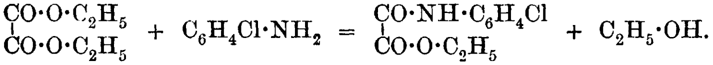
XIX.—*Halogen Derivatives of Substituted Oxamides.*

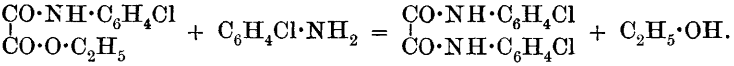
By FREDERICK DANIEL CHATTAWAY and WILLIAM HENRY LEWIS.

THE action of the halogens on substituted oxamides has been little studied, and the description of the substances formed is not satisfactory, inasmuch as the crude material was never subjected to any process of purification. By passing chlorine for different periods through a solution of oxanilide in boiling glacial acetic acid, Dyer and Mixter (*Amer. Chem. J.*, 1886, **8**, 349) obtained two products: one, the melting point of which is not given, they regard as being possibly a trichloro-oxanilide; the other, melting at 255°, they show to be somewhat impure tetrachloro-oxanilide.

In the course of the authors' study of substituted nitrogen chlorides, the action of chlorine on a boiling acetic acid solution of oxanilide has been investigated. In this action, a mixture of chloro-oxanilides is formed from which it is difficult to isolate any pure substance in quantity, although both *s*-di-*p*-chloro- and *s*-di-2 : 4-dichloro-oxanilides can be separated in sufficient amount for identification. For purposes of comparison, these two compounds and some closely related derivatives have been prepared from pure specimens of the anilines. The symmetrical disubstituted oxanilides or the ethyl esters of the corresponding substituted oxanilic acids are formed almost quantitatively when the substituted aniline is heated with ethyl oxalate, the product varying according as the aniline or the ethyl oxalate is present in excess.

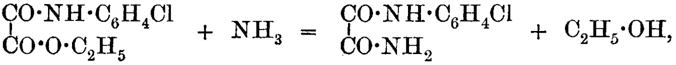


$$\begin{array}{l}\mathrm{CO{\cdot}O{\cdot}C_2H_5}\\ \mathrm{CO{\cdot}O{\cdot}C_2H_5}\end{array} + \mathrm{C_6H_4Cl{\cdot}NH_2} = \begin{array}{l}\mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\\ \mathrm{CO{\cdot}O{\cdot}C_2H_5}\end{array} + \mathrm{C_2H_5{\cdot}OH}.$$



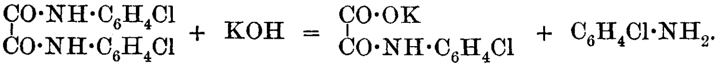
$$\begin{array}{l}\mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\\ \mathrm{CO{\cdot}O{\cdot}C_2H_5}\end{array} + \mathrm{C_6H_4Cl{\cdot}NH_2} = \begin{array}{l}\mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\\ \mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\end{array} + \mathrm{C_2H_5{\cdot}OH}.$$

Should the reaction yield a mixture of the two compounds, these can easily be separated from one another by dissolving out the oxanilic esters with alcohol, in which the disubstituted oxanilides are almost insoluble. When treated in alcoholic solution with ammonia, the oxanilic esters yield mono-substituted oxamides, thus:



$$\begin{array}{l}\mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\\ \mathrm{CO{\cdot}O{\cdot}C_2H_5}\end{array} + \mathrm{NH_3} = \begin{array}{l}\mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\\ \mathrm{CO{\cdot}NH_2}\end{array} + \mathrm{C_2H_5{\cdot}OH},$$

and when heated in alcoholic solution with the equivalent quantity of potassium hydroxide they yield the potassium salts of the substituted oxanilic acids, from which the acids are liberated on the addition of acetic acid:

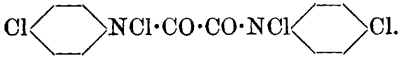


$$\begin{array}{l}\mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\\ \mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\end{array} + \mathrm{KOH} = \begin{array}{l}\mathrm{CO{\cdot}OK}\\ \mathrm{CO{\cdot}NH{\cdot}C_6H_4Cl}\end{array} + \mathrm{C_6H_4Cl{\cdot}NH_2}.$$

If to a boiling glacial acetic acid solution of oxanilide a saturated solution of bleaching powder is added, a white solid is deposited consisting mainly of a mixture of *s*-dichloro-oxanilide and its dichloroamino-derivative. The latter can be separated easily owing to its ready solubility in chloroform. Unlike most nitrogen chlorides containing phenyl residues with both ortho-positions to the nitrogen unoccupied, it is transformed into the isomeric oxanilide with the greatest difficulty, and its solution in acetic acid can be boiled until the whole is hydrolysed with regeneration of *s*-di-*p*-chloro-oxanilide; if any *s*-2:4-dichloro-oxanilide results, it is produced in too small a quantity to be recognised. Related to this reaction is the circumstance that if a saturated solution of bleaching powder is added to a boiling solution of *s*-2:4-dichloro-oxanilide in glacial acetic acid, the substituted oxamide is deposited from solution unchanged, no recognisable quantity of its chloroamino-derivative being formed. This behaviour is probably due to the hindrance offered to the addition of hypochlorous acid to the nitrogen by the spatial arrangement of the atoms forming the large molecule. It is less probable that it is due to the practical insolubility of the substituted oxanilides in even slightly diluted acetic acid.

That symmetrically disubstituted oxamides containing groups of less complexity can readily yield nitrogen chlorides and bromides is shown by the behaviour of *s*-dimethyloxamide and *s*-diethyloxamide, which are readily converted by hypochlorous or hypobromous acid into their *s*-dichloroamino- or *s*-dibromoamino-derivatives.

s-*Di*-p-*chlorophenyloxodichloroamide*,

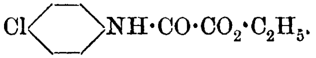


Oxanilide is so slightly soluble in water that an aqueous solution of hypochlorous acid has practically no action on it, and its dichloroamino-derivative has not up to the present been obtained. If to a solution of the anilide in boiling glacial acetic acid a saturated solution of bleaching powder is slowly added, a white solid is thrown out of solution, which consists of a mixture of *s*-di-*p*-chloro-oxanilide and its dichloroamino-derivative. If chloroform is added, the latter dissolves, and can be thus separated from the substituted anilide. To ensure complete conversion, the solution in chloroform is best shaken with a further quantity of bleaching powder solution acidified with acetic acid, and on separating the chloroform solution, drying, and evaporating off the solvent, the dichloroamino-derivative is left as a white, crystalline mass, which, after several crystallisations from a mixture of chloroform and petroleum, is obtained pure. It is readily soluble in boiling chloroform and sparingly so in petroleum; it crystallises from a mixture of the two in colourless, transparent rhombs (m. p. 169°).

0·3042 liberated I = 32·3 c.c. *N*/10 I. Cl as NCl = 18·82.
$C_{14}H_8O_2N_2Cl_4$ requires Cl as NCl = 18·76 per cent.

It is a stable substance, which undergoes transformation very slowly, if at all. On heating for some hours with boiling glacial acetic acid, hypochlorous acid or chlorine is gradually given off and *s*-di-*p*-chloro-oxanilide regenerated. *s*-Di-*p*-chlorophenyloxodichloroamide can be prepared also in a similar manner from *s*-di-*p*-chloro-oxanilide itself.

Ethyl p-*Chloro-oxanilate*,

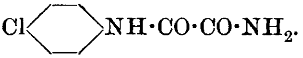


This compound is formed almost exclusively when ethyl oxalate (1 mol.) is heated to 180—200° for several hours with slightly less than the equivalent quantity (1 mol.) of *p*-chloroaniline. Ethyl alcohol is evolved and a clear, brown liquid obtained, which, on cooling, solidifies to a mass of crystals. On rubbing this to a paste with a little alcohol and pressing it on a porous plate, the ester is obtained as a white, soft, crystalline powder. It is moderately soluble in boiling alcohol, from which it crystallises well in thin, transparent, colourless plates (m. p. 155°), which have a pearly appearance when pressed together.

0·1886 yielded 0·1212 AgCl. Cl = 15·89.

$C_{10}H_{10}O_3NCl$ requires Cl = 15·58 per cent.

p-*Chloro-oxanilamide*,

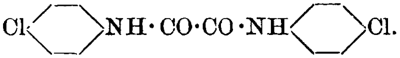


This compound, which is produced when a warm alcoholic solution of ethyl *p*-chloro-oxanilate is mixed with an alcoholic solution of ammonia, separates on cooling the liquid as a mass of fine needles and melts at 241°; it crystallises from boiling alcohol, in which it is sparingly soluble, in small, colourless needles, which form a felted mass from which the mother liquor can only be removed by considerable pressure.

0·1956 yielded 0·1435 AgCl. Cl = 18·14.

$C_8H_7O_2N_2Cl$ requires Cl = 17·85 per cent.

s-*Di*-p-*chloro-oxanilide*,

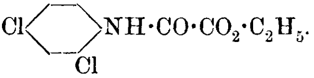


This compound, which is produced when ethyl *p*-chloro-oxanilate is heated with *p*-chloroaniline, is most easily made by heating *p*-chloroaniline in slight excess (2½ mols.) with ethyl oxalate (1 mol.) to 180—200° for three to four hours, the alcohol formed being allowed to escape. On cooling and extracting the crystalline mass repeatedly with boiling alcohol, the substituted oxanilide is left as a white, crystalline residue, scarcely soluble in any ordinary solvent. It can with some difficulty be recrystallised from boiling glacial acetic acid, in which, however, it is only slightly soluble and from which it separates in glittering, four-sided, rhombic plates. The best solvent for this and similarly substituted oxamides is hot nitrobenzene, in which they and oxanilide itself readily dissolve and from which they crystallise exceedingly well on cooling. The adhering nitrobenzene can be removed by boiling the crystals for a short time with alcohol. s-Di-*p*-chloro-oxanilide crystallises from hot nitrobenzene in glittering, long, colourless, transparent, thin plates, which are probably much flattened rhombic prisms (m. p. 288°).

0·4583 yielded 0·4189 AgCl. Cl = 22·60.
$C_{14}H_{10}O_2N_2Cl_2$ requires Cl = 22·94 per cent.

This compound can also be obtained by the direct chlorination of oxanilide dissolved in boiling glacial acetic acid, and is formed when *s*-di-*p*-chlorophenyloxodichloroamide is decomposed by a solution of hydriodic acid or by boiling alcohol.

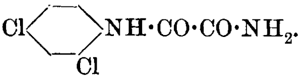
Ethyl 2 : 4-*Dichloro-oxanilate*,



This compound is prepared by heating 2 : 4-dichloroaniline (1 mol.) with rather more than the theoretical amount (1 mol.) of ethyl oxalate at 180—200° for two to three hours. On adding a little alcohol to the hot product and cooling, the ester separates as a felted mass of white needles. These, after washing with a little alcohol, can be recrystallised from boiling alcohol, in which the oxamate is moderately soluble; it crystallises from alcohol in colourless, transparent, long, hair-like crystals, seen under the microscope to be slender prisms (m. p. 119°).

0·2318 yielded 0·2556 AgCl. Cl = 27·26.
$C_{10}H_9O_3NCl_2$ requires Cl = 27·06 per cent.

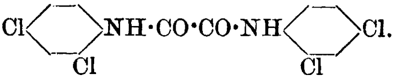
2 : 4-*Dichloro-oxanilamide*,



This compound separates as a mass of slender, white needles when a hot alcoholic solution of ethyl 2 : 4-dichloro-oxanilate is mixed with an alcoholic solution of ammonia. It is sparingly soluble in boiling alcohol, from which it crystallises as a network of colourless, branched, hair-like crystals (m. p. 234°).

0·1800 yielded 0·2228 AgCl. Cl = 30·60.
$C_8H_6O_2N_2Cl_2$ requires Cl = 30·43 per cent.

s-*Di*-2 : 4-*dichloro-oxanilide*,



This compound is produced when ethyl oxalate (1 mol.) is heated at 180—200° for three to four hours with a slight excess ($2\frac{1}{2}$ mols.) of 2 : 4-dichloroaniline. On cooling, a dark, semi-crystalline mass is left, from which *s*-di-2 : 4-dichloro-oxanilide is obtained as an insoluble crystalline powder on extracting with boiling alcohol. It is practically insoluble in all ordinary solvents, but can be recrystallised from boiling nitrobenzene, in which it is readily soluble, and from which it crystallises in colourless, glittering, transparent, very slender, flattened prisms (m. p. 276°).

0·2512 yielded 0·3800 AgCl. Cl = 37·40.
$C_{14}H_8O_2N_2Cl_4$ requires Cl = 37·52 per cent.

Action of Chlorine on Oxanilide.—It is not easy to obtain a pure product by the direct chlorination of oxanilide. If the latter compound is dissolved in a large excess of boiling glacial acetic acid and chlorine passed in to saturation, crystals resembling those of *s*-di-*p*-chloro-oxanilide separate on cooling. These are not pure, however, but contain some *s*-di-2 : 4-dichloro-oxanilide, and on repeatedly crystallising from nitrobenzene, the melting point of the substance, which at first, as a rule, melted not very sharply at about 245°, can be raised to about 280°. On passing chlorine for a long time into a glacial acetic acid solution of oxanilide, a little *s*-di-2 : 4-dichloro-oxanilide can be obtained, but the yield is poor and the process not a convenient one for preparing the compound.

s-*Dimethyloxodichloroamide*, $CH_3\cdot NCl\cdot CO\cdot CO\cdot NCl\cdot CH_3$.

This compound is easily prepared by suspending finely-divided *s*-dimethyloxamide in a solution of hypochlorous acid made by adding potassium hydrogen carbonate in excess to a solution of sodium hypochlorite. On adding a little chloroform and shaking, the dichloroamino-derivative is formed and dissolves in the chloroform. To ensure the complete conversion of the oxamide, the chloroform solution is again shaken with a fresh quantity of hypochlorous acid. On separating the chloroform solution, drying with calcium chloride, and driving off the solvent, the dichloroamino-derivative is left as a very pale yellow liquid, which solidifies on cooling and stirring with a little light petroleum. It forms a white, crystalline powder, easily soluble in light petroleum, from which it can be crystallised with some difficulty and from which it slowly separates in clusters of long, colourless, slender prisms (m. p. 37°). This substance and the other nitrogen chlorides described in this paper were analysed in the usual way by titrating with thiosulphate the iodine liberated by a weighed amount dissolved in acetic acid and mixed with excess of a solution of potassium iodide.

0·4070 liberated I = 87·9 c.c. *N*/10 I. Cl as NCl = 38·28.
$C_4H_6O_2N_2Cl_2$ requires Cl as NCl = 38·32 per cent.

s-*Diethyloxodichloroamide*, $C_2H_5·NCl·CO·CO·NCl·C_2H_5$.

This compound was prepared from *s*-diethyloxamide and isolated exactly as the compound previously described; it is a very pale yellow, viscid liquid, which, even after some months, shows no sign of crystallising. On strongly heating, it decomposes with evolution of gas.

0·4832 liberated I = 91·2 c.c. *N*/10 I. Cl as NCl = 33·45.
$C_6H_{10}O_2N_2Cl_2$ requires Cl as NCl = 33·28 per cent.

s-*Dimethyloxodibromoamide*, $CH_3·NBr·CO·CO·NBr·CH_3$.

This was prepared from *s*-dimethyloxamide in the same manner as the corresponding chlorine compound, using a solution of hypobromous acid made from mercuric oxide and bromine. A little free mercuric oxide was added to the solution to prevent the development of free bromine. On filtering off the chloroform solution, drying, and expelling the solvent, the dibromoamino-derivative was left as a very pale yellow, crystalline mass. It crystallises well from chloroform in long, flattened prisms or plates of a very pale yellow colour (m. p. 95°).

0·3373 liberated I = 49·2 c.c. *N*/10 I. Br as NBr = 58·32.
$C_4H_6O_2N_2Br_2$ requires Br as NBr = 58·35 per cent.

s-*Diethyloxodibromoamide*, $C_2H_5·NBr·CO·CO·NBr·C_2H_5$.

This compound was prepared from *s*-diethyloxamide and isolated exactly as the preceding compound; it crystallises from chloroform in brilliant, glittering plates having a very pale yellow colour (m. p. 82°).

0·2794 liberated I = 36·8 c.c. *N*/10 I. Br as NBr = 52·66.
$C_6H_{10}O_2N_2Br_2$ requires Br as NBr = 52·94 per cent.

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