175. *Mercuration of* O-*Trimethylgallaldehyde and Related Substances.*

By Thomas M. Sharp.

In an attempt to increase the yield of 2-nitro-3 : 4 : 5-trimethoxybenzaldehyde (Sharp, J., 1936, 1234), the aldehyde has been mercurated, giving a good yield of 2-*acetoxymercuri*-3 : 4 : 5-*trimethoxybenzaldehyde.* Attempts to replace the acetoxymercuri- by the nitro-group gave mixtures difficult to separate and offering no advantage over the direct nitration process. The method was therefore abandoned, but the mercury compound itself was of interest in being soluble in oils; as oil-solubility is a valuable therapeutic property, some similarly constituted compounds have been mercurated in the hope of obtaining a useful drug. Syringaldehyde, syringic acid, and *O*-trimethylgallic acid were selected for this purpose. All the substances were mercurated readily, but the acetoxymercuri-derivatives were difficult to purify owing to their sparing solubilities and they were, moreover, little soluble in oils. They were purified by conversion into chloromercuri- or bromomercuri-compounds; all these substances have a tendency to lose halogen in solution and this is most pronounced in the case of derivatives of *O*-trimethylgallic acid in alcohols. For example, recrystallisation of 2-bromomercuri-*O*-trimethylgallic acid gives a small amount of the normal salt, but most of the material, of sharp although lower melting point, approximates in composition to a basic salt, $3C_{10}H_{11}O_5HgBr,C_{10}H_{11}O_5HgOH$, and the chloromercuri-derivative has only been obtained as a basic salt, $4C_{10}H_{11}O_5HgCl,C_{10}H_{11}O_5HgOH$. It has not been proved whether these are true basic salts or mixtures of halogenomercuri- and hydroxymercuri-*O*-trimethylgallic acids, but repeated crystallisation failed to make an appreciable difference in the halogen–mercury ratio.

Syringaldehyde was prepared from *O*-trimethylgallaldehyde by partial demethylation with concentrated sulphuric acid at 40°, a method which has been used for the preparation of syringic acid from *O*-trimethylgallic acid (Alimchandani and Meldrum, J., 1920, **117**, 967; Bogert and Coyne, *J. Amer. Chem. Soc.*, 1929, **51**, 571).

The bactericidal action of the mercury compounds has been estimated by Major H. C. Brown, of the Wellcome Bureau of Scientific Research, using the method previously described (Henry, Sharp, and Brown, *Biochem. J.*, 1925, **19**, 515). He found that a 0·1% aqueous solution of 2-bromomercuri-*O*-trimethylgallic acid (as sodium salt) kills *B. typhosus*, Rawlings, in 5 minutes, whereas a 0·01% solution fails to kill. A 0·5% solution of acetoxymercuri-*O*-trimethylgallaldehyde in olive oil kills in 5 minutes, whereas a 0·05% solution fails. 2-Bromomercurisyringaldehyde and 2-chloromercurisyringic acid (as sodium salts) in concentrations of 0·5% and 1% respectively failed to kill the organism.

EXPERIMENTAL.

O-*Trimethylgallaldehyde.*—Molecular proportions of *O*-trimethylgallaldehyde and mercuric acetate in alcohol containing a few drops of acetic acid were boiled under reflux for 4 hours and filtered from mercurous acetate. 2-*Acetoxymercuri*-3 : 4 : 5-*trimethoxybenzaldehyde* slowly separated in soft colourless needles on cooling and more was obtained on concentration of the filtrate. The compound crystallised from alcohol, containing a little acetic acid, in colourless soft needles, m. p. 145—146°.* Yield, 80% of the theoretical (Found : C, 31·7; H, 3·1; Hg, 43·8. $C_{12}H_{14}O_6Hg$ requires C, 31·7; H, 3·1; Hg, 44·1%). It is readily soluble in fatty oils.

O-Trimethylgallic acid (16·96 g.) in alcohol (80 c.c.) was boiled under reflux for 4 hours with mercuric acetate (25·5 g.) in alcohol (160 c.c.) and acetic acid (4 c.c.). The solid which slowly separated was filtered off and a further quantity was obtained by evaporation of the filtrate (yield, 30·8 g.). The solid contained a little mercurous acetate, which was removed by filtration of the solution in sodium hydroxide. When the alkaline solution was poured into excess of 5% hydrobromic acid, 2-*bromomercuri*-3 : 4 : 5-*trimethoxybenzoic acid* was precipitated as a white solid, which after several crystallisations from methyl alcohol formed colourless needles, m. p. 194° (Found : Hg, 41·0; Br, 16·1. $C_{10}H_{11}O_5BrHg$ requires Hg, 40·8; Br, 16·25%). Later crops had m. p. 190° and appeared to be a *basic salt* (Found : Hg, 42·9; Br, 12·6. $C_{10}H_{11}O_5HgOH,3C_{10}H_{11}O_5HgBr$ requires Hg, 42·1; Br, 12·6%). The corresponding *chloromercuri*-compound, obtained by addition of an alkaline solution to hydrochloric acid, crystallised from chloroform or alcohol in colourless needles, m. p. 212°, having the composition of a basic salt (Found: C, 26·6; H, 2·6; Cl, 6·4; Hg, 45·5. $C_{10}H_{11}O_5HgOH,4C_{10}H_{11}O_5HgCl$ requires C, 27·1; H, 2·55; Cl, 6·4; Hg, 45·25%).

Syringaldehyde.—*O*-Trimethylgallaldehyde (5 g.) was added to 25 c.c. of sulphuric acid (*d* 1·84), kept at 40° for 6 hours and left overnight at room temperature. The solution was then poured into cold water (50 c.c.) and extracted with ether, and the aldehyde purified by extraction with sodium bisulphite solution. Yield of pure syringaldehyde, 3 g. It was mercurated by boiling for about 4 hours with an alcoholic solution of mercuric acetate. The acetoxymercuri-compound obtained was contaminated with mercurous acetate and was purified by conversion into 2-*bromomercuri*-4-*hydroxy*-3 : 5-*dimethoxybenzaldehyde* in the usual manner, the solubility in sodium hydroxide solution being due to the phenolic hydroxyl. This salt crystallised from methyl alcohol (in which it was very sparingly soluble) in soft colourless needles, m. p. 260—265° to a cloudy liquid (Found : Hg, 44·1; Br, 17·2. $C_9H_9O_4BrHg$ requires Hg, 43·95; Br, 17·3%).

Syringic Acid.—This was mercurated in the usual way and required about an hour. During the heating a bright yellow solid, presumably a basic salt, separated and was collected; concentration of the filtrate gave a white solid. These were mixed, dissolved in sodium hydroxide solution, filtered from mercurous oxide, and added to excess of hydrochloric acid. The white gelatinous precipitate of 2-*chloromercuri*-4-*hydroxy*-3 : 5-*dimethoxybenzoic acid* was filtered off, washed with water, and crystallised from acetone, from which it was obtained in colourless needles, m. p. 230° (decomp.) (Found : C, 25·1; H, 2·3; Hg, 46·0. $C_9H_9O_5ClHg$ requires C, 24·9; H, 2·1; Hg, 46·3%).

The author thanks Mr. A. G. Turner for assistance with the experimental work, and Messrs. A. Bennett and H. C. Clarke for a number of micro-analyses.

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[*Received, April* 13*th*, 1937.]