conditions. The reversal of the relative speeds of hydrolysis of lactose and maltose that was predicted by E. F. Armstrong and Caldwell has been realized.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

ORGANIC BISMUTH COMPOUNDS. I. PREPARATION OF TRICARBOXY-TRIPHENYLBISMUTH DICHLORIDES AND CERTAIN NITRO-TRIARYL BISMUTH COMPOUNDS

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During the past few years the administration of bismuth in one form or another in place of, or along with organic arsenic compounds in the treatment of spirochetosis has become quite frequent practice. The compounds most used are bismuthates formed from sodium potassium tartrate, gallic acid, pyrogallol, iodogallic acid, iodoquinine and other substances of less importance, the first one being in most general use; in all of these, bismuth is not attached to carbon but is in salt-like formation, and the compounds frequently have variable chemical composition and physical properties depending on the mode of preparation. Colloidal preparations of bismuth and bismuth oxide have also been used in practice.

The success in chemotherapy of organic arsenic compounds where arsenic is attached to carbon leads to the conclusion that among organic bismuth compounds where bismuth is attached to carbon might be found pure substances of low enough toxicity and high enough therapeutic action to replace the bismuth salts[1] used at present. Only one or two attempts to use true organic compounds of bismuth in chemotherapy have been reported. Giesma[2] obtained favorable results toward trypanosomes and spirochetes by the intramuscular injection of triphenyl bismuth in oil suspension or by percutaneous treatment. The object of this research has been the synthesis and study of various new organic bismuth compounds; the possibility of water-soluble carbon-bismuth compounds has been kept especially in mind.

All the compounds of the types R_3Bi, R_2BiX, $RBiX_2$, where R is aliphatic and X is halogen, are very unstable and in many cases spontaneously inflammable. Moisture causes the decomposition of most of them. No compounds of the above types where one R is aliphatic and the others aromatic have been prepared although many attempts are described; the products are always triaryl bismuthine and traces of trialkyl bismuthine. Compounds R_2BiX and $RBiX_2$ where R is aromatic and X halogen

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[1] Kolle, *Medizin. Klinik*, **20**, 1097 (1923).

[2] Giesma, *Dermatol. Wochenschr.*, **76**, 523 (1923); *Münch. med. Wochschr.*, **79**, 1452 (1923).

are also, in general, unstable to moisture. The compounds of satisfactory stability, therefore, are limited to R_3Bi where R is aromatic and to the corresponding dihalogen addition compounds R_3BiX_2 where X is fluorine, chlorine or bromine, the chlorine and sometimes the bromine derivatives being the only compounds readily prepared and sufficiently stable. Even the R_3Bi and to a less extent the R_3BiCl_2 compounds decompose by treatment with various reagents, especially acids, to give inorganic bismuth much more readily than do the corresponding compounds of arsenic or antimony. None of the compounds R_3Bi and R_3BiX_2 which have yet been described in the literature contains salt-forming groups.

The most convenient method of preparing the triaryl bismuth compounds is by means of aryl magnesium halides and bismuth halides as first described by Pfeiffer and Pietsch[3] and later by Challenger.[4] A slight change in the procedure for isolation of the products was introduced and rendered it easy to obtain them pure. The black product which was obtained from the reaction mixture was extracted with chloroform or carbon tetrachloride. The triaryl bismuthines could either be obtained from this solution or could be directly converted into the dihalides by adding chlorine or bromine.

A special study was made to prepare compounds containing the carboxyl group and the amino group. The carboxyl substituted compounds were finally formed through the oxidation of the tritolylbismuth dichlorides, the triaryl bismuth compounds themselves being far too unstable for treatment with vigorous oxidizing agents. Even the pentavalent bismuth compounds decomposed to a considerable extent during oxidation and only by careful control of conditions were yields of 15–25% of the tricarboxy derivatives obtained. Of a large variety of oxidizing agents, chromic acid in acetic acid at 68–70° proved to be most satisfactory, although the addition of aqueous potassium permanganate to an acetone suspension of the compound to be oxidized, gave satisfactory results at low temperature, providing small amounts of material were employed. The *o*-, *m*- and *p*-tolyl- and 1,3-xylylbismuth dichlorides were successfully oxidized. Of these only the *ortho* and *para* carboxyl derivatives were readily isolated and purified. These resulting acids were soluble in alkali but upon reprecipitation with hydrochloric acid frequently yielded low-melting products, due undoubtedly to partial hydrolysis of the chlorines attached to the bismuth. The alkaline solutions proved to be unstable, and on standing a yellowish solid precipitated.

It was hoped that tricarboxy compounds might be produced by brominating tritolylbismuth dibromide in the presence of the light from a mercury lamp to give the tribromomethyl-triphenylbismuth dibromides

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[3] Pfeiffer and Pietsch, *Ber.*, **37**, 4622 (1904).

[4] Challenger, *Proc. Chem. Soc.*, **29**, 76 (1913).

which could then be much more readily oxidized than the corresponding unsubstituted compounds. It was found, however, that the bromination gave bismuth bromide and *p*-bromo- or *o*-bromobenzyl bromide, quantitatively.

The oxidation of the tritolylbismuth dichlorides by means of lead tetra-acetate has given interesting and satisfactory results which will be reported later.

Challenger[5] reports the preparation of di-, tetra- and hexanitro compounds by the nitration of triphenyl-bismuth dinitrate under various conditions, the degree of substitution depending upon the time of reaction. In this investigation a trinitro compound was obtained. The nitration of the tri-*p*-tolyl-bismuth dinitrate took place with even greater ease and yielded a more readily purified trinitro product. On the other hand, the nitration of the tri-*o*-tolyl-bismuth dinitrate invariably resulted in an explosion when treated in an analogous way with fuming nitric acid and an indirect method had to be used for the preparation. The carboxylated compounds could not be nitrated, due to decomposition, but the corresponding ester of the *para* derivative was readily nitrated to form the corresponding trinitro compound.

All the dinitrates and especially the nitro derivatives exploded at a temperature that was not very definite and as a consequence, for identification, were best converted to the dichlorides by treatment with hydrochloric acid. Unfortunately, no method has yet been found which will yield pure amino derivatives by reduction of the nitro compounds; a certain amount of decomposition always occurs with the precipitation of bismuth or bismuth hydroxide, the presence of the amino group probably rendering the derivatives more unstable.

The reduction of pentavalent bismuth compounds of the general formula R_3BiX_2 to the corresponding triaryl bismuth compounds was carefully studied. The reduction has previously been carried out by means of ammonium sulfide[6] or silver oxide.[7] A very convenient reagent was found in sodium hydrosulfite at 0°. In the case of triphenyl- or tritolyl-bismuth dichlorides very little decomposition occurred and good yields resulted. With the nitro and especially the carboxyl substituted compounds a considerable amount of decomposition took place with the precipitation of metallic bismuth or bismuth hydroxide and consequently a lower yield of product. The same reducing reagent was excellent for the conversion of triphenylarsine dichloride and triphenylstibine dichloride to triphenylarsine and triphenyl-stibine.

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[5] Challenger and Wilkinson, *J. Chem. Soc.*, **126**, 675 (1924).

[6] Michaelis and Polis, *Ber.*, **20**, 55 (1887). Michaelis and Marquardt, *Ann.*, **251**, 324 (1889).

[7] Gildermeister, *Ber.*, **30**, 2846 (1891).

In addition to sodium hydrosulfite, other reagents were found which caused reduction. Formaldehyde or sodium and alcohol gave results but the isolation of the products was not always easy. Of more interest was that dimethyl sulfate and alkali converted the triphenyl- or tritolyl-bismuth dihalides into triphenyl- or tritolyl-bismuthine. Upon treatment of the tri-*o*- and *p*-carboxytriphenyl-bismuth dichlorides in a similar way it was hoped to obtain the tri-*o*- and -*p*-carbomethoxytriphenyl-bismuthines; esters were formed and the products were halogen-free. The structures of the products, however, were not those expected and have not yet been determined.

The tri-*o*-anisyl- and tri-*p*-anisyl-bismuthines were easily decomposed when an attempt was made to form the corresponding dichlorides or dibromides and only a small amount of dibromide of the *para* compounds was isolated. Attempts to hydrolyze the methoxyl groups by means of hydriodic acid or aluminum chloride resulted either in complete decomposition or in recovery of unchanged material.

Sulfonation of aryl bismuth compounds has also been attempted with some success up to the present in the case of tri-*o*-tolyl-bismuth dichloride. A product formed which is apparently hydrolyzed most readily in the presence of water and alkali so that an hydroxyl derivative results. This latter compound shows rather unexpected chemical properties which have not yet been investigated in detail.

An attempt to introduce bismuth into the benzene ring by a procedure similar to the Bart reaction for introducing arsenic was attempted by Challenger and gave negative results. This was confirmed in this investigation. The action of bismuth chloride in hydrochloric acid in the presence of tartaric acid with benzene-diazonium chloride resulted merely in the formation of a double salt of benzene-diazonium chloride and bismuth chloride.

The conclusions that can be drawn from this research are that the stability of the triaryl-bismuth dihalides and triaryl bismuthines varies markedly with the character and position of the substituting groups. In all of the compounds produced, the bismuth is more or less readily eliminated, a property desirable in compounds to be used therapeutically. Experiment has shown that many of them are less toxic than the bismuth salts which are now in common use.

Experimental Part

The melting points of the bismuth compounds are very variable, depending upon the mode of heating. For the most part the determinations were made with the temperature of the bath rising very slowly. A large majority of the compounds decompose at the melting point, which makes impossible an accurate determination.

Triaryl Bismuthines. General Procedure.—The Grignard reagent was made from three molecular equivalents of aromatic halogen compound and 3.3 molecular equivalents of magnesium in dry ether (100 g. of halogen compound to about 500 cc. of ether). The reaction mixture was kept cold while a solution of 1 molecular equivalent of melted, carefully powdered bismuth trichloride in dry ether (60 g. of bismuth trichloride in about 200 cc. of dry ether) was gradually added. When the spontaneous reaction was over the mixture was heated on a water-bath for 30 minutes and the ether distilled. The residue was treated with ice and 10% ammonium chloride solution after which a very small amount of dil. hydrochloric acid was added to take completely into solution the basic bismuth salts and the unchanged magnesium. The black precipitate which resulted was filtered off and dried at room temperature. It was then extracted in a Soxhlet apparatus with carbon tetrachloride or chloroform and after filtration and evaporation a crystalline solid was obtained. One recrystallization sufficed to give a pure product.

By this procedure several compounds were formed in yields varying from 30 to 65%. The tri-*p*-anisyl-bismuthine was obtained in 10% yields only. The melting points were essentially those reported in the literature.

. The tri-*m*-tolyl-bismuthine was best purified by a different procedure from that used with most of the other compounds. Because of its low melting point the removal of traces of toluene and *m*-bromotoluene was difficult. After extracting with chloroform according to the general procedure the solvent was evaporated and the residue was steam distilled to remove traces of impurities. The residue after the water had been removed was dissolved in acetone. Upon partial evaporation a white product resulted, which after recrystallization from alcohol melted at 65°. Even this product was not absolutely pure and the following procedure was used to obtain the purest product. The compound from the chloroform was converted into tri-*m*-tolyl-bismuth dichloride which in turn was reduced with sodium hydrosulfite to tri-*m*-tolyl-bismuth. The final product was recrystallized from ligroin, under which conditions a substance melting at 68° was obtained. The details for the reduction are described later.

The tri-1,3-xylyl-bismuth was best purified in a similar manner through the dichloride.

The tri-*o*- and tri-*p*-anisyl-bismuth compounds were very sensitive to cold, concd. hydrochloric acid and with which they decomposed rapidly.

Tri-*o*-anisyl-bismuth, $(o\text{-}CH_3OC_6H_4)_3Bi$.—This has not been previously prepared. It was purified from chloroform and then melted at 169–170°.

Anal. Subs., 0.3210: CO_2, 0.5595; H_2O, 0.1153. Calcd. for $C_{21}H_{21}O_3Bi$: C, 47.55; H, 3.99. Found: C, 47.54; H, 4.01.

Triaryl-bismuth Di-halides. General Procedure.—A carbon tetrachloride solution of triaryl bismuth as obtained by extraction of the black compound from the Grignard reaction was treated with chlorine gas at a low temperature. The reaction mixture was tested from time to time with a solution of bromine in carbon tetrachloride in order to determine when the calculated amount of chlorine had been added. When the reaction was complete, the carbon tetrachloride was partially evaporated and the resulting solution treated with three volumes of alcohol. A white, crystalline precipitate was formed which could be in practically every instance purified by crystallization from a mixture of alcohol and chloroform. The yields were nearly quantitative in most cases.

The corresponding bromides were made in a similar manner, using a 10% solution of bromine in carbon tetrachloride. The end-point was evidenced by a permanent brown color. Partial evaporation and precipitation with alcohol gives very good yields of the products.

The tri-*m*-tolyl-bismuth dichloride is best prepared by chlorinating the crude tri-*m*-tolyl-bismuth in ligroin; b. p., 60–80°. After removing the compound by chilling, it is recrystallized from acetone. The dibromide is prepared in a similar manner in poorer yields; it appears to be quite unstable and, therefore, cannot be recrystallized from acetone.

Tri-*m*-tolyl-bismuth Dichloride, $(m\text{-}CH_3C_6H_4)_3BiCl_2$.—This formed white crystals from acetone; m. p., 132–133°.

Anal. Subs., 0.3150: AgCl, 0.1649. Calcd. for $C_{21}H_{21}Cl_2Bi$: Cl, 12.80. Found: 13.01.

Tri-*m*-tolyl-bismuth Dibromide, $(m\text{-}CH_3C_6H_4)_3BiBr_2$.—This melted at 52° and could not be purified by crystallization. It decomposed quickly in the air.

Anal. Subs., 0.2413: AgBr, 0.1391. Calcd. for $C_{21}H_{21}Br_2Bi$: Br, 24.39. Found: 24.53.

The tri-*o*-anisyl and tri-*p*-anisyl compounds appear to be very unstable toward chlorine and bromine. Only the dibromide of the tri-*p*-anisyl compound could be isolated.

Triaryl-bismuth Diacetates.—Certain diacetates have been prepared previously by Challenger from silver acetate. A cheaper and somewhat more convenient method was to heat under a reflux condenser a solution of 10 g. of triaryl-bismuth dihalide in 150 cc. of glacial acetic acid with an excess of a saturated solution of lead acetate in glacial acetic acid. The lead chloride was filtered off and the filtrate upon cooling deposited white crystals. In this way triphenyl-bismuth diacetate was produced. It was purified by crystallization from acetone; m. p., 152–153°.

Anal. Subs., 0.3500: CO_2, 0.6032; H_2O, 0.1283. Calcd. for $C_{22}H_{21}O_4Bi$: C, 47.3; H, 3.79. Found: C, 47.0; H, 4.1.

In a similar manner the tri-*p*-tolyl compound was purified and melted at 162°, the same melting point that was reported by Challenger. The tri-*m*-tolyl compound when pure melted at 148–149°.

All three acetates were readily converted to the corresponding dichlorides by means of boiling hydrochloric acid and were thus identified.

Tri-*o*-carboxytriphenyl-bismuth Dichloride, $((o)HO_2CC_6H_4)_3BiCl_2$.—In a 1-liter beaker was placed 600 cc. of glacial acetic acid. This was heated to 68–70° and 1g. quantities of tri-*o*-tolyl-bismuth dichloride and about 2g. quantities of chromic acid were gradually introduced. After the first portion had been oxidized, another portion was added and this process continued until 20 g. of tri-*o*-tolyl-bismuth dichloride and 40 g. of chromic acid had been added. During the reaction the temperature had to be controlled very carefully between 68–70° or the yield of product was reduced considerably. It was necessary to keep water out of the reaction mixture if good results were to be obtained.

When the reaction was complete, the solution was poured into 1.5 liters of water. In the course of one-half hour a yellow precipitate formed which was filtered and washed with water. It was dissolved in 20% potassium hydroxide solution and filtered from about 8 g. of unoxidized tri-*o*-tolyl-bismuth dichloride. From the brown, alkaline solution the acid was precipitated with 10% hydrochloric acid, filtered and dried. It was purified by dissolving in acetone, filtering and partially evaporating the acetone at room temperature. When pure it was white and melted at 157–159° and was obtained in about 15% yields. For removing the brown color from the original precipitate, a mixture of formaldehyde and hydrochloric acid may be added in the cold, but at the same time some decomposition occurs.

Anal. Subs., 0.3753: CO_2, 0.5423; H_2O, 0.0815. Calcd. for $C_{21}H_{15}O_6Cl_2Bi$: C, 39.19; H, 2.35. Found: C, 39.41; H, 2.43.

Tri-*p*-carboxytriphenyl-bismuth Dichloride,[8] $((p)HO_2CC_6H_4)_3BiCl_2$.—The product could be made by the oxidation of the *p*-tolyl compound either by means of permanganate or chromic acid. A solution of 2.2 g. of tri-*p*-tolyl bismuth dichloride in 30 cc. of acetone was made and also a solution of 4.4 g. of potassium permanganate in 2.5% aqueous solution. These two solutions were added a small amount at a time to a flask containing 50 cc. of water. As soon as the first amount of potassium permanganate was reduced, a little more acetone solution was added and so on until the reaction was complete. The temperature must be kept below 20°. The reaction mixture was finally shaken for one-half hour, filtered from manganese dioxide and the organic matter precipitated from the filtrate by the addition of 10% hydrochloric acid. A yield of 1 g. of white compound was produced; m. p., 130°.

By dissolving the tricarboxy compound in water containing potassium or sodium hydroxide and adding alcohol or acetone, the corresponding potassium or sodium salt was precipitated in crystalline form. Upon allowing the alkaline solution to stand, decomposition took place with deposition of a yellow solid.

Anal. Subs., 0.1500, 0.1787: AgCl, 0.0734, 0.0831. Calcd. for $C_{21}H_{15}O_6BiCl_2$: Cl, 11.05. Found: 11.32, 11.38.

Tri-*p*-carbomethoxytriphenyl-bismuth Dichloride, $((p)CH_3O_2CC_6H_4)_3BiCl_2$.—A solution was made of 2 g. of acid in 50 cc. of absolute methyl alcohol saturated in the cold with dry hydrogen chloride. At the end of two hours, the alcohol was partially evaporated in a vacuum, the solution filtered from a small amount of precipitate and the filtrate added to ice and water. From methyl alcohol white crystals formed, which melted first at about 47–50°, but when completely pure at 103°. The yield is poor as bismuth hydroxide precipitates on warming with alcohol.

Anal. Subs., 0.1541: CO_2, 0.2402; H_2O, 0.0471. Calcd. for $C_{24}H_{21}O_6BiCl_2$: C, 42.04; H, 3.09. Found: C, 42.51; H, 3.42.

Tri-aryl-bismuth Dinitrates.—The general procedure was that used by Challenger, namely, the treatment of the corresponding dihalide in

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[8] This compound was first prepared in this Laboratory by means of chromic acid and glacial acetic acid by H. O. Calvery.

acetone solution with the calculated quantity of silver nitrate in 50% alcohol. The compounds resulting are white and are easily purified from acetone, or sometimes ethyl acetate. By this procedure the dinitrates of triphenyl-bismuth, tri-*o*-tolyl-bismuth, tri-*p*-tolyl-bismuth, tri-*m*-tolyl-bismuth and tri-*p*-carbomethoxytriphenyl-bismuth were prepared. The last two of these are new compounds but were not analyzed because they exploded violently on heating to about 150–160°. They have essentially the same properties as the triphenyl-bismuth dinitrate. It was noticeable that the *ortho* and *meta* compounds tended to decompose at lower temperatures with the formation of bismuth oxide.

Trinitrotriphenyl-bismuth Dinitrate, $((p)NO_2C_6H_4)_3Bi(NO_3)_2$.—To 100 cc. of fuming nitric acid which had been cooled to 0° was added 10 g. of triphenyl-bismuth dinitrate and the mixture allowed to stand at 0° for 12 hours. The reaction mixture was poured into 500 cc. of ice water, the precipitate filtered and washed with water, dried and recrystallized from ethyl acetate. A pale yellow product was formed which exploded when heated at about 147°.

Anal. Subs., 0.2380: N, 22 cc. (29°, 736.5 mm.). Calcd. for $C_{18}H_{12}O_{12}N_6Bi$: N, 10.02. Found: 9.71.

Upon crystallization from glacial acetic acid, the compound no longer exploded but decomposed at about 140°. Upon further crystallizations from the same solvent the melting point continued to drop, indicating that the nitrate radicals were gradually replaced by acetate radicals.

Trinitrotriphenyl-bismuth Dichloride, $((p)NO_2C_6H_4)_3BiCl_2$.—A solution of 10 g. of trinitrotriphenyl-bismuth dinitrate in 90 cc. of acetone was heated to boiling with 20 cc. of concd. hydrochloric acid. A white precipitate formed as oxides of nitrogen were evolved. The mixture was added to 500 cc. of water, the precipitate filtered, dried and recrystallized from ethyl acetate. The yield was 5 g. of a white crystalline powder; m. p., 132–134°.

Anal. Subs., 0.2473: Bi_2S_3, 0.0911. Calcd. for $C_{18}H_{12}O_6Cl_2Bi$: Bi, 32.24. Found: 32.24.

Trinitrotri-*p*-tolyl-bismuth Dinitrate, $(NO_2\ ,4\text{-}CH_3C_6H_3)_3Bi(NO_3)_2$.—This was made in a manner similar to that used in preparing the phenyl compound by nitrating tri-*p*-tolyl-bismuth dinitrate. The nitration required two hours at room temperature. The product was a white, crystalline powder which after crystallization from acetone or ethyl acetate explodes at about 160°.

Trinitrotri-*p*-tolyl-bismuth Dichloride, $(NO_2,\ 4\text{-}CH_3C_6H_3)_3BiCl_2$.—This was made in a similar manner to the corresponding phenyl compound; it forms a white powder which is purified from acetone and melts at 156°.

Anal. Subs., 0.1108, 0.1845: AgCl, 0.0474; Bi_2S_3, 0.0408; N, 10.5 cc. (26°, 745 mm.). Calcd. for $C_{21}H_{18}O_6N_3Cl_2Bi$: Cl, 10.03; Bi, 30.23; N, 6.11. Found: Cl, 10.58; Bi, 30.21; N, 6.23.

Trinitrotri-*o*-tolyl-bismuth Dichloride, $(NO_2,\ 2\text{-}CH_3C_6H_3)_3BiCl_2$.—A mixture of 10 g. of dry tri-*o*-tolyl-bismuth dichloride and 10 g. of finely pulverized silver nitrate was dissolved in 60 cc. of fuming nitric acid at 0°. After 12 hours, water was added and the precipitate which formed was filtered and extracted with acetone to remove the organic matter from the silver chloride. The acetone solution was boiled with hydrochloric acid and the precipitate recrystallized from ethyl acetate; m. p., 149–150°. The substance is quite unstable, decomposes on standing and always has an odor of nitrotoluene.

Anal. Subs., 0.3540: N, 19.3 cc. (24°, 745 mm.). Calcd. for $C_{21}H_{18}O_6N_3BiCl_2$: N, 6.11. Found: 6.01.

Trinitrotri-*p*-carbomethoxytriphenyl-bismuth Dinitrate, $(NO_2, 4\text{-}CH_3O_2CC_6H_3)_3Bi(NO_3)_2$.—This was formed by nitration at 0° by the method previously described. From acetone it formed a white, crystalline powder which exploded at about 150–160°.

Trinitrotri-*p*-carboxytriphenyl-bismuth Dichloride, $(NO_2, 4\text{-}CH_3O_2CC_6H_3)_3BiCl_2$.—The dinitrate just described was boiled for about one hour with 10% hydrochloric acid. The product was filtered off, dissolved in acetone and boiled with concd. hydrochloric acid. As this cooled, a white precipitate was formed which was purified by recrystallization from acetone; m. p., about 250–260°, with decomposition.

Anal. Subs., 0.2345: N, 12 cc. (20°, 751 mm.). Calcd. for $C_{21}H_{12}O_{12}N_3Cl_2Bi$: N, 5.4. Found: 5.81.

Reduction of Triaryl-bismuth Dihalides to Triaryl-bismuth Compounds.—The best way to carry out the reduction of these pentavalent compounds was to dissolve them in a few cubic centimeters of acetone, cool the solutions to 0° and treat gradually with excess of sodium hydrosulfite in a very concentrated aqueous solution. Generally a yellow precipitate formed which was filtered at low temperatures and washed with water. In general this yellow precipitate, upon solution in alcohol or in some other solvent which was to be used for crystallization, yielded a white precipitate of bismuth hydroxide which had to be filtered off before partial evaporation of the solution yielded the desired compound. By this procedure triphenyl-bismuth dichloride and tritolyl-bismuth dichloride gave about 80% yields of triphenyl-bismuth and tritolyl-bismuth. Trinitrotriphenyl-bismuth dichloride and trinitrotri-*p*-tolyl-bismuth dichloride gave yellow precipitates on reduction which, however, dissolved completely in acetone to give a yellow solution. These solutions when boiled deposited a black precipitate of metallic bismuth, and from the solvent was obtained trinitrotriphenyl bismuth and trinitro-*p*-tolyl-bismuth. The former was difficult but the latter easy to purify.

An attempt to esterify in the usual way the tricarboxytriphenyl-bismuth dihalides by means of potassium hydroxide solution and dimethyl sulfate gave an ester, the composition of which has not yet been determined but which was entirely free from chlorine, indicating that this combination had a reducing effect. With triphenyl or tri-*p*-tolyl-bismuth dihalides, triphenyl- or tri-*p*-tolyl-bismuth was readily obtained.

Trinitrotriphenyl-bismuth, $((p)NO_2C_6H_4)_3Bi$.—A solution of 2 g. of trinitrotriphenyl-bismuth dichloride in 10 cc. of acetone was cooled to 0° and treated with 8 g. of sodium hydrosulfite. A yellow precipitate formed which was filtered off at 0° and washed thrice with water. Upon dissolving this in acetone a yellow solution was produced which after spontaneous evaporation gave a yellow reduction product containing 45–60% of bismuth. When this was dissolved in alcohol and the solution heated to boiling a black precipitate of metallic bismuth was produced. Upon filtering and partial evaporation with alcohol a white powder was formed. After recrystallization from acetone, it melted at about 121°. The substance tends to decompose on standing.

Anal. Subs., 0.2513, 0.1970: N, 17.0 cc. (22°, 743 mm.); Bi_2S_3, 0.0871. Calcd. for $C_{18}H_{12}O_6N_3Bi$: N, 7.31; Bi, 36.17. Found: N, 7.51; Bi, 35.91.

Trinitrotri-*p*-tolyl-bismuth, $(NO_2, 4\text{-}CH_3C_6H_3)_3Bi$.—The yellow compound formed in a similar manner to the phenyl derivative contains 34.5% of bismuth. Upon boiling with alcohol it yields metallic bismuth and a white compound which is purified from ethyl acetate and melts at 126°.

Anal. Subs., 0.1940, 0.0983: N, 12.4 cc. (30°, 748 mm.); Bi_2S_3, 0.0398. Calcd. for $C_{24}H_{18}O_6N_3Bi$: N, 6.81; Bi, 37.23. Found: N, 6.93; Bi, 37.0.

Sulfonation of Tri-*o*-tolyl-bismuth Dichloride.—One hundred and twenty g. of tri-*o*-tolyl-bismuth dichloride was dissolved in 250 cc. of 98% sulfuric acid. Hydrogen chloride was evolved. At the end of 20 minutes the yellow solution was mixed with ice and the white precipitate which formed was filtered off, washed with water and treated with 20% potassium hydroxide solution. After two hours the mixture was diluted and the insoluble material filtered off. The filtrate was treated with dil. hydrochloric acid which caused a precipitation. This precipitate was washed with water, dried and dissolved in chloroform, the solution filtered and the substance precipitated with six volumes of methyl alcohol. The reprecipitation was carried out thrice according to the same method. Upon drying the compound at 100° it decomposed into a substance insoluble in cold alkali, melting sharply at 154°. Without drying it is soluble in cold potassium hydroxide solution and is precipitated from the alkaline solution by carbon dioxide or other acids. After some days the material decomposes and a solid material gradually precipitates.

Anal. Subs., 0.3427, 0.2086: CO_2, 0.5516; H_2O, 0.1101; AgCl, 0.0521. Calcd. for $(CH_3, (OH)C_6H_3)_3BiOHCl$: C, 43.26; H, 3.81; Cl, 6.09. Found: C, 43.90; H, 3.6; Cl, 6.18.

Benzene-diazonium Chloride and Bismuth Trichloride, $C_6H_5N_2lC.BiCl_3$.—To a cold solution of 28 g. of aniline in 180 cc. of hydrochloric acid diazotized with 21 g. of sodium nitrite were added a mixture of 150 cc. of hydrochloric acid and 95 g. of bismuth chloride and finally 50 g. of tartaric acid. A white, crystalline precipitate was formed which was filtered off and washed with alcohol. The product explodes at about 120°. It is soluble in concd. hydrochloric acid but insoluble in organic solvents. With water and alkali, decomposition takes place with the formation of bismuth hydroxide, nitrogen and a tarry material.

Anal. Subs., 0.2346: AgCl, 0.3002; Bi_2S_3, 0.1352. Calcd. for $C_6H_5N_2Cl_4Bi$: Bi, 46.85; Cl, 31.80. Found: Bi, 46.85; Cl, 31.80.

***o*-Bromobenzylmethyl Ether.**—To 81 g. of *o*-bromotoluene was added gradually 71 g. of bromine in the presence of light from a mercury lamp. The reaction took place rapidly and crude *o*-bromobenzyl bromide was produced. To the crude reaction mixture was added 300 cc. of methyl alcohol containing 45 g. of potassium hydroxide. As soon as the spontaneous reaction was over the mixture was refluxed for one hour. The reaction product was poured into water, the heavy oil separated, washed, dried and distilled. It formed a colorless oil; b. p., 225° (745 mm.).

Anal. Subs., 0.2000: CO_2, 0.3485; H_2O, 0.0830. Calcd. for C_6H_3OBr: C, 47.76; H, 4.51. Found: C, 47.52; H, 4.61.

***p*-Bromobenzylmethyl Ether.**—This was prepared by a similar method to the *ortho* compound. From 171 g. of *p*-bromotoluene was obtained 200 g. of product boiling at 201° (750 mm.) or 127° (30 mm.).

Anal. Subs., 0.1709: CO_2, 0.2857; H_2O, 0.0711. Calcd. for C_8H_9OBr: C, 47.76; H, 4.55. Found: C,47.11; H, 4.55.

Attempts to make the Grignard reagent from the *o*- and *p*-bromobenzyl methyl ethers in order to form the corresponding triaryl bismuthines were unsuccessful.

Summary

1. A method has been developed for oxidizing tritolyl-bismuth dihalides to the corresponding carboxy compounds.

2. Various nitro-triaryl bismuthines and bismuth dihalides have been prepared.

3. A careful study of the reduction of triaryl bismuth dihalides to triaryl bismuthines has been completed with the result that sodium hydrosulfite has proved to be a very satisfactory reagent.

4. Preliminary work on sulfonation of triaryl bismuth dihalides is reported.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE HAVEMEYER CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

THE BASIS FOR THE PHYSIOLOGICAL ACTIVITY OF CERTAIN -ONIUM COMPOUNDS[1,2]

IV. THE SULFUR ANALOG OF CHOLINE

BY R. R. RENSHAW, N. BACON AND J. H. ROBLYER

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Little work seems to have been reported on the preparation of substituted alkyl sulfonium derivatives. It is possible that this is due to the fact that the sulfonium compounds with a few exceptions are much more slowly formed and are very much less stable than many of the other -onium compounds. This instability is associated with the ready dissociation of the -onium structure.

It has been shown that when a number of different halogen compounds are heated with dimethyl sulfide, trimethylsulfonium halides are formed. Cahours[3] demonstrated this fact with methylene iodide, ethylene bromide, acetyl iodide and bromocyanogen and Carrara[4] with iodine. The mechanism in these cases was undoubtedly similar to the one operating when Klinger and Maassen[5] obtained trimethylsulfonium iodide by distilling both dimethyl-ethylsulfonium iodide and methyl-diethylsulfonium iodide.

It seems clear from the results of these earlier investigators and from

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[1] Study of this problem is being carried on in coöperation with Dr. Reid Hunt of the Harvard Medical School. The physiological data are the basis of another series of papers published elsewhere by him.

[2] A general discussion of this problem may be found in the introductory paper, *Sci.*, **62**, 384 (1925).

[3] Cahours, *Ann. chim. phys.*, [5] **10**, 29 (1878).

[4] Carrara, *Gazz. chim. ital.*, **22**, I, 408 (1892).

[5] Klinger and Maassen, *Ann.*, **252**, 246 (1889).