and the products often differ according to different conditions. (See also Das Gupta.⁴) Urea has thus been included in the list of the amides tried in these condensations. It has been condensed with *n*-heptaldehyde (Pandya and Sodhi, H. S.¹⁸) and also with the two chloro-salicylaldehydes included in the present paper. The yields here have not been high.

Similarly benzenesulphonamide presents another type of an amide, having an $-\text{SO}_2\text{NH}_2$ group instead of the $-\text{CONH}_2$ group. Earlier workers in this Laboratory (notably George⁵) failed to obtain a condensation-product from it with some aldehydes. We, however, succeeded in obtaining mono-amide products, in one case in theoretical yields, from the two aldehydes considered in this paper. Later another worker (Mhala⁶) also succeeded in condensing it with another aldehyde (3:5-dibromo-salicylaldehyde).

EXPERIMENTAL

Preparation of the Chloro-salicylaldehydes

5-Chlorosalicylaldehyde.—Biltz and Stepf³ prepared it by passing for one hour a stream of chlorine in salicylaldehyde kept on water-bath, and reported an yield of 66.7% and the melting-point 99.5°. We found that the room-temperature (23°) gave a better yield, 77.5%, and the final melting-point was 101°.

3:5-Dichlorosalicylaldehyde.—Biltz and Stepf³ prepared this by passing dry chlorine for one hour into a glacial acetic acid solution of salicylaldehyde kept on waterbath. While they reported an yield of 90%, only a 58% yield

was obtained by us: but by changing the proportion of glacial acetic acid solution, from 1:5 to 1:3.2 grams, it was found that the yield rose to 85%: the melting-point was identical, 95°.

Condensations with Acetamide

5-Chlorosalicylaldehyde (0.8 gr.) and acetamide (0.6 gr.), (1:2 mol.), were heated alone on water-bath (98°) for eight hours. The pale yellow hard solid with a buff-coloured rim was washed with hot water and then with ether: it gave a crude product that melted at 208°, and, after recrystallisation from alcohol, melted finally at 227°. It came out then in white crystalline needles. Cl, found 13.61%: monochlorosalicylidene*bis*acetamide $C_{11}H_{13}O_3N_2Cl$ requires 13.84%, and monochlorosalicylidene*mono*acetamide $C_9H_9O_2NCl$ requires 17.97%. The yield here was 45.75% of theory. Heating at 100–110° gave a 53% yield.

3: *5-Dichlorosalicylaldehyde* (1.0 gr.) and acetamide (0.6 gr.: 1:2 mol.) were heated in the same way. Within ten minutes the mass fused to a clear liquid and crystals began to be formed in 45 minutes, after which the whole began to set to a hard yellow mass. After the usual treatment the crude product melted at 199°, and, after recrystallisation (warm alcohol), finally at 204.5°. Cl, found 24.25%: dichlorosalicylidene*bis*acetamide $C_{11}H_{12}O_3N_2Cl_2$ requires 24.39%, dichlorosalicylidene*mono*acetamide $C_9H_7O_2NCl_2$ requires 30.6%. The yield was 46.46%.

In the presence of pyridine (1:2:0.15 mol.) the yield decreased to 20%, but when the heating was carried on at 100–110°, in the absence of a condensing agent, the yield increased to 86.28%.

Condensations with Propionamide

5-Chlorosalicylaldehyde (0.8 gr.) and propionamide (0.75 gr., 1:2 mol.) were heated on water-bath as above. The product, recrystallised from alcohol, melted at 188°. Cl, found 12.35%: monochlorosalicylidene*bis*propionamide $C_{13}H_{17}O_3N_2Cl$ requires 12.47%, while the monochlorosalicylidene*mono*propionamide $C_{10}H_{11}O_2NCl$ requires 16.78%. The yield was 35% of theory, but it increased to 44% when the condensation was carried out at 100–110°.

3: *5-Dichlorosalicylaldehyde* (1.0 gr.) and propionamide (0.75 gr., 1:2 mol.) were heated on water-bath in the same way. White needle crystals, recrystallised from alcohol, melted at 195.5° and regenerated the aldehyde and the amide when heated with mineral acids. Cl, found 22.11%: dichlorosalicylidene*bis*propionamide $C_{13}H_{16}O_3N_2Cl_2$ requires 22.26%, while the dichlorosalicylidene*mono*propionamide $C_{10}H_9O_2NCl_2$ requires 28.86%.

The yield was 65.8% of theory. When the same condensation was carried out by heating for 24 hours in the presence of pyridine acetate (1:2:0.15 mol.), the yield was 48.6%, and in the presence of pyridine, 68.4%. But on heating without any condensing agent at 100–110°, the yield became nearly quantitative (99.6%).

Condensation with *n*-Butyramide

5-Chlorosalicylaldehyde (0.8 gr.) and *n*-butyramide (0.9 gr., 1:2 mol.) were heated as usual on water-bath, and gave a product melting at 166° after several recrystallisations from alcohol. Cl, found 11.58%: monochlorosalicylidenebis-butyramide $C_{15}H_{21}O_3N_2Cl$ requires 11.36%, while monochlorosalicylidene*mono*butyramide $C_{11}H_{13}O_2NCl$ requires 15.75%. The yield is 73.27% of theory: a higher temperature gave a lesser yield 40%.

3:5-Dichlorosalicylaldehyde (1.0 gr.) and *n*-butyramide (0.87 gr., 1:2 mol.), when heated as usual on water-bath, gave a milk-white product melting at 175–177°, and at 179° after recrystallisation from alcohol. Cl, found 20.84%: dichlorosalicylidenebisbutyramide $C_{15}H_{20}O_3N_2Cl_2$ requires 20.46%, while dichlorosalicylidene*mono*butyramide requires 27.31%. The yield was about 53%, but increased to 85% of theory when the heating during the condensation was 100–110°.

Condensations with *n*-Heptamide

5-Chlorosalicylaldehyde (0.8 gr.) and *n*-heptamide (1.3 gr., 1:2 mol.), when heated alone on water-bath, gave no solid product even after six hours. The temperature was gradually raised to 140–150°, when solidification took place. Washing with water and with petroleum ether (b.p. 55–70°) gave a lemon-yellow solid almost insoluble in the ordinary organic solvents. After frequent washings with hot alcohol it decomposed at 268°. Cl, found: 13.19%: monochlorosalicylidenebisheptamide $C_{21}H_{23}O_3N_2Cl$ requires 8.95%, while monochlorosalicylidene*mono*heptamide $C_{14}H_{18}O_2NCl$ requires 13.27%. The monoheptamide decolorised Baeyer's reagent rather slowly and gave a deep red colour with concentrated sulphuric acid. The yield was only 18.6%.

3:5-Dichlorosalicylaldehyde (1.0 gr.) and *n*-heptamide (1.3 gr., 1:2 mol.), heated on water-bath as usual, gave a product melting at 144°, or at 147° after recrystallisation (alcohol). Cl, found: 16.21%: dichlorosalicylidenebisheptamide $C_{21}H_{22}O_3N_2Cl_2$ requires 16.47%, while dichlorosalicylidene*mono*heptamide requires 23.51%. The yield was 46% of theory but increased to 79% when the heating was at 100–110°.

Condensation with Benzamide

5-Chlorosalicylaldehyde (0.8 gr.), benzamide (1.2 gr.) and pyridine acetate (1 : 2 : 0.15 mol.) were heated on waterbath for 24 hours, after which by the usual procedure a product melting at 194°, after a recrystallisation from 90% alcohol, was separated. Cl, found: 9.81%: monochlorosalicylidene-*bis*benzamide $C_{21}H_{17}O_3N_2Cl$ requires 9.32%, while monochlorosalicylidene-*monobenzamide* $C_{14}H_{10}O_2NCl$ requires 13.68%. The yield was 46.26% of theory. It decolorised Baeyer's reagent but gave no colour with cold concentrated sulphuric acid.

A second experiment under the same circumstances, except that the heating was for 48 hours, gave 56.54% yield.

A third experiment of heating the aldehyde and the amide alone at 150–160° for eight hours gave a different product. It was a hard solid and after repeated washings with ether, hot alcohol and petroleum ether (b.p. 55–75°), it decomposed at 269° without melting. Cl, found: 13.98%, corresponding to the monochlorosalicylenemobenzamide which requires 13.68% (*vide* above). The yield was 40.7% and the product might have been a polymer. It decolorised Baeyer's reagent and also gave a deep red colour with cold concentrated sulphuric acid.

3: *5-Dichlorosalicylaldehyde* (1.0 gr.), benzamide (1.2 gr.) and pyridine (1 : 2 : 0.15 mol.) were heated for 8 hours on water-bath. The hard yellow cake, after purification, melted at 202°. Cl, found: 17.47%: dichlorosalicylidene-*bis*benzamide $C_{21}H_{16}O_3N_2Cl_2$ requires 17.10%, while dichlorosalicylidene-*monobenzamide* $C_{14}H_9O_2NCl_2$ requires 24.15%. The yield was 28.46% but increase to 47.43% when the two were heated without pyridine, and to 85.7% when, without pyridine, the temperature of the bath was 100–110°.

Condensations with Benzenesulphonamide

5-Chlorosalicylaldehyde (0.2 gr.) and benzenesulphonamide (0.4 gr., 1 : 2 mol.) were heated for 8 hours at 140–150° (there being no reaction below this). The product melted at 170°, the melting-point remaining unchanged on recrystallisation (hot alcohol). Cl, found: 11.99%: chlorosalicylidene-*bis*benzenesulphonamide $C_{19}H_{17}O_5S_2N_2Cl$ requires 7.4%, while the chlorosalicylidene-*monobenzenesulphonamide* $C_{13}H_{10}O_3SNCl$ requires 12.01%. The yield of the monoamide was 37.4%, which increased to 60% when the condensation was carried out at 150–160°. The product was soluble in alcohol, benzene, acetone and chloroform; it decolorised immediately Baeyer's reagent and gave a deep red colour with cold concentrated sulphuric acid.

3: 5-Dichlorosalicylaldehyde (0.25 gr.) and benzenesulphonamide (0.4 gr., 1:2 mol.) were heated at 120–130° for 8 hours and gave, after a recrystallisation from cold alcohol, a white product melting at 196°. Warming with even rectified spirit decomposed it back into the original aldehyde and the amide. It decolorised neither Baeyer's reagent nor bromine water. S, found: 9.96%; Cl, found: 21.71%; dichlorosalicylidenebisbenzenesulphonamide $C_{19}H_{18}O_5N_2S_2Cl_2$ requires 13.14% and 14.58% respectively, while dichlorosalicylidene*monobenzenesulphonamide* $C_{13}H_9O_3NSCl_2$ requires 9.69 and 21.51% respectively. The yield of the monoamide was 37.5%, and rose to 61.9%, when the heating was at 130–140°, for five hours: at 140–150°, the reaction took only four hours and the yield was nearly theoretical.

Condensations with Urea

5-Chlorosalicylaldehyde (0.8 gr.), urea (0.6 gr.) and pyridine (1:2:0.15 mol.) were heated at 140–150° for seven hours when a deep orange-coloured liquid was obtained. It solidified overnight and was washed respectively with water, dilute hydrochloric acid and ether. Recrystallisation (twice from alcohol) gave a yellow product melting at 241° (dec.). Cl, found: 14.27%; chlorosalicylidenebiuret $C_9H_8O_3N_3Cl$ requires 14.69%. The yield was 44.5%.

When the same experiment was repeated at a temperature below the melting-point of urea, at 120–125°, a different product was obtained melting at 226°. The same product came out also in the presence of pyridine, but the yield in both cases was meagre. The yield was improved in the presence of 2 c.c. of 90% alcohol (on water-bath). The alcohol evaporated leaving behind an orange mass, which on purification melted at 226° (dec.). Cl, found: 13.34%; chlorosalicylidenediurea $C_9H_{12}O_3N_4Cl$ requires 13.69%. The yields were 37.8 and 27.7% respectively without and with pyridine.

3: 5-Dichlorosalicylaldehyde (1.0 gr.) and urea (0.6 gr.) were heated, in two separate flasks, with and without pyridine as before at 150–160° for seven hours, but charring took place in both. In another experiment a lower temperature (132–140°) was tried, which in seven hours gave a yellowish substance melting at 261°. It was insoluble in water or in ordinary organic solvents, but dissolved in alkalis from which it could be reprecipitated. Cl, found: 25.28%; dichlorosalicylidenebiuret $C_9H_7N_3O_3Cl_2$ requires 25.72%. The yields were 35.9 and 21.13% respectively.

The same experiments when repeated on a water-bath gave a product melting at 175° with an orange colour and resembling the above in its general insolubility. It also decomposed into the original aldehyde and urea when

it was heated with mineral acids. Cl, found: 23.96%: dichlorosalicylidene-diurea $C_9H_{10}N_4O_3Cl_2$ requires 24.23%. The yields were poor but increased to 11.9 and 9.3%, when the heating was at 128–130°.

Condensations with Formamide

5-Chlorosalicylaldehyde (0.8 gr.) and formamide (0.45 gr., 1:2 mols.), heated on water-bath for 8 hours, gave, after the usual treatment and recrystallisation (hot alcohol), a yellow substance melting at 270°. Cl, found: 24.62%: monochlorosalicylidene-*mono*formamide $C_8H_8O_2NCl$ requires 19.34%, chlorosalicylidene-*bis*formamide $C_9H_9O_3N_2Cl$ requires 15.53%, and tetramonochlorosalicylpyrazine $C_{28}H_{16}N_2O_4Cl_4$ requires 24.23%. The yield was 80%. The product affected neither Baeyer's reagent nor cold concentrated sulphuric acid.

3:5-Dichlorosalicylaldehyde (1.0 gr.) and formamide (0.45 gr.) were heated at 100–105° for 8 hours, when an orange mass was obtained: it was left soaking in water for twenty-four hours when it changed into a yellow plastic. There was much resin, but it was resolved into two parts, one soluble, the other insoluble, in alcohol. The former, coming out in white needle crystals, melted at 207°. The latter melted at 227°. Cl, found in the first 26.91%; dichlorosalicylidene-*bis*formamide $C_9H_8O_3N_2Cl_2$ requires 26.99%, while dichlorosalicylidene-*mono*formamide $C_8H_7O_2NCl_2$ requires 32.56%. Cl, found in the second was 39.01%; tetradichlorosalicylpyrazine $C_{28}H_{12}O_4N_2Cl_8$ requires 39.22%. The yield of the first was only 3.6% and that of the second was 10.5%. When the condensation was conducted at 120–130°, the former disappeared and the latter increased to 21.1%.

SUMMARY

5-Chloro- and 3:5-dichlorosalicylaldehydes have been condensed with different amides under different conditions. In contrast with the *-mono-*amides obtained in all the salicylaldehyde-amide condensations,⁷ the monochlorosalicylaldehyde gave monoamides with only three amides, of which one, benzamide, gave the *bis-* product as well. The 3:5-dichlorosalicylaldehyde gave the monoamide only once, in its condensation with benzenesulphonamide: for all the rest the *-bis* product was the usual rule. This may be one of the effects of the chlorine on the aromatic ring of the aldehyde. Except in one case the yields in the dichlorosalicylaldehyde-amides condensations were all higher than those of the monochloro-aldehyde-amide condensations, reaching, in condensations with propionamide and benzenesulphonamide, the quantitative limits. Usually the highest yields were obtained at 100–110° and in the absence of any condensing agent.

TABLE

Amides	Maximum yields with Salicylaldehyde?	5-Chlorosalicylaldehyde	3 : 5-Dichlorosalicylaldehyde	
Formamide	.. 100 -mono-	0	10.5	-bis-pyrazine deriva.
Acetamide	.. 98 "	80 -bis-	21.1	-bis-
Propionamide	.. 88.2 "	53 -bis-	86.28	-bis-
n-Butyramide	.. not tried	44 "	99	"
n-Heptamide	.. "	73 "	85	"
Benzamide	.. 96.4 -mono-	18 -mono-	79.5	"
		40 "	85.7	"
		56 -bis-		
Benzenesuphonamide	.. not tried	60 -mono-	100	-mono-
Urea	.. "	44 diurea	11.3	diurea
		37.8 biuret	36	biuret

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