CXXI.—*The Aldehydosalicylic Acids and their Derivatives.*

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By the action of chloroform and sodium hydroxide on salicylic acid two isomeric aldehydo-acids are formed which Tiemann and Reimer (*Ber.*, 1876, **9**, 1268), who first studied this reaction, named respectively ortho- and para-aldehydosalicylic acid. These substances, containing as they do three different reactive groups, are specially interesting, but have so far received little attention. We have therefore undertaken a careful examination of them as well as of similar derivatives of other hydroxy-acids, which will form the subject of a future communication. For convenience of nomenclature, the above two acids will be referred to as the 3- and 5-aldehydosalicylic acids.

Preparation of 3- and 5-Aldehydosalicylic Acids.

The method used, with slight modifications, is that described by Tiemann and Reimer (*loc. cit.*). After precipitating the mixed acids with hydrochloric acid, filtering, and washing, instead of extracting with ether and separating the acids by shaking the ethereal solution with sodium hydrogen sulphite, a simpler and more effective method of separation is to crystallise the mixed acids, after precipitation, from alcohol. The 5-acid, which is the chief product, is much less soluble than the 3-compound or salicylic acid and in this way complete separation of the acid may be effected, with little loss, by not more than two crystallisations. On the average, one-third of the weight of the original salicylic acid in the form of the pure 5-compound was obtained. The mother-liquors contain a small quantity of the 3-compound mixed with salicylic acid and some resinous matter, from which the first can be separated by treatment of the ether solution with sodium hydrogen sulphite as described by Tiemann and Reimer.

The Methyl Esters of 3- and 5-Aldehydosalicylic Acids.

The methyl esters were prepared by the action of methyl iodide on the dry silver salts suspended in ether, separating the ether solution, and removing the ether.

The 5-compound crystallises from alcohol in pale buff-coloured needles, m. p. 78° , but may be obtained quite colourless by conversion into the bisulphite compound, reprecipitation, and recrystallisation. It then melts at $82-83^{\circ}$ (Found: C = 59.7; H = 4.5. $C_9H_8O_4$ requires C = 60.0; H = 4.44 per cent.). The *ethyl* ester, which was prepared in a similar way, melts at 75° .

The 3-compound, prepared as above, crystallises from alcohol in needles and melts at 87° (Found: C = 60.03; H = 4.77. $C_9H_8O_4$ requires C = 60.0; H = 4.44 per cent.).

Methyl 2-Methoxy-5-aldehydobenzoate.—Three grams of the ester were mixed with 7 to 8 grams of methyl sulphate, and 2 grams of sodium hydroxide in 45 c.c. of water were gradually added while the mixture was gently warmed and shaken. The solid sodium compound first separated and was subsequently replaced by an oily liquid. The solution finally became acid and the excess of methyl sulphate was then decomposed by heating for a short time on the water-bath. On cooling and stirring, the oil solidified. It was ground up with a solution of sodium carbonate to remove the unchanged hydroxy-ester and then crystallised from boiling water, from which it separated in colourless, silky needles, m. p. $86-87^{\circ}$. It is insoluble in sodium carbonate solution, and is readily distinguished from the original hydroxy-ester by the fact that both dissolve in a hot solution of sodium carbonate, but the hydroxy-ester does not separate on cooling, whereas the methoxy-compound crystallises out (Found: C = 61.74; H = 5.22. $C_{10}H_{10}O_4$ requires C = 61.86; H = 5.16 per cent.). Various condensation products were prepared by methods similar to those described on p. 1026. The *phenylhydrazone* crystallises from alcohol in pale yellow needles, m. p. $133-135^{\circ}$; the *nitrophenylhydrazone*, which was obtained by adding a solution of nitrophenylhydrazine to the methoxy-ester, both dissolved in ethyl acetate, was crystallised from pyridine and alcohol and formed clusters of dark red needles, m. p. 200° . The *oxime* crystallises from dilute alcohol in clusters of colourless needles, m. p. $145-147^{\circ}$, and the *semicarbazone* from pyridine in small rectangular plates, m. p. 190° . *2-Methoxy-5-aldehydobenzoic acid* was obtained by hydrolysis of the above ester. It crystallises from water in long, nearly colourless needles, m. p. 170° .

Acyl Derivatives of 5-Aldehydosalicylic Ester.

The *benzoyl* derivative was prepared by dissolving 1 gram of the ester in sodium hydroxide solution; on adding the equivalent quantity of benzoyl chloride and gently warming the mixture with the occasional addition of sodium hydroxide solution, the oily liquid eventually solidified. It was separated, washed, and

recrystallised from a small quantity of alcohol, in which it is very soluble. It crystallises in colourless prisms with pointed ends and melts at 99–101° (Found : C = 67.69; H = 4.39. $C_{16}H_{12}O_5$ requires C = 67.61; H = 4.23 per cent.).

The *acetyl* derivative was obtained by heating 1 gram of the ester with 1 gram of acetyl chloride on the water-bath for half an hour. The product was then poured into water and a little ammonia added to decompose the excess of acetyl chloride. The solid product was crystallised from alcohol and formed colourless needles melting at 81–82° (Found : C = 59.55; H = 4.48. $C_{11}H_{10}O_5$ requires C = 59.45; H = 4.5 per cent.).

Bromination of 5-Aldehydosalicylic Ester.

The ester was dissolved in four times its weight of glacial acetic acid, and an equal weight of bromine in twice its weight of acetic acid was added; the mixture was kept for a short time and then poured into water. The product was filtered, washed, and crystallised twice from dilute alcohol, from which it separated in colourless needles, m. p. 115–116° (Found : C = 41.56; H = 2.84. $C_9H_7O_4Br$ requires C = 41.7; H = 2.7 per cent.). The substance is therefore a monobromo-derivative. The bromine atom probably occupies the 3-position, which is ortho to the hydroxyl and meta to the carboxyl group. The *phenylhydrazone* of the bromine derivative was obtained by dissolving the latter in acetic acid and adding half the weight of phenylhydrazine in the same solvent. The phenylhydrazone was thrown down as a yellow precipitate, which was filtered, washed, and crystallised twice from acetic acid. It forms greenish-yellow needles, m. p. 155–157° (Found : N = 8.17. $C_{15}H_{12}O_3N_2Br$ requires N = 8.05 per cent.).

Nitration of 5-Aldehydosalicylic Ester.

Mononitro-derivative.—Five grams of the ester were slowly added to four times the weight of a mixture of equal parts of fuming nitric acid and concentrated sulphuric acid and cooled to 5°, whilst the temperature was maintained below 10° during the process. When the ester had completely dissolved, the mixture was kept for half an hour, then poured on to ice, and the solid was filtered and washed. It yielded 6.3 grams of the crude nitro-product, which may be crystallised from ethyl acetate or benzene and forms glistening plates, m. p. 161–163° (Found : N = 6.43. $C_9H_7O_6N$ requires N = 6.24 per cent.).

On the addition of sodium hydroxide, the sodium compound separates in the form of clusters of orange needles. The nitro-compound also dissolves in pyridine with a deep yellow colour, indicating the formation of a pyridine salt.

An attempt was made to prepare the amino-derivative of the above by reduction with tin and hydrochloric acid, but no pure product could be isolated. After removal of the tin with hydrogen sulphide and evaporating the filtrate, a sticky residue was obtained, from which no crystalline product could be prepared.

Dinitro-derivative.—In one nitration experiment in which the substance was probably longer in contact with the acid, a second nitro-derivative was isolated similar in appearance to the above nitro-compound but melting at 128—130°. The analysis indicated a dinitro-derivative (Found : N = 10.39. $C_9H_6O_8N_2$ requires N = 10.41 per cent.).

Nitration of 5-Aldehydosalicylic Acid.

Five grams of the aldehydo-acid were added to 25 c.c. of fuming nitric acid, cooled and maintained at about 0—5° in ice. The mixture was left for a few minutes until all was dissolved and then poured on to ice. The yield of the crude nitro-compound was 6 grams. It was purified by converting it into the sodium salt by adding sodium carbonate to the concentrated solution of the nitro-compound. The sodium salt separates in red needles. It was filtered and decomposed with hydrochloric acid. When crystallised from hot water, the nitro-derivative melts at 172—173°, but at 182—183° when crystallised from alcohol. The difference is due to the presence of water of crystallisation in the former compound. The substance proved to be identical with dinitrosalicylic acid prepared from salicylic acid by Hübner (*Annalen*, 1879, **195**, 47), who gives the melting point as 173°. When dehydrated at 120°, it melts at 182°, a fact not mentioned by Hübner. The hydrated acid was analysed (Found : N = 11.58; H_2O = 7.74. $C_7H_4O_7N_2 \cdot H_2O$ requires N = 11.39; H_2O = 7.44 per cent.).

The action of nitric acid is probably to oxidise the aldehyde group to carboxyl, then to replace the carboxyl by splitting off carbon dioxide, and at the same time a nitro-group enters the nucleus in the ortho-position to the hydroxyl group, thus :

Oxidation of 5-Aldehydosalicylic Acid.

The action of permanganate on the acid was examined by Tiemann and Reimer (*Ber.*, 1877, **10**, 1571), who obtained in this way *o*-hydroxyisophthalic acid. We have repeated the process in a slightly modified form as follows : 3.4 grams of the acid were dissolved

in sodium hydroxide solution containing 1 gram of NaOH in 50 c.c. of water. To this solution 1.5 grams of permanganate in 300 c.c. of water were added. The colour of the permanganate changed at once to brown, and on standing the peroxide separated. On passing in sulphur dioxide, the hydroxyisophthalic acid separated, whilst any unchanged acid remained in solution. The precipitate was filtered, washed, and crystallised from dilute alcohol. The filtrate was concentrated to a small bulk and the unchanged acid precipitated with hydrochloric acid, filtered, and treated with the same quantity of permanganate as before, and if necessary the process was again repeated. In this way, practically the whole of the aldehydosalicylic acid may be oxidised. On heating in a capillary tube, it began to decompose at 285° , turning brown and giving off bubbles of gas. Tiemann and Reimer give 300° as the melting point, but do not refer to any decomposition.

Condensation Products of 5-Aldehydosalicylic Ester.

The *oxime* was prepared by mixing together 0.5 gram of the ester, dissolved in a little alcohol, 0.2 gram of hydroxylamine hydrochloride in water, and 0.15 gram of anhydrous sodium carbonate, also dissolved in water. On warming, a rapid effervescence occurred and a white precipitate was immediately thrown down. It was filtered, washed, and crystallised from dilute alcohol and formed clusters of colourless needles, m. p. $147-148^{\circ}$ (Found : N = 7.15. $C_9H_9O_4N$ requires N = 7.18 per cent.).

The *hydrazone* was obtained by mixing together 0.5 gram of ester, 0.43 gram of hydrazine sulphate dissolved in water, and 0.35 gram of anhydrous sodium carbonate dissolved in water. An immediate precipitate was formed and was filtered, washed, and crystallised either from glacial acetic acid or nitrobenzene. From the former it separates in colourless needles, m. p. $239-240^{\circ}$. It is insoluble in alcohol and benzene (Found : N = 7.96. $C_{18}H_{16}O_6N_2$ requires N = 7.91 per cent.).

The compound is therefore a di-aldehydosalicylic ester hydrazone,

The *semicarbazone* was obtained by dissolving 1 gram of the ester in 0.22 gram of sodium hydroxide in 20 c.c. of water and then adding 0.8 gram of semicarbazide hydrochloride. The solution, which was faintly acid, was heated on the water-bath for half an hour, cooled, and the semicarbazone which separated was filtered and washed. It was crystallised from pyridine, from which it separates

in small prisms with pointed ends, m. p. 215—216° (Found : N = 17·76, 17·68. $C_{10}H_{11}O_4N_3$ requires N = 17·72 per cent.).

In the first experiment, the product was crystallised from glacial acetic acid. It was then found that, on heating, acetic acid was evolved, and analysis showed that the semicarbazone acetate was present (Found : N = 14·32, 14·07, 14·16. $C_{12}H_{15}O_6N_3$ requires N = 14·14 per cent.).

The *phenylhydrazone* was prepared by mixing together concentrated alcoholic solutions containing 0·6 gram of ester and 0·4 gram of phenylhydrazine and heating on the water-bath first with reflux and then in an open vessel until the alcohol was driven off. On cooling and adding a crystal of the phenylhydrazone, the mass solidified and was washed free from phenylhydrazine with light petroleum. It crystallised from alcohol in pale yellow aggregates of blunt prisms, m. p. 120—121° (Found : N = 10·29. $C_{15}H_{14}O_3N_2$ requires N = 10·36 per cent.).

The *nitrophenylhydrazone* was obtained by mixing equal weights of nitrophenylhydrazine and the ester in alcoholic solution. In a short time dark red crystals of the hydrazone separated and were filtered and washed. The substance is slightly soluble in glacial acetic acid or alcohol and insoluble in benzene. It crystallises most readily from nitrobenzene or pyridine (in both of which it is fairly soluble), forming flat prisms with pointed ends. It melts at 265—267° (Found : N = 13·36. $C_{15}H_{13}O_5N_3$ requires N = 13·32 per cent.).

Condensation of 5-Aldehydosalicylic Ester with 1 : 3-Diketones.

An attempt was made to condense the aldehydo-ester with aldehydes and ketones and also to apply Knoevenagel's reaction by mixing it with acetoacetic ester, malonic ester, acetylacetone, etc., in presence of alkali or piperidine; but although it was clear that in most cases some condensation had occurred, it was only in the case of acetylacetone that a definite product was isolated. One gram of the ester was dissolved in acetylacetone and a drop of piperidine added. On standing, the mixture solidified, forming brown crystals, m. p. 93—94°. On crystallisation from alcohol, colourless needles were obtained, m. p. 94—95° (Found : C = 64·08; H = 5·41. $C_{14}H_{14}O_5$ requires C = 64·14; H = 5·34 per cent.).

5-Aldehydosalicylic Ester Cyanohydrin.

On adding 10 c.c. of strong sodium hydrogen sulphite solution to 2·5 grams of the ester, in a few minutes the mixture became semi-solid from the formation of the crystalline aldehydo-bisulphite compound. It was separated by filtration and pressed down.

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To the moist bisulphite compound 2 grams of potassium cyanide in 5 c.c. of water were added and the mixture was warmed on the water-bath, when a brown oil of the cyanohydrin separated. This was extracted with ether, the ether removed, and the residue heated with concentrated hydrochloric acid to convert the cyanohydrin into the corresponding hydroxy-acid; but although the reaction was repeated with modifications, the original aldehydo-ester was each time regenerated.

2-Hydroxy-3-carboxy- and 4-Hydroxy-5-carboxy-cinnamic Acids.

By the action of acetic anhydride and fused sodium acetate on the 5-aldehydo-acid at the boiling point of the anhydride, slight effervescence occurred, due probably to the splitting off of carbon dioxide. On boiling the resulting mass with potassium hydroxide and acidifying, a viscous, yellow oil was obtained, which could not be crystallised or otherwise purified. Recourse was then had to the method used by Sir W. H. Perkin for the preparation of coumarin (*Annalen*, 1868, **147**, 230), which consists in acting on the sodium salt of the phenol-aldehyde with acetic anhydride and sodium acetate. The sodium salts of the esters were therefore first prepared by dissolving the esters in methyl alcohol and adding the calculated quantity of sodium as sodium methoxide, also in methyl alcohol. A crystalline precipitate was immediately thrown down, which was filtered, washed with alcohol and ether, and dried in a vacuum.

Sodium 5-aldehydosalicylic ester has a straw colour, is slightly soluble in alcohol and insoluble in ether (Found: Na = 11.17. $C_9H_7O_4Na$ requires Na = 11.38 per cent.).

Sodium 3-aldehydosalicylic ester has an orange colour, but in other respects is similar to the 5-aldehydo-ester compound (Found: Na = 11.8. $C_9H_7O_4Na$ requires Na = 11.38 per cent.).

Each of the above compounds was heated with an equal weight of fused sodium acetate and 2.5 parts of acetic anhydride at 160° for four to five hours. The resulting dark-coloured mass was boiled with potassium hydroxide solution, filtered from a small quantity of resinous matter, and the cinnamic acid precipitated by the addition of hydrochloric acid. After recrystallisation from water or dilute alcohol, the two acids were obtained as straw-coloured, crystalline powders very similar in appearance. *4-Hydroxy-5-carboxycinnamic acid* was analysed (Found: C = 57.41; H = 4.03. $C_{10}H_8O_5$ requires C = 57.69; H = 3.84 per cent.).

On heating, *2-hydroxy-3-carboxycinnamic acid* melts, darkens, and evolves water and carbon dioxide, and at the same time a crystalline substance sublimes in colourless needles, which can be

crystallised from hot water. It possesses the m. p. and the characteristic smell of coumarin.

This experiment therefore determines the position of the aldehyde group in the 3-aldehydo-acid.

Owing to the difficulty of obtaining the 3-aldehydo-acid in sufficient quantity, we have been unable to prepare a complete set of derivatives of this substance; but we hope to improve the yield and to publish further results in a subsequent paper.

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