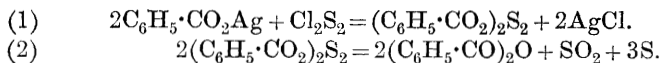


CCII.—*The Action of Sulphur Chloride and of Thionyl Chloride on Metallic Salts of Organic Acids: Preparation of Anhydrides.*

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(Carnegie Scholar).

THE preparation of anhydrides of organic acids by the action of sulphur chloride on metallic salts in the presence of an indifferent solvent has already been described by one of the authors (T., 1909, 95, 1237). The reaction proceeds in two stages, which are represented for the case of silver benzoate by the equations:

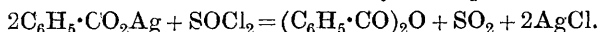


The intermediate compounds of the general formula $(\text{R}\cdot\text{CO}_2)_2\text{S}_2$ can, as a rule, be isolated, but very soon decompose spontaneously in the manner indicated by equation (2).

A compound of the type $(\text{R}\cdot\text{CO}_2)_2\text{S}_2$ may be regarded as a mixed anhydride of the organic acid and of an unknown sulphur acid, $\text{S}_2(\text{OH})_2$, of which sulphur monochloride, S_2Cl_2 , would be the chloride. Other derivatives of this acid are already known, as, for example, the substituted amides $\text{S}_2(\text{NMe}_2)_2$ and $\text{S}_2(\text{NEt}_2)_2$, which are readily obtained by the interaction of the alkylamines and

sulphur chloride (Michaelis, *Ber.*, 1895, **28**, 165). Lengfeld (*Ber.*, 1895, **28**, 449) describes esters which he terms methyl and ethyl thiosulphites, obtained by the action of sulphur chloride on sodium methoxide and on sodium ethoxide in the presence of light petroleum. The authors, although their attempts to prepare these compounds were unsuccessful and yielded only chlorinated products which evolved hydrochloric acid on keeping, propose to retain the term "thiosulphite" as a convenient designation for the acyl compounds now described.

The acyl thiosulphites should be compounds of considerable interest, and in the hope of isolating stable representatives of this class the salts of a large number of acids have been subjected to the reaction with sulphur chloride, but, despite minor variations in the degree of stability, a stable acyl thiosulphite was not obtained. The reaction, which proceeds smoothly as a rule, is, however, of general application as a method of preparing anhydrides, but fails in the cases of hydroxy- and amino-acids when more complex reactions occur, and it is inferior as a practical method to that in which thionyl chloride is used (P., 1909, **25**, 294). In this method equivalent quantities of the silver salt and thionyl chloride are shaken together in presence of ether or other indifferent solvent, when silver chloride, sulphur dioxide, and the anhydride are formed, the last-mentioned product being obtained nearly pure on filtration and removal of the solvent. The formation of benzoic anhydride in this manner is indicated by the equation:



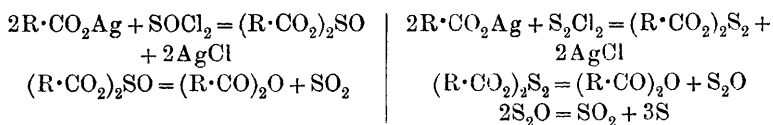
This method also is a general one, but, as with sulphur dioxide, fails in the case of amino-acids, whilst the reaction with hydroxy-acids appears to be abnormal. The preparation of bromoacetic anhydride from the sodium salt according to this method is described in the experimental part of this paper.

The salts of hydroxy-acids are exceptional in their behaviour towards both sulphur chloride and thionyl chloride. Sulphur chloride has little action on silver glycollate, it reacts only slowly with silver malate, whilst, with silver mandelate, reaction occurs more readily, but apparently in a less simple manner than usual. Thionyl chloride, on the other hand, reacts at once with all three salts. In the case of silver glycollate, a white, crystalline compound separates from the filtrate, the composition of which is represented by the formula $(\text{HO}\cdot\text{CH}_2\cdot\text{CO}_2)_2\text{SO}$; similar compounds are formed from silver mandelate and silver malate, although they have not been isolated in a pure condition. All these compounds part with sulphur dioxide only slowly in dry air even when they

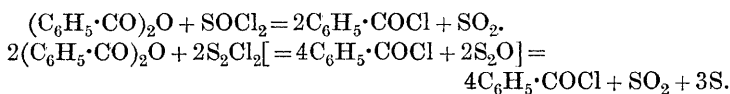
are heated. The formation of intermediate thionyl compounds was not observed in the preparation of anhydrides of other acids by this method, and as silver methoxyacetate does not yield a thionyl compound, it appears probable that the hydroxyl group plays a specific part in the reaction when salts of hydroxy-acids are used. Jarrard, however, on applying the method to the preparation of mellitic trianhydride, noted the formation of an intermediate compound which was not decomposed at once by boiling the solution (P., 1913, **29**, 106). From the products of the reactions between thionyl chloride and the salts of these hydroxy-acids it has been found possible to separate substances of undetermined constitution which have the same percentage composition as would be possessed by anhydrides of normal type; the conditions for their preparation having now been established, their investigation will be continued. The anhydride derived from malic acid is crystalline, and appears to be a chemical individual; it differs, probably, from the substance of the same composition obtained by Walden by heating the acid. The anhydride derived from mandelic acid is a glass, and, whilst similar to the anhydrides described by Bischoff and Walden (*Annalen*, 1899, **279**, 129), Staudinger (*Ber.*, 1911, **44**, 545), and Stutz (*Ber.*, 1911, **44**, 3485), may be represented by a simpler empirical formula.

The results just recapitulated are of some interest in connexion with the much-discussed question of the constitution of sulphur chloride. At present opinion seems to be divided between the constitutions represented by the formulæ $\begin{smallmatrix} \text{S} \cdot \text{Cl} \\ | \\ \text{S} \cdot \text{Cl} \end{smallmatrix}$ and $\text{S} : \text{S} \begin{smallmatrix} \text{Cl} \\ \diagup \\ \text{Cl} \end{smallmatrix}$, the latter representing the compound as the sulphur analogue of thionyl chloride. Although either formula is sufficient for the representation of the reactions at present under consideration, it may be pointed out, in view of the possible similarity in constitution of the two chlorides, that the analogy between the two series of reactions may be made more striking on the assumption that the first product of the interaction of the silver salt and thionyl chloride is the unstable mixed anhydride $(\text{R} \cdot \text{CO}_2)_2\text{SO}$, an assumption which finds support in Jarrard's observation just mentioned, even if the formation of a thionyl compound from silver glycollate is thought to be inadmissible as evidence on account of the possible participation of the hydroxyl groups in the reaction. Further, the intermediate compound, $(\text{R} \cdot \text{CO}_2)_2\text{S}_2$, derived from sulphur chloride may be regarded as giving as the first products of decomposition the anhydride $(\text{R} \cdot \text{CO})_2\text{O}$, and an oxide of sulphur, S_2O , which immediately decomposes into sulphur dioxide and sulphur.

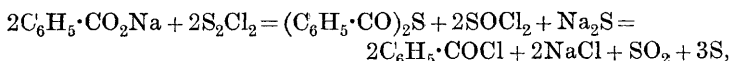
The fact that the decomposition of the acyl thiosulphite proceeds as a reaction of the first order is in harmony with this view. The changes which occur would then be represented as follows:



It may not be superfluous to point out that the analogy extends further, for, if silver benzoate is treated in the presence of ether with twice the quantity of thionyl chloride that is required for the formation of the anhydride, the filtrate, on evaporation of the solvent, gives benzoyl chloride in good yield. The preparation of acid chlorides of hydroxy-acids according to this method has been patented (Kopetschni and Karczag, Fr. Pat. 450227). Similarly, although less readily and less smoothly, sodium benzoate when heated with sulphur chloride in equimolecular proportions gives essentially benzoyl chloride, sodium chloride, sulphur dioxide, and free sulphur (Carius, *Annalen*, 1858, **106**, 291). Benzoyl chloride is formed also when benzoic anhydride is heated with sulphur chloride. The following equations represent similar reactions:



The two stages represented by the equations:



in which Carius thought the reaction between sodium benzoate and sulphur chloride to occur, appear to be less probable.

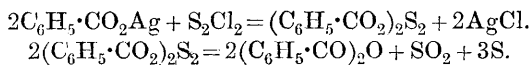
EXPERIMENTAL.

The products obtained by the action of sulphur chloride on sodium benzoate and on the silver salts of acetic, propionic, benzoic, *o*-toluic, *m*-toluic, *p*-toluic, and phenylacetic acids have already been described (T., 1909, **95**, 1235). Additional data are here given regarding the benzoyl compound, and a record of experiments with salts of other acids, which were carried out in the search for a stable compound of the type.

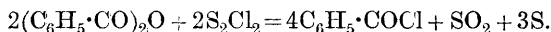
Action of Sulphur Chloride on Silver Salts.

Sulphur Chloride and Silver Benzoate.—12.5 Grams (instead of 11.5 grams) of silver benzoate suspended in 50 c.c. of dry ether

were treated with 3·4 grams of sulphur chloride, and the mixture was shaken vigorously. After filtration from the silver chloride and removal of the ether, 7·5 grams of benzoyl thiosulphite were obtained as a colourless syrup, which soon crystallised with marked evolution of heat, and afterwards decomposed. From the products of decomposition 5·6 grams of the crude anhydride were extracted by means of ether, and 0·96 gram of sulphur was left. The calculated quantities (reckoning on the amount of sulphur chloride used) are 7·6 grams of benzoyl thiosulphite, 5·65 grams of benzoic anhydride, and 0·95 gram of sulphur, if the reactions which occur are represented by the equations:



The crude anhydride was now mixed with 3·4 grams of sulphur chloride and heated under reflux for four hours. On extraction of the product with ether, 1 gram of sulphur was left, and the ethereal extract contained 6 grams of dissolved matter, which consisted chiefly of benzoyl chloride. The calculated amounts are 1·2 grams of sulphur and 7·1 grams of benzoyl chloride on the assumption that the reaction is represented by the equation:



Determination of the Velocity Constant for the Decomposition of Benzoyl Thiosulphite.

The sulphur dioxide evolved from a solution of the compound in boiling toluene was expelled from the containing flask by means of a regular current of dry carbon dioxide, and passed through a reflux condenser into a dilute solution of iodine in potassium iodide, which was replaced from time to time.

The total volume of iodine solution used (after some hours) = a = 71·2 c.c.

Minutes.	x = c.c. Iodine.	$a - x$.	$1/t \log a/a - x$.
10	9·1	62·1	0·0059
26	21·4	49·8	0·0060
45	33·0	38·2	0·0060
71	43·7	27·5	0·0059
85	48·2	23·0	0·0058

Sulphur chloride and silver n-butyrate gave a viscous liquid, which closely resembled the acetyl compound:

0·3199 gave 0·6220 BaSO_4 . $\text{S} = 26\cdot71$.

0·4805, in 12·25 benzene, gave $\Delta t = -0\cdot08^\circ$. $\text{M.W.} = 213$.

$\text{C}_8\text{H}_{14}\text{O}_4\text{S}_2$ requires $\text{S} = 26\cdot89$ per cent. $\text{M.W.} = 238$.

Sulphur chloride and silver isobutyrate reacted in the usual way, but the intermediate product was so unstable that a sample could not be obtained for analysis.

Sulphur chloride and silver isovalerate gave an oil which decomposed almost immediately after preparation:

0.3437 gave 0.5954 BaSO_4 . $S=23.76$.

0.3972, in 9.07 benzene, gave $\Delta t = -0.055^\circ$. $M.W.=233$.

$\text{C}_{10}\text{H}_{18}\text{O}_4\text{S}_2$ requires $S=24.06$ per cent. $M.W.=266$.

The decomposition products from these preparations reacted immediately with aniline, giving about the same yields of anilide as is obtained from acetic anhydride.

Sulphur chloride and silver palmitate gave an intermediate product, which was only sparingly soluble in ether. The reaction mixture was therefore warmed, and, on filtering the solution, palmityl thiosulphite crystallised in soft, feathery crystals, which closely resembled those of palmitic acid:

0.2417 gave 0.2050 BaSO_4 . $S=11.64$.

0.7049, in 25.05 benzene, gave $\Delta t = -0.30^\circ$. $M.W.=469$.

$\text{C}_{32}\text{H}_{62}\text{O}_4\text{S}_2$ requires $S=11.15$ per cent. $M.W.=574$.

The compound decomposed normally, but the anhydride was not easily obtained free from sulphur.

Sulphur chloride and silver α -naphthoate gave a product which separated from the ethereal solution as a white, crystalline mass:

0.3212 gave 0.3688 BaSO_4 . $S=15.77$.

$\text{C}_{22}\text{H}_{14}\text{O}_4\text{S}_2$ requires $S=15.76$ per cent.

The anhydride presumably formed when this substance decomposed, either at the ordinary temperature or on heating, could not be obtained free from a small quantity of sulphur. After dissolving it in a solution of sodium hydroxide and filtering from the undissolved sulphur, addition of hydrochloric acid to the solution precipitated α -naphthoic acid in a pure state.

Sulphur chloride and silver monochloroacetate reacted normally, and yielded a compound which is similar to the acetyl compound, but is less stable:

0.4750 gave 0.8997 BaSO_4 . $S=26.02$.

0.649, in 10.51 benzene, gave $\Delta t = -1.57^\circ$. $M.W.=197$.

$\text{C}_4\text{H}_4\text{O}_4\text{Cl}_2\text{S}_2$ requires $S=25.50$ per cent. $M.W.=251$.

Sulphur chloride and silver tribromoacetate gave a dark brown oil, which deposited sulphur before the ether was completely removed.

Sulphur chloride and the silver bromobenzoates reacted normally. The products are probably less stable than the benzoyl compound;

for this reason and on account of its sparing solubility the para-compound was not obtained pure:

o-compound: 0.2162 gave 0.2070 BaSO₄. S=13.15.

m-compound: 0.4156 „ 0.4272 BaSO₄. S=14.11.

p-compound: 0.2350 „ 0.1730 BaSO₄. S=10.11.

C₁₄H₈O₄Br₂S₂ requires S=13.79 per cent.

Sulphur chloride and the silver nitrobenzoates react normally, and the products which, like the anhydrides themselves, are only sparingly soluble in the usual solvents, undergo normal decomposition. The reactions were carried out in the presence of carbon disulphide, and the anhydrides were extracted from the decomposition products by means of ethyl acetate, and were recrystallised from that solvent:

o-compound: 0.3352 gave 0.4194 BaSO₄. S=17.19.

m-compound: 0.1894 „ 0.2150 BaSO₄. S=15.56.

p-compound: 0.1062 „ 0.1204 BaSO₄. S=15.55.

C₁₄H₈O₈N₂S₂ requires S=16.16 per cent.

Sulphur chloride and the silver aminobenzoates react at once in presence of ether. After concentration of the yellow ethereal solution and addition of light petroleum a yellowish-brown substance is precipitated, the sulphur content of which agrees approximately with that of a substance of the formula (NH₂·C₆H₄·CO₂)₂S₂, but this compound, if formed, is not of the usual type, and although some sulphur separates on keeping, the residue still contains combined sulphur.

Sulphur Chloride and Silver Salts of Hydroxy-acids.—Reaction between sulphur chloride and silver glycolate or silver malate proceeds only slowly in the presence of ether. The products are syrups which deposit sulphur and evolve sulphur dioxide, but no definite compounds were obtained from the decomposition products. In the case of silver mandelate reaction occurs at once on the addition of an ethereal solution of sulphur chloride to a suspension of the salt in ether. After filtration from the silver chloride and removal of part of the ether by distillation, addition of light petroleum causes the precipitation of a crystalline paste, which at once decomposes with deposition of sulphur and evolution of sulphur dioxide. The only pure substance that could be obtained from the decomposition product was mandelic acid.

The behaviour of sulphur chloride towards the silver salts of the hydroxybenzoic acids appears to be irregular.

Action of Thionyl Chloride on Silver Salts.

Action of Thionyl Chloride on Silver Benzoate.—4.7 Grams of silver benzoate (instead of 4.6 grams) were treated with 1.2 grams of thionyl chloride in the presence of 30 c.c. of ether. On distillation of the ether from the filtered solution, 2.1 grams of nearly pure benzoic anhydride were obtained. The calculated amount is 2.3 grams. The method has been further tested by the preparation in a similar manner of the anhydrides of acetic, monobromoacetic, palmitic, *o*-bromobenzoic, *m*-nitrobenzoic, and α -naphthoic acids. The preparation of the anhydride of *o*-bromobenzoic acid does not appear to have been previously recorded.

Preparation of o-Bromobenzoic Anhydride.—0.6 Gram of thionyl chloride was shaken with 3.2 grams (instead of 3.1 grams) of silver bromobenzoate in the presence of 60 c.c. of ether. 1.65 Grams of a yellow, crystalline substance separated from the viscous liquid which remained after removal of the ether by distillation from the filtered solution. The calculated yield of anhydride is 1.99 grams. The yellow impurity was removed by recrystallisation from ether after treatment with animal charcoal. The anhydride melts at 75–76°:

0.1512 gave 0.1470 AgBr. Br=41.37.

$C_{14}H_8O_3Br_2$ requires Br=41.65 per cent.

Gerhardt (*Annalen*, 1853, **87**, 158) was unable to obtain *m*-nitrobenzoic anhydride in the pure state by the action of phosphoryl chloride on the sodium salt. Autenrieth (*Ber.*, 1901, **34**, 184) gives 47° as the melting point for the anhydride prepared by boiling *m*-nitrobenzoic acid with acetic anhydride. The melting point of the anhydride prepared as described below was 160°.

Preparation of m-Nitrobenzoic Anhydride.—Six grams of silver *m*-nitrobenzoate (instead of 5.5 grams) were shaken with 1.2 grams of thionyl chloride in 30 c.c. of ether. The ether was removed by distillation, and the residual mixture of silver chloride and anhydride was extracted twice by boiling with 20 c.c. of ethyl acetate each time. The crude product was recrystallised from ethyl acetate:

0.2116 gave 0.4114 CO_2 and 0.0502 H_2O . C=53.02; H=2.63.

$C_{14}H_8O_7N_2$ requires C=53.16; H=2.53 per cent.

Preparation of Bromoacetic Anhydride.—Twenty grams of thionyl chloride were added gradually to a slightly warm mixture of 55 grams of sodium bromoacetate (Bischoff and Walden, *Annalen*, 1894, **46**, 279) and 250 c.c. of dry light petroleum contained in a 500 c.c. flask fitted with a reflux condenser and a

mercury-sealed stirrer. After the vigorous reaction was over the mixture was boiled to remove the remaining sulphur dioxide, and then filtered while still warm; the residual sodium chloride was washed with ether, and further extracted for some hours with the same solvent in a Soxhlet apparatus. The combined solutions were washed with a cold aqueous solution of sodium hydrogen carbonate and dried with anhydrous magnesium sulphate. The total yield after purification by fractional distillation under diminished pressure was 80 per cent. of the calculated amount.

Thionyl Chloride and Silver Glycollate.—To 1.9 grams of silver glycollate (1 mol.) suspended in 30 c.c. of ether, 0.6 gram of thionyl chloride ($\frac{1}{2}$ mol.) was added, and the mixture shaken. The syrup left after filtration and distillation of the ether crystallised suddenly. The compound was purified by dissolving it in ether and reprecipitating with light petroleum, the process being repeated two or three times until the substance was free from halogen:

0.1984 gave 0.1796 CO_2 and 0.0536 H_2O . $\text{C}=24.69$; $\text{H}=3.00$.

0.2350 „ 0.2752 BaSO_4 . $\text{S}=15.99$.

$\text{C}_4\text{H}_6\text{O}_7\text{S}$ requires $\text{C}=24.24$; $\text{H}=3.03$; $\text{S}=16.16$ per cent.

The compound has thus the composition of a thionyl derivative of glycollic acid. The decomposition of this substance, although apparent very soon after its preparation by the odour of sulphur dioxide, does not proceed rapidly; a sample which had been left in an evacuated desiccator at the ordinary temperature still contained, nine days after preparation, 11.32 per cent. of sulphur. A small quantity of the thionyl compound which had remained for about a fortnight at the ordinary temperature was washed quickly with ether, which removed a more soluble portion, and analysed:

0.1190 gave 0.1574 CO_2 and 0.0482 H_2O . $\text{C}=36.07$; $\text{H}=4.50$.

$\text{C}_4\text{H}_6\text{O}_5$ requires $\text{C}=35.82$; $\text{H}=4.48$ per cent.

The substance has thus the composition of an anhydride of glycollic acid. It softens at about 90° , and is completely melted at $102\text{--}103^\circ$.

Thionyl chloride and silver methoxyacetate react at once without the formation of a thionyl compound. The reaction appears to proceed normally; fractional distillation of the product under diminished pressure did not, however, yield the anhydride in the pure state.

Thionyl chloride and silver mandelate in the presence of ether yield a crystalline thionyl derivative, mixed, however, with chlorinated products. If, after repeated solution in ether and reprecipitation with light petroleum, it is heated for several days at $60\text{--}70^\circ$

in a current of dry carbon dioxide to remove sulphur dioxide and then extracted with cold benzene, a glass-like product is obtained on removal of the benzene in a vacuum, which, although of undetermined constitution and possibly a mixture, has a composition nearly that of an anhydride of normal type:

0.1650 gave 0.4020 CO_2 and 0.0760 H_2O . $\text{C}=66.45$; $\text{H}=4.71$.

$\text{C}_{16}\text{H}_{14}\text{O}_5$ requires $\text{C}=67.13$; $\text{H}=4.90$ per cent.

0.5365 gram neutralised 75.3 c.c. *N*/20-baryta solution, in which it dissolved on boiling; 70.6 c.c. would be required by the same quantity of mandelic acid, and 75.0 c.c. by an anhydride, $\text{C}_{16}\text{H}_{14}\text{O}_5$.

Thionyl Chloride and Silver Malate.—Four grams (a considerable excess) of silver malate suspended in 30 c.c. of ether were shaken with 1.2 grams of thionyl chloride. Sulphur dioxide was expelled from the filtered solution by passing carbon dioxide through it for twenty-four hours. The syrup which remained after distillation of the ether yielded a small quantity of crystalline product, which was washed with ether and analysed:

0.1169 gave 0.1732 CO_2 and 0.0372 H_2O . $\text{C}=40.44$; $\text{H}=3.54$.

$\text{C}_4\text{H}_4\text{O}_4$ requires $\text{C}=41.38$; $\text{H}=3.45$ per cent.

This *malic anhydride* softens below 70° , and is completely melted at $75\text{--}76^\circ$. It may be recrystallised from ether, and dissolves readily in cold water; the aqueous solution crystallises completely on evaporation in a desiccator at the ordinary temperature, yielding malic acid in an almost pure state.

The authors' thanks are due to Mr. William Dickson, who carried out a number of the above experiments, to Mr. R. Fraser Thomson for contributing an account of the preparation of bromoacetic anhydride, and to the Carnegie Trust, which has defrayed part of the cost of the investigation.

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