XXVII.—*Applications of Thallium Compounds in Organic Chemistry. Part IV. Thallium Compounds of Polyhydroxy-compounds.*

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In Part I (Menzies and Wilkins, J., 1924, **125**, 1151), the qualitative reactions of thallous hydroxide with the sugars were described and it was shown that colour changes took place on heating, which were marked in the cases of glucose and fructose, the metal being reduced as a mirror under suitable conditions.

On boiling sucrose and mannitol, however, with 10% thallous hydroxide solution a faint yellow colour alone appears.

The precipitates formed in the cold when concentrated aqueous solutions of fructose, glucose, and galactose are mixed with a solution of thallous hydroxide give indefinite analytical figures, but definite compounds are formed by methylglucoside, and methylarabinoside, in which the reducing group is masked, and also by *thallous gluconate* and by sorbitol, from which it is absent. As a useful criterion of the purity of these compounds is a comparison of the total thallium content estimated by precipitation as iodide or as chromate with that estimated by titration, it is recalled that thallium replacing hydrogen in non-acidic hydroxyl groups is hydrolysed by water and may be estimated by titration with acid, 1 c.c. of *N*-acid indicating 0·2044 g. of the metal (see Part II, J., 1925, **127**, 2372).

The hydrolysis of thallous ethoxide, thallous phenoxide, and *trithallium methylarabinoside*, for instance, is so complete that estimations of the metal by titration and by precipitation give the same percentage figure. The normal thallous salts of acids, such as thallous tartrate, are not hydrolysed by water, the aqueous solutions have a neutral reaction, and none of the thallium is estimable by titration. In hydroxy-acids in which thallium has replaced the hydrogen of both carboxyl and hydroxyl groups, that replacing the latter only is hydrolysed by water, so that part only of the metal is estimated by titration; *e.g.*, the thallium estimated by titration of tetrathallium tartrate, $C_2H_2(OTl)_2(CO_2Tl)_2$ (Part II), is half that estimated by precipitation as iodide, and titration of *hexathallium gluconate*, $C_5H_6(OTl)_5(CO_2Tl)$, indicates five-sixths of the total thallium, which may be estimated by precipitation. The formation of acid oxidation or decomposition products may lead to the contamination of the compounds with the thallium salts of these acids and thus depress the titration value, the total thallium content not being changed to the same extent, so that determinations of both values are necessary for the characterisation of the pure compounds.

The most marked example of this contamination yet encountered is afforded by a precipitate, obtained by treating fructose with 3·5 equivalents of thallous hydroxide [$C_6H_9O_3(OTl)_3$, $C_6H_8O_2(OTl)_4$, and $C_6H_7O(OTl)_5$ require Tl, 77·6, 82·3, and 85·4%, respectively], which gave 79·2% of metal as iodide but 54·9% by titration, indicating that acid products had been formed by oxidation of the fructose in amount sufficient to neutralise rather less than one-third of the thallous hydroxide formed by hydrolysis. Treatment of solutions of glucose and galactose in the cold with six equivalents of aqueous thallous hydroxide gave precipitates which showed high analytical figures—from glucose, Tl, 83·8, 83·5% by precipitation, 76·0, 77·1% by titration : from galactose, Tl, 81·6% by precipitation, 76·4% by titration—but here again the divergence is evidence of decomposition, and none of the three precipitates can be regarded as a well-defined compound, the combined action of the easily reducible metal and of atmospheric oxygen (not excluded in any of the experiments described) attacking the sugars in the alkaline solution even in the cold.

A closer approximation to a definite composition is shown by trithallium methylglucoside, the thallium estimated by precipitation being in good agreement with that required by the formula $C_7H_{11}O_3(OTl)_3$ (Fear and Menzies, J., 1926, 937). The thallium estimated by titration, however, is always less than that found by precipitation, the difference increasing the longer the aqueous solutions of the samples have been boiled; *e.g.*, a specimen which was filtered off shortly after the hot solutions of methylglucoside and thallous hydroxide were mixed gave Tl 76·4% by precipitation and 73·4% by titration, whereas a second crop, indistinguishable from the first in appearance, obtained by concentrating the mother-liquor to half its bulk by boiling, gave corresponding values of 76·15 and 69·2% (the above formula requires Tl, 76·2%). For specimens rapidly prepared, titration values exceeding 75% have been obtained.

Methylarabinoside, which resembles methylglucoside in containing three secondary alcoholic groups but differs from it in containing no primary alcoholic group (Hirst, J., 1925, **127**, 358), also forms a trithallium derivative, the precipitation and titration values of which are in close agreement (Found : Tl, by precipitation 78·7, by titration 78·8. $C_6H_9O_5Tl_3$ requires Tl, 79·2%). In a second crop, obtained from the mother-liquor concentrated to small bulk by boiling, the thallium found by precipitation was 79%, and by titration, 78·1%. A solution of trithallium methylarabinoside, however, which had been boiled and allowed to cool slowly, gave on titration Tl 74·2%, suggesting that the greater ease with which this substance can be obtained pure may be due to the greater solubility of the impurity formed on heating. The non-substitution of one of the four hydroxylic hydrogen atoms of methylglucoside may be connected with the lack of activity of one of the hydroxyl groups of glucose to which attention has been directed by Schlubach and Firgau (*Ber.*, 1926, **59**, 2100), but a complete explanation cannot yet be attempted, as both gluconic acid and sorbitol form thallium derivatives in which all six available hydrogens are replaced by thallium, whereas solutions of sucrose mixed with thallous hydroxide in widely differing molecular proportions deposit tetrathallium sucrose, which it is hoped to describe in a future communication.

EXPERIMENTAL.

The two crops of *trithallium methylarabinoside*, details of the analyses of which have been given above, weighed together 1·14 g. and were prepared from 0·8 g. of α-methylarabinoside (kindly presented by Dr. A. K. Macbeth) and slightly more than 3 equivs. of thallous hydroxide, made by boiling 3·85 g. of thallous ethoxide (theoretical quantity for 3 equivs., 3·75 g.) with water until much hydroxide separated on cooling. The substance is exceedingly soluble in water, the first crop being obtained by concentrating the solution to small bulk by boiling, and the second from the mother-liquor in the same way. Both crops were filtered off with suction, washed with a little water, and dried on a porous plate over phosphoric anhydride. They darkened at 160°, became black between 200° and 210°, and melted and frothed at 215—220°.

When the mother-liquor was evaporated to dryness in a desiccator, yellow scales (0·77 g.) were formed which did not adhere to the bottom of the dish (Found by titration : Tl, 72·6%). There was also a very small amount of a substance which adhered firmly to the bottom of the dish in rounded aggregates; these appeared white in reflected light, yellowish-brown in transmitted light, and as red circles with dark crosses in polarised light between crossed Nicols.

When 4 equivalents of thallous ethoxide were used, a first crop of 1·3 g. was obtained (Found : Tl, 78·8 as iodide; 78·0 by titration. Calc. : Tl, 79·2%). The second crop obtained by boiling was very small in amount, a colourless, transparent jelly being also formed. Trithallium methylarabinoside is unaltered by daylight.

Thallous Gluconate.—The preparation of crystalline *thallous gluconate* was delayed for 3 years owing to inability to obtain a nucleus. Treatment of a well-crystallised sample of mercury gluconate (Heffer, *Ber.*, 1889, **22**, 1049) with metallic thallium and water until the solution was free from mercury, and subsequent evaporation, gave a syrup which, after being flooded with methyl alcohol, crystallised over-night and then served to nucleate larger-scale preparations. By double decomposition of 11·2 g. of barium gluconate with a slight excess of thallous sulphate 10·5 g. of crude thallous gluconate (yield, 68%) were obtained. Several preparations of gluconic acid, each made from 50 g. of glucose by oxidation with bromine in the usual way, gave yields of 20—25 g. of thallous gluconate on neutralisation with thallous hydroxide solution, followed by evaporation to small bulk, nucleation, and subsequent recrystallisation.

Thallous gluconate is very soluble in water, a saturated solution forming a heavy viscous syrup from which rosettes of prisms crystallise slowly on nucleation. A sample prepared from barium gluconate and thallous sulphate had $[\alpha]_D + 3{\cdot}3^\circ$ in water ($c = 4{\cdot}24\%$). It darkened at 134° and melted at 134—144° to a clear brown liquid (Found : Tl, 50·8, 51·2. $C_6H_{11}O_7Tl$ requires Tl, 51·2%). A sample prepared from gluconic acid and thallous hydroxide had $[\alpha]_D + 4{\cdot}4^\circ$ in water ($c = 3{\cdot}9\%$). It darkened at 136° and melted at 133—138° to a very dark liquid (Found : Tl, 50·3, 50·6%). Thallous gluconate crystallises without water of crystallisation : a sample left over-night over phosphoric anhydride lost no further weight at 100°.

Hexathallium Gluconate.—Thallous gluconate (22 g.) in 80 c.c. of water was heated with a thallous hydroxide solution prepared by boiling 66 g. of thallous ethoxide (theoretical quantity for 5 equivs., 68·7 g.) with 100 c.c. of water until the alcohol formed was expelled; 44·3 g. of crude *hexathallium gluconate* were obtained as a yellow powder [Found : Tl, 85·2 by precipitation, 70·6 by titration. $C_5H_6(OTl)_5{\cdot}CO_2Tl$ requires Tl, 86·6% by precipitation, 72·2% by titration]. After some weeks the crude compound, which was superficially darkened by light, was washed with a little hot water, filtered off with suction, and again dried to constant weight (Found by precipitation: Tl, 85·3, 85·35%. Found by titration, the standard acid being run directly on to the dried solid: Tl, 70·9, 69·8%. Found by titration in three separate experiments in which the salt had previously been dissolved in warm water: Tl, 65·75, 66·7, and 68%). A solution of the salt which had been boiled and allowed to stand for ½ hour gave Tl 65·6% on titration, and a sample which had been heated dry at 100° for 1 hour gave Tl 63·1%.

Theoretical figures, however, were obtained for a sample made from 4 g. of thallous gluconate and 12·3 g. of thallous ethoxide treated with water as before, and analysed immediately after it had dried to constant weight (Found: Tl, 86·6% by precipitation, 72·1% by titration).

Aqueous solutions of hexathallium gluconate are lævorotatory.

Thallium Compound of Sorbitol.—12·25 G. of the crude compound were obtained from 2 g. of sorbitol and an aqueous solution of thallous hydroxide made by treating 18 g. (6½ equivs.) of thallous ethoxide with water [Found: Tl, 86·6 by precipitation, 84·4 by titration. $C_6H_8(OTl)_6$ requires Tl, 87·5%]. After being washed with 15 c.c. of hot water, filtered off with suction, and again dried to constant weight, the substance gave Tl 86·8% by precipitation and 86·4% by titration. A sample which had been kept for 6 months gave Tl 80·7% on titration. The compound is superficially darkened by daylight.

9·4 G. of the compound were obtained in a second preparation from 2 g. of sorbitol and thallous hydroxide prepared from 12·4 g. of thallous ethoxide (4½ equivs.) (Found: Tl, 86·4% by precipitation, 87·9, 87·4% by titration). After being washed with water and treated as described above, the substance gave Tl 86·9% by precipitation and 87·7% by titration.

The first of the above washings contained 9·6 g. of dissolved solid in 100 c.c., was faintly dextrorotatory, and gave strikingly different figures on analysis by the two methods (Found: Tl, 78·3% by precipitation, 57·5% by titration).

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