ORGANOBISMUTH COMPOUNDS

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Received November 22, 1941

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I. FOREWORD

The synthesis of triethylbismuth in 1850 by Löwig and Schweizer (76) inaugurated the study of the chemistry of organobismuth compounds. The spontaneous inflammability of these trialkyl derivatives limited investigation in the field until Michaelis and Polis (84) prepared triphenylbismuth in 1887. This aromatic compound was stable in air and could be converted to a pentavalent dichloride or dibromide which possessed unusual stability. In 1913, Challenger reported the beginning of an investigation on the preparation of optically active organobismuth compounds. In the years which followed, up until 1934, Challenger and his coworkers (13–27, 118), although they did not

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accomplish their original purpose, did make contributions of paramount importance in the field of organobismuth compounds.

The effectiveness of triphenylbismuth, used as a salve, in the treatment of canine syphilis was reported by Giemsa (39, 40, 41) in 1923. Two years later, Supniewski and Adams (111) and Supniewski (109, 110) prepared a number of water-soluble organobismuth compounds for possible therapeutic utilization. Bismuth therapy in the past had been based entirely upon the use of colloidal bismuth, inorganic bismuth salts, or bismuth salts of organic acids. With these, in general, absorption by body fluids was slow and toxicity high.

The use of water-soluble organobismuth compounds offers new opportunities for investigation into bismuth therapy, but the synthesis of these compounds presents numerous difficulties. Organobismuth compounds undergo a limited number of reactions, and it is rarely possible, starting with known compounds, to prepare new derivatives possessing amino, carboxylic, or related groups. Of the many reactions reported, the synthesis of organobismuth compounds in liquid ammonia (52) and through the decomposition of aryldiazonium chloride–bismuth chloride complexes (53) appear to hold most promise.

II. The Chemistry of Organobismuth Compounds

A. INTRODUCTION

A study of the relative reactivities of organometallic compounds would indicate that reactivity, in part, is dependent upon the strength of the carbon–metal bond in the organometallic molecule. The organoalkali compounds which possess a weak and highly polar bond represent a highly reactive type. Hein and coworkers (65a) have demonstrated the highly polar character of these compounds by showing their ability to conduct an electric current when dissolved in the proper medium. The strength of the carbon–metal bond, and consequently reactivity, may be correlated also with the metallic nature of the central atom of the organometallic molecule, since with enhanced metallicity the bond becomes increasingly weaker. It has been predicted, therefore, on the basis of these generalizations, that Element 87 will form the most reactive organometallic compounds.

In their thorough investigation of the triphenyl compounds of the elements of the B family of Group V, Smith and Andrews (106) have observed a definite increase in molal heat capacity with increasing atomic weight of the central atom. As an explanation of this they have suggested the possibility that the greater atomic volume of the element would give the R groups attached to it increased freedom of motion and hence less stability. It should be noted, however, that their data, numerically, give little indication of the difference in stability and reactivity between two adjacent members of this family, e.g., antimony and bismuth.

It has been observed that the relative reactivities of many RM compounds parallel and may be related directly to the ionization potentials of the corresponding metallic atoms (45a). In a given group or subgroup, the lower the ionization potential of the metal the more reactive will be its simple organometallic compound. There appear to be some exceptions but, by and large, this generalization holds true. The ionization potentials for bismuth and antimony are not known with certainty, but are given as 8 and 9 volts, respectively. This difference of approximately 1 volt is large when it is seen that the difference between the potentials of lithium and cesium is only 1.49 volts. Thus the ionization potentials of the corresponding gaseous metallic atoms would indicate marked distinctions between the reactivities of organoantimony and organobismuth compounds, and this is actually the case. The carbon–antimony linkage is extremely stable, whereas the weakness of the carbon–bismuth bond is the most characteristic property of organobismuth compounds.

Organobismuth compounds resemble organomercury, organolead, and organotin compounds in reactivity. Cleavage reactions with hydrogen chloride and trichloroacetic acid,

$$(C_6H_5)_3Bi + \begin{cases} HO_2CCCl_3 & \rightarrow C_6H_6 + (C_6H_5)_2BiO_2CCCl_3 \\ HCl & \rightarrow C_6H_6 + (C_6H_5)_2BiCl \end{cases}$$

would indicate that tetraphenyllead and diphenylmercury are more reactive than triphenylbismuth and that tetraphenyltin is extremely unreactive (12). Cleavage with formic and acetic acids, however, would give triphenylbismuth a greater reactivity than diphenylmercury or tetraphenyllead (71). Again, diphenylmercury and bismuth bromide yield triphenylbismuth in quantitative yields (18), whereas trivalent or pentavalent aromatic bismuth compounds and mercuric chloride do not form R_2Hg compounds (77). Thus, organomercury compounds might be considered more reactive than organobismuth compounds, since the preparation of a less reactive organometallic compound is accomplished, in general, by the reaction between a more reactive organometallic compound and a metal halide. The reaction between diphenylmercury and bismuth bromide is not a reaction of general application, however, since di-*p*-tolylmercury, di-*p*-bromophenylmercury, di-*o*-carbomethoxyphenylmercury, or di-*p*-carboethoxyphenylmercury and bismuth bromide do not yield organobismuth compounds (55). A similar behavior has been noted also by Michaelis and Reese (85, 86) and by Hasenbäumer (64) in the reaction between diphenylmercury and antimony chloride. The former authors could not obtain organoantimony compounds by the fusion of diphenylmercury and antimony chloride alone, or in the presence of solvents, whereas the latter obtained traces of triphenylantimony dichloride and diphenylantimony trichloride from the same reactants in dry xylene at 130°C. in a sealed tube.

Hilpert and Grüttner (67) have reported that diphenylmercury and bismuth metal at 250°C. in a stream of hydrogen gave a 41 per cent yield of triphenylbismuth, while triphenylbismuth and mercury under the same conditions gave but a 25 per cent yield of diphenylmercury. The yield of triphenylbismuth in the first experiment may have been higher, since organobismuth compounds are cleaved by hydrogen (68). The bismuth compound was not isolated, but the residue remaining from the xylene extraction of the reaction mixture was analyzed for bismuth. On this basis, organobismuth compounds might be considered more reactive than organomercury compounds. It has not been possible to extend this reaction, since di-*p*-tolylmercury and bismuth metal at 233°C. yield only free mercury and toluene. Both di-*p*-tolylmercury and tri-*p*-tolylbismuth are pyrolyzed even at the boiling point of *p*-cymene. No pyrolysis occurs in benzene or xylene, and at these temperatures di-*p*-tolylmercury and bismuth metal do not react. With mercury, neither tri-*p*-tolylbismuth nor triphenylbismuth yields organomercury compounds when refluxed in benzene (55), but under the same conditions triphenylthallium and diphenylcadmium react with mercury to form diphenylmercury (45a). On the basis of cleavage reactions with *n*-butylmercaptan and selenophenol, Nelson (47, 89) has shown organomercury compounds to be less reactive than both organobismuth and organolead compounds. Further complications are introduced by cleavage reactions with thiophenol which indicate the order Hg > Bi > Pb > Sn (55.)

As Nelson has pointed out, the reactivity of organolead, organobismuth, and organomercury compounds toward the —SH and —SeH groups is anomalous, since these compounds are cleaved more readily by thiols and selenols than by more acidic carboxylic acids. He has suggested that a reactivity series based on cleavage by acidic hydrogens exclude those hydrogens of the selenol and thiol types. It is probable, too, that the tellurols would show the same anomalous behavior.

On the basis of the cleavage reactions with the carboxylic acids, Nelson has proposed the order of reactivity Pb > Hg > Bi > Sn, and for cleavage by —SH and —SeH compounds, the order Bi > Pb > Hg > Sn. In all probability his first series is the more accurate one, although it is the reverse of the Koton series, Bi > Hg > Pb, which is based on cleavage by carboxylic acids also.

It is very apparent, because of these conflicting data, that the term "relative reactivities" when applied to a series of organometallic compounds must be based on *true* equilibrium reactions which have been allowed to come to equilibrium. This is very difficult with organometallic compounds, where solubility, solvent, instability, and diverse unknown but significant factors seriously limit the number of suitable reactions. Of the reactions described above, only one appears to have a real significance. Hilpert and Grüttner (67) made an attempt to approach the true equilibrium between triphenylbismuth and mercury, and diphenylmercury and bismuth. In the other reactions all that has been measured is the *rate* at which a reaction is proceeding.

Although compounds containing $>\mathrm{As{-}As}<$ and $>\mathrm{Sb{-}Sb}<$ groups have been prepared, Paneth and Loleit (93) mention only the possible formation of bisdimethylbismuth, $(CH_3)_2BiBi(CH_3)_2$, and bisdiethylbismuth, $(C_2H_5)_2BiBi(C_2H_5)_2$, in the reactions between heated bismuth mirrors and free methyl and ethyl radicals.[2] The dimethylbismuth reported by Denham (32) may have been

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[2] F. O. Rice and A. L. Glasebrook (J. Am. Chem. Soc. **56**, 2381 (1934)) have found that the methylene radical, prepared by the thermal decomposition of diazomethane, will not remove bismuth mirrors. Antimony and arsenic mirrors, however, are removed.

bisdimethylbismuth. Ganassini and Santi (38) have prepared this compound or its oxide, $(CH_3)_2BiOBi(CH_3)_2$, by the reaction between sodium acetate and bismuth oxide. Blicke, Oakdale, and Smith (7) and Rozenblumówna and Weil (100) were unable to prepare bisdiphenylbismuth by treating diphenylbismuth halides with various reducing agents. The probable formation of the diarylbismuth radical in liquid ammonia has been reported recently (52). For example, di-*p*-tolylbismuth halide and one atom of sodium yield an intensely green colored solution.

$$(p\text{-}CH_3C_6H_4)_2BiX + Na \rightarrow (p\text{-}CH_3C_6H_4)_2Bi + NaX$$

The addition of a second atom of the metal replaces the green color by a dark red color which is characteristic of diarylbismuth sodium compounds.

$$(p\text{-}CH_3C_6H_4)_2Bi + Na \rightarrow (p\text{-}CH_3C_6H_4)_2BiNa$$

The first reaction has been used to prepare a variety of free radicals in liquid ammonia (44).

Compounds containing —As═As— and —Sb═Sb— groups are known, but the corresponding bismuth compounds have never been prepared. Bismuth compounds with mixed metal-metal bonds, e.g., —Bi═As—, are unstable, easily oxidized by air, and decomposed by boiling water (35). Triphenylbismuth dichloride and copper bronze do not yield $(C_6H_5)_3Bi{=}Bi(C_6H_5)_3$, even though pentavalent bismuth compounds like $(Aryl)_3BiX_2$ possess unusual stability (19). Phenylbismuth dibromide and copper bronze yield only triphenylbismuth (18).

No bismuth compounds analogous to the aromatic arsonic and stibonic acids, $RAsO(OH)_2$ and $RSbO(OH)_2$, have been prepared. Actually, H_3BiO_3 is a moderately strong base, and basic bismuth salts of these acids have been made and investigated as spirocheticidal and treponemicidal agents. Lecoq (74) has reported the preparation of phenylbismuth oxide, C_6H_5BiO, which may hydrate to a pentavalent form, but this is questionable. Triarylbismuth dihydroxides, $R_3Bi(OH)_2$, have been prepared (22, 55) and are easily soluble in water.

$$R_3BiCl_2 + 2AgOH \rightarrow R_3Bi(OH)_2 + 2AgCl$$

The pH of such a solution is approximately 7.2, and after removal of the silver chloride by centrifuging, the solution may be used therapeutically (55). The aqueous solution undergoes gradual decomposition, particularly in the presence of light. By evaporation of the aqueous solution the dihydroxide may be obtained as a pale yellow powder which does not redissolve in water but dissolves readily in 95 per cent ethanol. Ethanolic solutions also undergo decomposition, yielding acetaldehyde and bismuth hydroxide.

Primary and secondary arsines, $RAsH_2$ and R_2AsH, where R is aliphatic or aromatic, are known, but the corresponding antimony or bismuth compounds have not been prepared.

Tertiary aromatic and aliphatic arsenic compounds and tertiary alkyl- and some mixed alkylaryl-antimony compounds add alkyl halides to form "onium" compounds. Tertiary bismuth compounds, both aliphatic and aromatic, do not add alkyl halides even at elevated temperatures. Generally, a secondary cleavage reaction takes place.

$$(CH_3)_3Bi + 2CH_3I \xrightarrow{200°C.} CH_3BiI_2 + 2C_2H_6$$

The reaction between triphenylbismuth dibromide and ethylmagnesium bromide might have yielded a bismuthonium compound.

$$(C_6H_5)_3BiBr_2 + C_2H_5MgBr \rightarrow (C_6H_5)_3(C_2H_5)BiBr + MgBr_2$$

The products, instead, were triphenylbismuth, diphenylbismuth bromide, and bromobenzene (14). It cannot be assumed that ethyltriphenylbismuthonium bromide was formed as an intermediate and decomposed in a manner similar to that which takes place when trimethylphenylarsonium iodide is heated (119),

$$(CH_3)_3(C_6H_5)AsI \rightarrow (CH_3)_2(C_6H_5)As + CH_3I$$

since no onium compound was formed when triphenylarsenic dihalide was treated with methylmagnesium iodide. There occurred, instead, reduction to triphenylarsenic.

The most stable valence in organobismuth compounds is 5. This valence is not demonstrated by the trialkylbismuth compounds, although it has been proposed that pentavalent derivatives are formed as intermediates and decompose spontaneously (80). The pentavalent aromatic bismuth compounds are comparatively stable. The various derivatives with halogens and pseudohalogens show a regular decrease in stability, the difluoride being the most stable. On the basis of decomposition temperatures, these derivatives, in the order of decreasing stability are: difluoride, dichloride, dicyanate, dibromide, diazide, and diiodide. The dithiocyanate and diselenocyanate have not been prepared.

Birchenbach and Kellermann (6) have determined the decomposition potentials of a large number of potassium halides and pseudohalides. Since the decomposition potential is related directly to stability, it was possible to obtain a series of halogens and pseudohalogens based on the relative ease of decomposition. This series,—F, CNO, OCN, Cl, N_3, Br, CN, SCN, I, SeCN, TeCN,—agrees well with the series described above.

Trivalent bismuth compounds are cleaved quantitatively by inorganic acids. In contrast, the pentavalent compounds are but little affected by fuming nitric acid, boiling hydrochloric acid, or sulfuric acid, except for nuclear substitution. This stability is demonstrated by the following reactions:

$$(C_6H_5)_3Bi(NO_3)_2 \xrightarrow{\text{concd. HCl}} (C_6H_5)_3BiCl_2$$

$$(C_6H_5)_3Bi(NO_3)_2 \xrightarrow{\text{fuming } HNO_3} (O_2NC_6H_4)_3Bi(NO_3)_2$$

$$(C_6H_5)_3BiCl_2 \xrightarrow{\text{concd. } H_2SO_4} (C_6H_5)_3BiSO_4$$

B. GENERAL METHODS FOR THE PREPARATION OF TERTIARY BISMUTH COMPOUNDS

Organobismuth compounds are best prepared by interaction of a Grignard reagent and bismuth chloride. The yields range from 60 to 80 per cent with most aromatic bismuth compounds. Triethylbismuth has been obtained in 86 per cent yield by this method (47). It has not been possible to introduce bismuth into the aromatic nucleus by means of the Bart reaction (3) or its modifications (26, 111). The synthesis of organobismuth compounds by the copper bronze decomposition of aryldiazonium chloride–bismuth chloride complexes has been described recently (48, 53).

Tertiary bismuth compounds have been prepared by the following methods:

(*a*) *Reaction of a bismuth–sodium or bismuth–potassium alloy with an alkyl or aryl halide:* Löwig and Schweizer (76) synthesized triethylbismuth by this method in 1850. This was the first organobismuth compound reported in the literature. The reaction may be represented as follows:

$$3C_2H_5X + BiK_3 \rightarrow (C_2H_5)_3Bi + 3KX$$

Breed (8) and Dünhaupt (34) also prepared triethylbismuth, using a bismuth–potassium alloy. Michaelis and Polis (84), Michaelis and Marquardt (83), and Gillmeister (43) obtained aromatic bismuth compounds by means of a bismuth–sodium alloy and an aryl halide. Rozenblumówna and Weil (100) have reported more recently a modification of the Gillmeister method which gave improved yields. Stilp (108) has prepared triphenylbismuth in 75 per cent yield by the Michaelis method.

(*b*) *Reaction between aluminum carbide and bismuth chloride in hydrochloric acid:* Hilpert and Ditmar (66) obtained trimethylbismuth by the slow addition of aluminum carbide to bismuth chloride in 20 per cent hydrochloric acid solution.

$$2Al_4C_3 + 2BiCl_3 + 18HCl \rightarrow 2(CH_3)_3Bi + 8AlCl_3$$

It is apparent that this reaction is limited to the preparation of trimethylbismuth and that the yield would be affected by acid cleavage.

(*c*) *Reaction of a dialkylzinc compound and a bismuth halide:* Marquardt (80, 81) prepared trialkylbismuth compounds by the addition of an ether solution of a bismuth halide to a similar solution of a dialkylzinc compound. The difficulty in handling the spontaneously inflammable alkylzinc compounds has made it necessary to replace this method by the equally effective but more easily handled Grignard reagent.

(*d*) *Reaction of the Grignard reagent and a bismuth halide:* Pfeiffer and Pietsch (97) were the first to prepare organobismuth compounds by means of the Grignard reagent. This method was later employed by Stilp (108), Challenger and coworkers (14, 15, 18, 23), Worrall (120), Supniewski and Adams (111), Supniewski (109, 110), Classen and Ney (29), Krause and Renwanz (72), Blicke, Oakdale, and Smith (7), Davies, Norvick, and Jones (31), Gilman and coworkers (47, 51, 54), Grüttner (62, 63), Fr. Fabrikant (37), and Zhitkova and coworkers (121). With phenyllithium and bismuth bromide, the yield of triphenylbismuth is

44 per cent (121); this method is therefore inferior to the Grignard method, which gives yields of about 80 per cent. It should be noted that, regardless of the quantity of bismuth halide used, except when it exceeds the quantity demanded by the equation

$$3RMgX + BiX_3 \rightarrow R_3Bi + 3MgX_2$$

the tertiary compound is formed. The reaction can be used to prepare $RBiX_2$ and R_2BiX compounds but not in good yields (63, 74, 114).

(*f*) *Reaction between diphenylmercury and bismuth metal:* Hilpert and Grüttner (67) have reported a 41 per cent yield of triphenylbismuth when bismuth metal and diphenylmercury are heated at 250°C. Frankland and Duppa (36) prepared triethylbismuth by heating diethylmercury and powdered bismuth at 100–130°C. Tetraethyllead and powdered bismuth do not react after 5 hr. heating at 100–130°C. Tetraethyllead and bismuth chloride yield a mixture of ethylbismuth chlorides and probably some triethylbismuth (50). Phenylmercuric chloride and bismuth–sodium alloy yield traces of triphenylbismuth (121).

(*g*) *Reaction between bismuth electrodes and a gaseous hydrocarbon under the influence of an electrical discharge:* Trimethylbismuth is formed by an electrical discharge between two bismuth electrodes if a stream of methane is passed between the electrodes simultaneously with the electrical discharge (92).

(*h*) *Reaction between free radicals and bismuth mirrors:* Paneth and Hofeditz (92), Paneth (94), and Rice and coworkers (98) have reported that free methyl and ethyl radicals dissolve bismuth mirrors. Paneth and Loleit (93) have obtained trialkylbismuth compounds with cold mirrors and methyl and ethyl radicals. With heated mirrors, in addition to the trialkyl compounds, there was evidence of the possible formation of bisdimethylbismuth and bisdiethylbismuth.

(*i*) *Spontaneous decomposition of diphenylbismuth sodium in liquid ammonia:* The spontaneous decomposition of diphenylbismuth sodium in liquid ammonia leads to the formation of triphenylbismuth in 49 per cent yield (52). Sodium–bismuth alloy and iodobenzene do not form triphenylbismuth in liquid ammonia, owing probably to the insolubility of the alloy in this solvent (52).

(*j*) *Decomposition of an aryldiazonium chloride–bismuth chloride complex, followed by treatment with ammonia or hydrazine:* The recently described preparation of triarylbismuth compounds by the decomposition of an aryldiazonium chloride–bismuth chloride complex by copper, followed by treatment with ammonia (48), has unusual possibilities for the synthesis of therapeutically active organobismuth compounds. Thus far, however, it has not been possible to obtain experimental conditions favorable to the preparation of compounds like tri-*p*-carboxyphenylbismuth or tri-*p*-sulfophenylbismuth. In any case the reaction has some advantages, since it has made possible the preparation of di-*o*-carbomethoxyphenylbismuth chloride, di-*o*-carboethoxyphenylbismuth chloride, and *o*-carbomethoxyphenylbismuth dichloride, which could not have been prepared so readily by other methods. It affords a simplified procedure, also, for the preparation of tri-*p*-bromophenylbismuth (53).

The mechanism of this reaction has been established by isolating the intermediary $RBiX_2$ and R_2BiX compounds formed. It has been found, in addition, that hydrazine is a reagent of choice for the conversion of these intermediates to R_3Bi compounds.

$$(C_6H_5N_2Cl)_2 \cdot BiCl_3 + 4Cu \longrightarrow (C_6H_5)_2BiCl + 4CuCl + 2N_2$$

$$(C_6H_5)_2BiCl \xrightarrow{H_2NNH_2} (C_6H_5)_3Bi$$

(*k*) *Reaction between an* R_2BiX *or* $RBiX_2$ *compound and the Grignard reagent:* This reaction was first used by Challenger (14) to prepare diphenyl-α-naphthylbismuth, and later by Norvick (90) to prepare diethylamylbismuth. A modified procedure employing low temperatures has been utilized successfully in the preparation of a large number of related $R_2R'Bi$ compounds (51).

(*l*) *Reaction between a diarylbismuth sodium compound and an aryl iodide or bromide:* Unsymmetrical organobismuth compounds have been prepared by the reaction of an R_2BiNa compound and α-iodonaphthalene in liquid ammonia. Some aryl bromides react also, but substituents ortho to the halogen inhibit reaction (52).

$$(C_6H_5)_2BiNa + \alpha\text{-}C_{10}H_7I \rightarrow (C_6H_5)_2(\alpha\text{-}C_{10}H_7)Bi + NaI$$

(*m*) *Conversion of triarylbismuth dihalides to triarylbismuth compounds:* Tri-*m*-tolylbismuth, because of its low melting point, is best purified as the pentavalent dichloride (111). Diphenyl-α-naphthylbismuth dichloride may be separated from triphenylbismuth dichloride by virtue of the insolubility of the latter compound in acetone (20). Impure oily unsymmetrical bismuth compounds have been converted to their dichlorides in order to facilitate purification (51). These halogens may be removed by hydrogen sulfide (84), ammonium sulfide (83), moist silver oxide (19, 43), sodium hydrosulfite, formaldehyde, sodium and alcohol, and dimethyl sulfate and alkali (111). Hydrazine hydrate is a reagent of choice for this reaction (49).

(*n*) *Conversion of arylbismuth dihalides and diarylbismuth halides to triarylbismuth compounds:* Hydrazine hydrate converts $RBiX_2$ and R_2BiX compounds to R_3Bi in excellent yields. Alcoholic ammonia has been used also, but no data are available as to its effectiveness (23, 83).

(*o*) *Formation of trimethylbismuth by the spontaneous disintegration of tetramethylradium D:* Mortensen and Leighton (87) have investigated the molecular changes accompanying radioactive transformations by measuring the β-activity of tetramethyllead containing small quantities of tetramethylradium D. These authors were interested in determining whether the molecule was completely decomposed, or whether it adjusted itself to the new valence conditions. The transformation of radium D into radium E and then into radium F is essentially the change of an atom of lead into bismuth and then into polonium. Radium D emits only β-rays which are too feeble to produce an appreciable effect upon an electroscope, while radium E and radium F possess strong α- and β-ray activity. By the examination of the vapor above the radioactive tetramethyllead, these authors found indisputable evidence for the presence of radium E (presumably as trimethylbismuth) and radium F (presumably as dimethylpolonium). From this they concluded that the tetramethylradium D molecule was not completely broken down by radioactive transformation, but adjusted itself to the new valence conditions by the loss of a methyl group and the completion of the electron pair by the acquisition of an electron from its surroundings. The disintegration apparently involves the rupture of one bond only.

(*p*) *Formation of organobismuth compounds by metal–metal interchange:* Leigh-Smith and Richardson (75) have obtained evidence which suggests that bismuth metal, deposited presumably as the oxide on a metallic surface, can exchange with lead in tetramethyllead to form trimethylbismuth. This they demonstrated in the following manner:

A piece of gold which had been activated with Th(B + C + C′ + C″) was immersed in an ether solution of tetramethyllead for 2 hr. Then a small quantity of the solution was introduced into a small pot inside a Wilson expansion chamber filled with nitrogen. As the solution evaporated from the pot, characteristic tracks of Th(C + C′) were observed starting from parts of the chamber remote from the pot, thus proving that a volatile compound had been formed which evaporated with the rest of the solution, and this compound, presumably, is trimethylbismuth. This exchange process occurs apparently between atoms of the same atomic number and without the breaking up of the molecule.

The reaction between *n*-butyllithium or *n*-butylsodium and triarylbismuth compound does not lead to the expected metalation of the aromatic nucleus (54). Instead, a metal–metal interconversion takes place.

$$(p\text{-}CH_3C_6H_4)_3Bi + 3n\text{-}C_4H_9Li \rightarrow (n\text{-}C_4H_9)_3Bi + 3p\text{-}CH_3C_6H_4Li$$

Phenyllithium and bismuth metal do not yield triphenylbismuth, whereas phenyllithium and antimony give triphenylantimony (113). This again demonstrates the sharp differences between antimony and bismuth. Many reactions which can be used to prepare organoantimony compounds in good yields fail entirely in the preparation of organobismuth compounds.

(*q*) *Reaction between* R_3Bi *and* RX *compounds:* Marquardt (81) has reported that, in the course of heating triisobutylbismuth with methyl or ethyl iodide at 150°C., he obtained no quaternary iodides but, instead, trimethylbismuth and triethylbismuth, respectively.

(*r*) *Electrolysis of ethylsodium in diethylzinc, using bismuth as the anode:* The electrolysis of an ethylsodium–diethylzinc solution probably gives free ethyl radicals. Triethylbismuth was obtained when the electrolysis was carried out with bismuth as the anode (65b).

C. ORGANOBISMUTH COMPOUNDS

1. *Symmetrical trialkylbismuth compounds*

The trialkylbismuth compounds are heavy, highly refractive, colorless or pale yellow, oily liquids. Tricyclohexylbismuth appears to be a solid at room temperature. The methyl and ethyl compounds possess unpleasant odors, but the higher homologs are odorless. Their vapors irritate mucous membranes. Because of their inflammability in air they must be isolated under an inert atmosphere, and with the exception of the trimethyl compound they cannot be distilled at ordinary pressures without decomposition. Triethylbismuth, for example, explodes when heated to 150°C. (8, 34). Dünhaupt (34) has reported that the presence of water or ether makes possible a distillation of triethylbismuth at atmospheric pressure. Seifter (105) has found that it is possible to distil a trialkylbismuth-etherate without decomposition. Triethylbismuth becomes cloudy when exposed to atmospheric oxygen, and this clouding effect has been proposed as a delicate test for the presence of oxygen (47).

Moureu, Dufraisse, and Badoche (88) have shown that trialkylbismuth compounds can function both as catalyst and inhibitor in the autoöxidation of organic compounds. Triethylbismuth effectively retards the oxidation of benzaldehyde, furfural, butyraldehyde, and alkaline solutions of sodium sulfite but accelerates the oxidation of styrene, turpentine, and acid solutions of sodium sulfite.

The boiling points of the trialkylbismuth compounds increase normally, and the branched-chain compounds have lower boiling points than the normal isomers. Their specific gravities, as one might predict, decrease with increasing carbon content. They are soluble in alcohol, ether, petroleum ether, carbon tetrachloride, and benzene, and are insoluble in water.

Trialkylantimony compounds combine readily with oxygen, but the ease of oxidation decreases with increasing molecular weight. They ignite when warmed in air, with the formation of antimony trioxide. Trimethylantimony oxide, triethylantimony oxide, and triamylantimony oxide can be prepared directly by the regulated oxidation of the respective tertiary compounds. With chlorine, bromine, iodine, cyanogen bromide, cyanogen iodide, sulfur, and selenium, the trialkylantimony compounds form stable pentavalent compounds. They also form double salts with platinum and palladium chlorides. Mercuric, auric, and silver salts are reduced to the free metal. With alkyl halides they readily form stibonium halides. They dissolve in nitric acid to form dinitrates.

The trialkylbismuth compounds, in contrast, form no stable pentavalent derivatives. With the exception of the trimethyl compound, which is the most stable of the trialkylbismuth compounds, they ignite spontaneously and burn to bismuth oxide, although the ease of oxidation decreases with increasing molecular weight. In the presence of pure oxygen, tributylbismuth explodes violently (54).[3] With chlorine or bromine, trialkylbismuth compounds undergo

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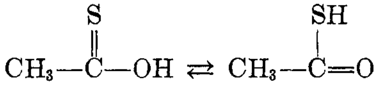
[3] G. Calingaert, H. Soroos, and V. Hnizda (J. Am. Chem. Soc. **64**, 392 (1942)) have found that the oxidation of triethylbismuth with pure oxygen under controlled temperature yielded bismuth oxide, diethylbismuth ethoxide, ethoxybismuth oxide, diethyl peroxide, diethyl ether, ethyl alcohol, and ethylene.

cleavage even at 0°C. to form R_2BiX compounds. Inorganic acids cleave the bismuth compounds and with concentrated nitric and sulfuric acids the reaction proceeds explosively. With alkyl iodides, quaternary bismuthonium iodides do not form even at elevated temperatures. Hydrogen sulfide cleaves the bismuth compounds. Both silver nitrate and mercuric chloride readily cleave these compounds and are themselves reduced to the free metal.

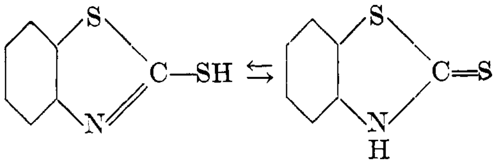
It has been reported that triethylbismuth may be used for the detection of the —SH group (47). The test is based on the cleavage of triethylbismuth by acid hydrogens,

$$(C_2H_5)_3Bi + R{-}{-}{-}H \rightarrow C_2H_6 + (C_2H_5)_2Bi{-}{-}{-}R$$

and is carried out using the ordinary Zerewitinoff technique. No cleavage occurs with the hydrogens in —NH, —C≡CH, or simple —OH groups, although some strong carboxylic acids give limited reactions. There is no interference by azo or nitro groups. The existence of thioenolization in thioacetic acid and 1-mercaptobenzothiazole, for example, is shown quite definitely.



$$CH_3-\overset{\overset{S}{\|}}{C}-OH \rightleftarrows CH_3-\overset{\overset{SH}{|}}{C}=O$$



2. *Symmetrical triarylbismuth compounds*

The tertiary aromatic bismuth compounds are colorless crystalline solids, unaffected by oxygen and possessing generally a characteristic pleasant odor. They are soluble in ethanol, ether, chloroform, ethyl acetate, acetone, petroleum ether, dioxane, and benzene and are insoluble in water. Triphenylbismuth may be distilled or sublimed without decomposition at very low pressures and can be obtained so pure that it has been used in determinations of the atomic weight of bismuth (28, 29, 30). The molecular weights of triphenylbismuth, tri-α-naphthylbismuth, and tri-*p*-tolylbismuth determined cryoscopically in benzene are normal. This is further evidence that even the more stable aromatic compounds show no tendency to form bismuth–bismuth bonds,

$$\geqslant Bi{=}Bi \leqslant$$

even in view of their greater stability when the maximum valence has been satisfied. The aromatic groups are held loosely by bismuth and are cleaved readily by inorganic and organic acids, thiophenol, hydrogen, and inorganic halides.

With either chlorine or bromine, tertiary aromatic bismuth compounds form dichlorides and dibromides (R_3BiX_2), respectively. Triphenylbismuth diiodide is stable only at −78°C. It is formed by titrating triphenylbismuth at this temperature with iodine, using starch as the indicator. The end point occurs when exactly two equivalents of iodine have been added. Raising the temperature but a few degrees causes a spontaneous decomposition. If the temperature is kept at −78°C., however, the diiodide may be kept unchanged for days. The difluoride is prepared by a double decomposition reaction between the dichloride and potassium fluoride.

With sulfuryl chloride, sulfur monochloride, and thionyl chloride tertiary compounds yield dichlorides (15, 18). With the halogen halides or halogen pseudohalides,—iodine chloride, iodine bromide, cyanogen chloride, etc.,—the tertiary compounds are cleaved. The more negative group or atom attaches itself to the bismuth, while the more positive group or atom is eliminated as part of the aromatic nucleus (17, 18, 19, 118). Such reactions give further confirmation to the stability series of halogens and pseudohalogens mentioned previously (page 12).

$$(C_6H_5)_3Bi + \left\{\begin{array}{llll} ICl & \longrightarrow & (C_6H_5)_2BiCl & + C_6H_5I \\ CNI & \longrightarrow & (C_6H_5)_2BiCN & + C_6H_5I \\ CNBr & \longrightarrow & (C_6H_5)_2BiBr & + C_6H_5CN \\ IBr & \longrightarrow & (C_6H_5)_2BiBr & + C_6H_5I \end{array}\right.$$

The ease with which bismuth exchanges its aromatic groups for the halogens of inorganic halides is evidence again of the weak carbon–bismuth bond. Under conditions where triphenylantimony reacts to form R_3SbX_2 compounds, triphenylbismuth cleaves to yield R_2BiX and $RBiX_2$ compounds (21, 23, 57, 59).

$$(C_6H_5)_3Bi + \left\{\begin{array}{llll} BiCl_3 & \rightarrow & (C_6H_5)_2BiCl & + C_6H_5BiCl_2 \\ SbCl_3 & \rightarrow & (C_6H_5)_2BiCl & + (C_6H_5)_3SbCl_2 \\ AsCl_3 & \rightarrow & (C_6H_5)_2BiCl & + C_6H_5AsCl_2 \\ PCl_3 & \rightarrow & (C_6H_5)_2BiCl & + C_6H_5PCl_2 \\ SiCl_4 & \rightarrow & (C_6H_5)_2BiCl & + \quad - - - \\ CuCl_2 & \rightarrow & (C_6H_5)_2BiCl & + \quad - - - \\ TiCl_4 & \rightarrow & (C_6H_5)_2BiCl & + \quad - - - \\ HgCl_2 & \rightarrow & (C_6H_5)_2BiCl & + C_6H_5HgCl \\ TlCl_3 & \rightarrow & (C_6H_5)_2BiCl & + (C_6H_5)_2TlCl \\ AgNO_3 & \rightarrow & \text{Probably } (C_6H_5Ag)_2 \cdot AgNO_3 & \end{array}\right.$$

The reaction with silicon tetrachloride yields an unidentified organosilicon compound; with cupric chloride there was no mention of the possible formation of organocopper compounds. No reduction to trivalent titanium occurs in the reaction with titanium tetrachloride. Considerable reduction occurs in the interaction of a Grignard reagent and titanium tetrachloride.

Stilp (108) has been the only one to report the formation of double salts in the reaction between tertiary aromatic bismuth compounds and mercuric chloride. Gillmeister (43) had reported previously that no double salt was formed between triphenylbismuth and mercuric chloride. Stilp did not prepare this salt but he was able to form others: $(p\text{-}CH_3C_6H_4)_3Bi \cdot HgCl_2$, $(o\text{-}CH_3C_6H_4)_3Bi \cdot HgCl_2$, $(m\text{-}(CH_3)_2C_6H_3)_3Bi \cdot HgCl_2$, and $(\alpha\text{-}C_{10}H_7)_3Bi \cdot HgCl_2$. The preparation of the tri-*p*-tolylbismuth double salt has been confirmed (55). These compounds are colorless crystalline solids which can be recrystallized without decomposition from glacial acetic acid. Compounds of this type could be useful as derivatives, since they possess sharp melting points and are easily purified.

Challenger and Pritchard (21) have found that migration of phenyl groups from bismuth may be effected either to the comparatively electropositive tin and mercury or to electronegative elements like arsenic and phosphorus. It was earlier proposed by Hilpert and Grüttner (67) that such migration took place only from the less positive to the more positive element, although the presence of halogens appeared to modify the reaction. The former authors consider that many of the ready migrations of phenyl groups are partly conditioned by the insolubility of one of the possible products.

With triphenylantimony, migration of phenyl groups occurs very rarely at ordinary temperatures. It has been observed with silicon tetrachloride, mercuric chloride, phosphorus trichloride, and with antimony trichloride only at 240°C. Addition compounds are produced almost always with triphenylarsenic. This is further evidence of the stability of the bond between carbon and the more electronegative elements.

Organobismuth compounds do not add to benzaldehyde, benzalacetophenone (55), or Michler's ketone (79). They do react, however, to a limited extent with acid halides (23) to give ketones in small yields. Under similar conditions, triphenylantimony does not react with acid halides. With chloroform in a sealed tube at 160°C. triphenylbismuth forms small quantities of triphenylmethane (26), and with benzyl chloride it forms diphenylmethane (23).

Triphenylbismuth reacts with benzoyl peroxide to form triphenylbismuth dibenzoate, $(C_6H_5)_3Bi(O_2CC_6H_5)_2$ (27), and with benzoyl nitrate to form triphenylbismuth dinitrate (118). It has been reported that triphenylbismuth gives color reactions with certain nitro derivatives (15), but no details are available.

Tribenzylbismuth oxidizes spontaneously when exposed to air, yielding benzaldehyde and inorganic bismuth (23). Tri-β-phenylethylbismuth undergoes a similar oxidation (55). This may account for the reported failure to prepare tri-*p*-methoxybenzylbismuth and tri-*o*-methoxybenzylbismuth (111). It has been reported also that bromophenacetin, *p*-chlorophenol, and *o*-iodoaniline with sodium–bismuth alloy do not yield tertiary bismuth compounds (100).

Makarova and Nesmeyanov (78) have prepared benzenediazonium nitrate by the reaction between triphenylbismuth, nitric oxide, and nitrogen trioxide. Supniewski and Adams (111) were unable to obtain triarylbismuth compounds possessing amino groups by the reduction of trinitroarylbismuth compounds. Unstable mixtures were the only products. Tri-*p*-dimethylaminophenylbismuth has been prepared by the interaction of *p*-dimethylaminophenyllithium and bismuth chloride, but this compound was cleaved by acetic acid in preference to forming a water-soluble acetate. It was cleaved also by chlorine even at 0°C., so that the preparation of a more stable pentavalent derivative was not possible (51).

Challenger, Peters, and Halévy (20) have attempted the preparation of triphenylbismuth diselenocyanate, $(C_6H_5)_3Bi(SeCN)_2$, by the interaction of triphenylbismuth dichloride and potassium selenocyanate (KSeCN). They obtained, instead, the unstable diphenylbismuth selenocyanate, $(C_6H_5)_2BiSeCN$. Tri-*p*-tolylbismuth dichloride and potassium selenocyanate underwent a similar reaction. The instability of the pentavalent compound was to be predicted. Triphenylbismuth and tellurium dicyanide, $Te(CN)_2$, gave diphenylbismuth cyanide.

When triarylbismuth compounds are heated to high temperatures, they

TABLE 1

*Tertiary bismuth compounds**

AROMATIC COMPOUNDS	MELTING POINT	REFERENCES
	°C.	
Tri-*o*-anisyl-	171	(108, 110, 111)
Tri-*p*-anisyl-	190	(43, 108, 110)
Tribenzyl-	85	(13, 26, 55)
Tribiphenyl-	183	(120)
Tri-*p*-bromophenyl-	149	(23, 53)
Tri-*p*-carboxyphenyl-	162	(110)
Tri-*o*-chlorophenyl-	141	(51)
Tri-*p*-chlorophenyl-	116	(23, 53, 54)
Tri-2-*p*-cymyl-	87	(51)
Tri-*p*-cumyl-	159	(43)
Tri-*p*-dimethylaminophenyl-	230	(51)
Tri-*p*-fluorophenyl-	94	(51)
Trimesityl-	137	(51, 121)
Tri-α-naphthyl-	235	(14, 53, 54, 108)
Tri-β-naphthyl-	84	(108)
Tri-*p*-nitrophenyl-	121	(109, 111)
Trinitrophenyl-	159	(118)
Tri-2-nitro-*p*-tolyl-	126	(111)
Tri-*o*-phenetyl-	122	(54)
Tri-*p*-phenetyl-	73	(43, 54)
Tri-β-phenylethyl-		(55)
Triphenyl-	77.6	(14, 18, 29, 67, 83, 84, 97, 100, 108, 121)
Tristyryl-		(37)
Trithymyl-		(37)
Tri-α-thienyl-	137.5	(72)
Tri-*o*-tolyl-	129	(43, 53, 108, 110)
Tri-*m*-tolyl-	65	(18)
Tri-*p*-tolyl-	120	(15, 48, 53, 54, 83, 108, 109)
Tri-*m*-xylyl-	175	(83, 108, 110)
Tri-*p*-xylyl-	194.5	(43, 108)
Diphenyl-α-naphthyl-	119	(13, 14, 18, 23, 51, 52)
Di-*p*-tolyl-α-naphthyl-	130	(51, 52)
Di-*p*-chlorophenyl-α-naphthyl-	139	(51, 52)
Di-*p*-anisyl-α-naphthyl-	136	(51)
Di-*p*-phenetyl-α-naphthyl-	132	(51)
Dimesityl-α-naphthyl-	151.5	(51)
Di-*p*-chlorophenyl-*o*-tolyl-	104.5	(51)
Di-*p*-tolyl-*p*-chlorophenyl-	97	(51)
Di-*o*-tolyl-α-naphthyl-	114	(51)
Diphenyl-*p*-chlorophenyl-	83.5	(51)
Diphenyl-*p*-hydroxyphenyl-	180	(52)

TABLE 1—*Concluded*

ALIPHATIC COMPOUNDS	BOILING POINT	REFERENCES
	°C.	
Trimethyl-	110 at 760 mm.	(66, 75, 80, 81, 87, 92, 93)
Triethyl-	96 at 50 mm. 107 at 79 mm. 123 at 150 mm.	(8, 31, 34, 36, 47, 76, 80, 81, 93)
Tri-*n*-propyl-	87 at 8 mm. 127 at 50 mm.	(31)
Tri-*n*-butyl-	124 at 7 mm. 173 at 50 mm.	(31, 54)
Tri-*tert*-butyl-	Decomposes	(55)
Triisobutyl-	162 at 74 mm.	(15, 81)
Tri-*n*-amyl-	158 at 7 mm. 209 at 50 mm.	(31)
Triisoamyl-	200 at 70 mm.	(81)
Tricyclohexyl-		(16, 62, 112)
Diethylamyl-		(90)
Ethylcyclopentamethylene-	118 at 20 mm.	(63)
Trilauryl-		(107)
Tricetyl-		(107)

* Where more than one value for a melting point is given, the highest value is recorded in this and other tables.

decompose into the metal and biaryl compounds. Cambi (10) found that triphenylbismuth and diphenylmercury form no bimolecular compound. Challenger and Ridgway (23) have reported the interchange of aromatic radicals between bismuth and mercury compounds at high temperatures. Tri-α-naphthylbismuth and diphenylmercury at 200°C. gave di-α-naphthylmercury, triphenylbismuth, and diphenyl-α-naphthylbismuth. Tri-*p*-tolylbismuth and diphenylmercury at 180°C. gave triphenylbismuth and di-*p*-tolylmercury. No exchange occurred between tri-*p*-tolylbismuth and di-α-naphthylmercury at this temperature.

Calingaert and Beatty (11b) have described similar reactions as the "random intermolecular exchange of organic radicals." Thus, a mixture of tetraethyllead and tetramethyltin, after undergoing redistribution, yielded all ten possible R_4M compounds. Later, Calingaert, Soroos, and Thomson (11c) showed that tetramethyllead and diethylmercury, and tetraethyllead and dimethylmercury, both underwent a similar reaction to yield all the possible redistribution products.

There appears to be an exchange of radicals when two bismuth compounds are fused, since tri-α-naphthylbismuth and triphenylbismuth at 190°C. yield diphenyl-α-naphthylbismuth. No reaction occurred between tri-*p*-tolylbismuth and tri-α-naphthylbismuth at 200°C. There is evidence that the former reaction is reversible, and Calingaert, Soroos, and Hnizda (11a) have proposed this reaction as an example of random distribution (51).

With strong inorganic acids triarylbismuth compounds are cleaved quantitatively to the hydrocarbon and the inorganic bismuth salt (84). With the more weakly acidic compounds it is possible to isolate intermediate products (25, 55).

$$(C_6H_5)_3Bi + \left\{\begin{array}{lll} HSCN & \rightarrow (C_6H_5)_2BiSCN & + C_6H_6 \\ 2HSCN & \rightarrow C_6H_5Bi(SCN)_2 & + 2C_6H_6 \\ 2HSC_6H_5 & \rightarrow C_6H_5Bi(SC_6H_5)_2 & + 2C_6H_6 \end{array}\right.$$

Triphenylantimony is not cleaved by thiophenol under similar conditions (55). Tri-α-naphthylbismuth is not cleaved by this reagent under conditions which give 43.6 per cent cleavage with triphenylbismuth. Cleavage reactions with the halogens and pseudohalogens also indicate that the α-naphthyl radical is held more firmly to bismuth than is the phenyl radical (17, 18).

Table 1 lists all the known tertiary organobismuth compounds.

3. Unsymmetrical triarylbismuth compounds

Prior to a recent publication (51) the only unsymmetrical organobismuth compound which had been described in any detail was diphenyl-α-naphthylbismuth, prepared by Challenger and coworkers (13, 14, 15, 16, 17, 18, 19, 23).

$$(C_6H_5)_2BiBr + \alpha\text{-}C_{10}H_7MgBr \rightarrow (C_6H_5)_2BiC_{10}H_7\text{-}\alpha + MgBr_2 \tag{a}$$

Incidental to studies concerned with optically active organobismuth compounds, these authors tried unsuccessfully to prepare other unsymmetrical organobismuth compounds. More recently, Norvick (90) reported the formation of diethylamylbismuth, together with triethylbismuth and triamylbismuth, from the reaction between amylbismuth dichloride and ethylmagnesium bromide, but no physical data on this compound were provided.

On the basis of general observations concerned with the relative reactivities of organometallic compounds, it appeared quite probable that a variety of unsymmetrical compounds could be made and would be found to be reasonably stable. This was found to be the case. The procedures used are illustrated in the following reactions for the synthesis of di-p-tolyl-α-naphthylbismuth.

$$(p\text{-}CH_3C_6H_4)_2BiX + \alpha\text{-}C_{10}H_7MgBr \rightarrow (p\text{-}CH_3C_6H_4)_2BiC_{10}H_7\text{-}\alpha + MgXBr \tag{b}$$

$$2p\text{-}CH_3C_6H_4MgBr + \alpha\text{-}C_{10}H_7BiBr_2 \rightarrow (p\text{-}CH_3C_6H_4)_2BiC_{10}H_7\text{-}\alpha + 2MgBr_2 \tag{c}$$

$$(p\text{-}CH_3C_6H_4)_2BiNa + \alpha\text{-}C_{10}H_7I \rightarrow (p\text{-}CH_3C_6H_4)_2BiC_{10}H_7\text{-}\alpha + NaI \tag{d}$$

Reaction (d) was carried out in liquid ammonia (52). Diarylbismuth halides react in liquid ammonia with sodium, potassium, lithium, calcium, and barium to form highly reactive R_2BiM or $(R_2Bi)_2M$ compounds which upon treatment with α-iodonaphthalene yield the corresponding unsymmetrical compound.

Once obtained in a pure condition, the unsymmetrical compounds were found to have a distinctly higher stability than might have been expected. For example, a sample of diphenyl-α-naphthylbismuth was kept in a stoppered bottle for three years without alteration in melting point. In this connection it is interesting to recall the observations of Calingaert, Soroos, and Hnizda (11a) that the reputedly unstable, unsymmetrical methylethylmercury was in reality quite stable and could be distilled without undergoing disproportionation, provided that traces of RHgX or other related catalysts are absent.

The general problem of redistribution or disproportionation of radicals is closely related to other reactions leading to the synthesis of the unsymmetrical organobismuth compounds. Challenger and coworkers found that, with the single exception of reaction (a), R_2BiX and $R'MgX$ compounds always yielded R_3Bi compounds. This indicated to them the possibility that an R_2BiX compound was a double salt of R_3Bi and BiX_3. The use of a sufficient excess of $R'MgX$ should have yielded two symmetrical organobismuth compounds.

$$\left.\begin{matrix}R_3Bi\\ BiX_3\end{matrix}\right\rangle \xrightarrow{(3R'MgX)} R_3Bi + R'_3Bi + 3MgX_2$$

Although this did not occur when R and R′ were aryl radicals (since only R_3Bi was isolated), when R′ was an alkyl radical the odor of an alkylbismuth compound was evident. It is our opinion that, although organometallic salts in general show the equilibria,

$$R_2MX \rightleftarrows RMX_2 \rightleftarrows R_3M + MX_3$$

some of the unsymmetrical $R_2R'Bi$ compound was formed initially and then may have undergone redistribution, in part or in whole, to R_3Bi and R'_3Bi, to account for the formation of a trialkylbismuth compound.

4. The preferential cleavage of radicals from bismuth in unsymmetrical triarylbismuth compounds

Challenger and Allpress (17) first demonstrated the preferential cleavage of radicals in unsymmetrical organobismuth compounds when they reported that diphenyl-α-naphthylbismuth and iodine bromide yielded α-iodonaphthalene and diphenylbismuth bromide.

$$(C_6H_5)_2BiC_{10}H_7\text{-}\alpha + IBr \rightarrow (C_6H_5)_2BiBr + \alpha\text{-}C_{10}H_7I$$

It was found possible to extend the metal–metal interconversion reaction between organobismuth compounds and *n*-butyllithium (54),

$$(p\text{-}CH_3C_6H_4)_3Bi + 3n\text{-}C_4H_9Li \rightarrow 3p\text{-}CH_3C_6H_4Li + (n\text{-}C_4H_9)_3Bi$$

to determine the relative labilities of radicals attached to bismuth. When an unsymmetrical organobismuth compound, $R_2R'Bi$, was treated with one equivalent of *n*-butyllithium, there was a preferential replacement of one of two available radicals (55). In most instances both R and R′ were cleaved; for example, when diphenyl-α-naphthylbismuth and one equivalent of *n*-butyllithium were allowed to react for 10 min., in diethyl ether, there was obtained, subsequent to carbonation, yields of 21.6 per cent of α-naphthoic acid and 1.7 per cent of benzoic acid. This single experiment had a particular significance, since it might have appeared that the ratio of 2R:R′ in an $R_2R'Bi$ compound was unfavorable to R′ in the determination of the preferential cleavage of either R or R′. If the relative amounts of the two radicals were the sole consideration, the law of probability would have indicated that more R groups would cleave than would R′. This was not found to be true, however, with the above compound or with a number of other $R_2R'Bi$ compounds. Furthermore, while cleavage of diphenyl-α-naphthylbismuth by *n*-butyllithium showed the α-naphthyl and phenyl radicals to possess labilities which might have been predicted on the basis of the series of radicals obtained by the cleavage of unsymmetrical RR′Hg compounds by hydrogen chloride (69b), this was the exception. Anomalously, the *p*-chlorophenyl radical was cleaved as readily as the α-naphthyl, while the phenyl radical was cleaved in preference to the *p*-tolyl and *o*-tolyl groups.

Similar reactions between symmetrical R_3Bi compounds and *n*-butyllithium gave confirmation to the data obtained with the unsymmetrical bismuth compounds, and, in addition, provided further exceptions to the series of radicals mentioned above (69b).

The series of radicals obtained by this metal–metal interconversion reaction, in order of decreasing ease of cleavage from bismuth, was as follows: (*p*-chlorophenyl, *p*-bromophenyl, *p*-fluorophenyl, α-naphthyl), phenyl, *p*-tolyl, *p*-ethoxyphenyl, (*o*-tolyl, mesityl, *o*-chlorophenyl).

On the basis of cleavage from unsymmetrical mercurials by hydrogen chloride, these radicals possess the following order of decreasing lability: mesityl, α-naphthyl, *o*-tolyl, *p*-tolyl, *p*-fluorophenyl, phenyl, (*p*-chlorophenyl, *p*-bromophenyl), *o*-chlorophenyl.

The *p*-ethoxyphenyl radical is not listed in this latter series, but the *p*-methoxyphenyl radical is placed above the *p*-tolyl radical and approximately equal to the mesityl radical in lability. One may arbitrarily assume that the *p*-methoxyphenyl group would occupy a position similar to the *p*-ethoxyphenyl radical.

It is interesting to note that dimesitylmercury was cleaved to the extent of 72.5 per cent under the same conditions which gave no cleavage with trimesitylbismuth.

The solvent played an important rôle in all of these reactions. Cleavage of the *p*-chlorophenyl radical proceeded to the extent of 50 per cent in diethyl ether, but no cleavage occurred in a mixture of petroleum ether and benzene. The effect of the solvent manifested itself, also, in the low order of reaction between tri-α-naphthylbismuth and *n*-butyllithium, where the yield of α-naphthoic acid was 1.2 per cent. In all the other reactions described above, the bismuth compounds were completely dissolved in the solvent prior to the addition of the *n*-butyllithium. Tri-α-naphthylbismuth is practically insoluble in diethyl ether and the slow rate of reaction was due probably to this. With the ether-soluble unsymmetrical bismuth compounds containing the α-naphthyl groups, the radical showed itself to have a lability equal to that of the *p*-chlorophenyl radical. The use of a benzene–ether mixture, in which tri-α-naphthylbismuth is soluble, decreased the yield of α-naphthoic acid to 0.6 per cent.

5. Compounds of the general formulas R_2BiX *and* $RBiX_2$

(a) Alkyl compounds

Alkyl bismuth compounds of the type R_2BiX (where X is Cl or Br) are crystalline solids which burn spontaneously in air and must, therefore, be isolated under an inert atmosphere. They are soluble in alcohol and insoluble in ether. The following methods have been employed in their preparation:

(*a*) *Reaction between a trialkylbismuth compound and chlorine or bromine:* The cooled ether solution of the trialkylbismuth compound is treated with the calculated quantity of the halogen (80, 81).

(*b*) *Reaction between tetraethyllead and bismuth chloride:* The reaction between tetraethyllead and bismuth chloride yields a colorless solid which ignites spontaneously in air and appears to consist in part of diethylbismuth chloride (50).

Compounds of the general formula $RBiX_2$ are more stable than the R_2BiX type discussed above. These, too, are solids possessing high melting points and are stable in air. They are somewhat soluble in alcohol and almost insoluble in ether and petroleum ether. The following methods have been employed in their preparation:

(*a*) *Reaction between a bismuth halide and a tertiary bismuth compound:* To a solution of bismuth chloride or bromide is added the calculated quantity of the R_3Bi compound. The $RBiX_2$ compound separates out as a yellow powder (80, 81).

(*b*) *Reaction between a Grignard reagent and a bismuth halide:* Methylbismuth dibromide has been prepared in small yields by the reaction between methylmagnesium iodide and bismuth bromide (114). Dimethylzinc and bismuth bromide also yield methylbismuth dibromide (80). Ethylbismuth dibromide has been obtained by the interaction of bismuth bromide and ethylmagnesium bromide (63).

(*c*) *Reaction between an* $RBiCl_2$ *compound and potassium iodide:* Dünhaupt (34) prepared ethylbismuth diiodide by treating the corresponding dichloride with potassium iodide.

(*d*) *Reaction between a tertiary bismuth compound and an alkyl iodide:* Derivatives of the type $RBiI_2$ are produced when a tertiary bismuth compound and an alkyl iodide are heated to about 200°C.

(*e*) *Reaction between a tertiary bismuth compound and an inorganic halide:* Inorganic halides, e. g., silver nitrate or mercuric chloride, readily cleave bismuth compounds and are themselves reduced to the free metal.

When an alkylbismuth dihalide is treated with aqueous ammonia or sodium hydroxide, an oxide, RBiO, is formed. This oxide is easily oxidized further by air. With ethylbismuth diiodide, alcoholic silver nitrate forms ethylbismuth dinitrate. Marquardt (80) has reported that dimethylbismuth bromide forms a double salt with zinc bromide. This double salt when treated with alcoholic ammonia yields methylbismuth oxide; with methyl iodide it forms methylbismuth diiodide, and with water it forms dimethylbismuth hydroxide.

(b) Aryl compounds

Aromatic bismuth halides of the general formula R_2BiX or $RBiX_2$ are crystalline solids possessing high melting points. Generally speaking, compounds of these types are decomposed by moisture, alcohol, and ammonia. It was found, however, that *o*-carbomethoxyphenylbismuth dichloride, di-*o*-carbomethoxyphenylbismuth chloride, and di-*o*-carboethoxyphenylbismuth chloride were unaffected by moisture or alcohol and could be kept indefinitely without any precautions being taken (53).

Extensive studies of compounds like $(C_6H_5)_3BiX_2$ have shown that the order of decreasing stability of the dihalides is R_3BiCl_2, R_3BiBr_2, R_3BiI_2. With R_2BiX compounds the order seems to be reversed, based on ammonolytic and hydrolytic reactions, as well as conversion to R_3Bi by hydrazine (49, 52).

Compounds of the general formula R_2BiX and $RBiX_2$ have been obtained in a variety of ways:

(*a*) *Reaction between a tertiary bismuth compound and a bismuth halide:* The calculated quantity of anhydrous bismuth chloride or bismuth bromide in dry ether is added to an ether solution of the tertiary bismuth compound. Two moles of bismuth compound and one of bismuth halide yield R_2BiX compounds.

$$2R_3Bi + BiX_3 \rightarrow 3R_2BiX$$

The yields are very good, in many instances almost quantitative (51). The diarylbismuth chlorides are insoluble in most organic solvents but can be recrystallized from large volumes of dry benzene. The diarylbismuth bromides are slightly soluble in ether. If the molar ratio of bismuth halide and bismuth compound is reversed, $RBiX_2$ compounds are formed.

$$R_3Bi + 2BiX_3 \rightarrow 3RBiX_2$$

Yields, here, are also good. The dichlorides are extremely insoluble, but the dibromides, with the exception of α-naphthylbismuth dibromide, are quite soluble in ether. These are the best methods available for the preparation of aromatic R_2BiX and $RBiX_2$ compounds.

(*b*) *Reaction between a tertiary bismuth compound and an inorganic halide other than bismuth chloride:* See page 293.

(*c*) *Reaction between tetraphenyllead and a bismuth halide:* Tetraphenyllead and bismuth bromide yield diphenylbismuth bromide and diphenyllead dibromide (58).

(*d*) *Reaction between an* R_2BiCl *compound and potassium iodide:* Diphenylbismuth iodide, di-*p*-chlorophenylbismuth iodide, and di-*p*-tolylbismuth iodide have been prepared by the interaction of the corresponding chloride and potassium iodide in absolute alcohol (7, 51).

(*e*) *Reaction between a tertiary compound and a halogen, halogen halide, or halogen pseudohalide:* See page 292.

(*f*) *Reaction between an* R_2BiX *compound and a halogen:* Challenger (14) prepared phenylbismuth dibromide by treating diphenylbismuth bromide with bromine in chloroform. Diphenylbismuth bromide and iodine monochloride

TABLE 2

R_2BiX *and* $RBiX_2$ *compounds*

COMPOUND	MELTING POINT °C.	REFERENCES
Dibiphenylbismuth chloride		(120)
Di-*p*-chlorophenylbismuth chloride	160	(51)
Di-*p*-chlorophenylbismuth bromide	159	(23)
Di-*p*-chlorophenylbismuth iodide	140	(23, 51)
Di-α-naphthylbismuth chloride	168	(17, 18, 59)
Di-α-naphthylbismuth bromide (?)*		(17)
Di-α-naphthylbismuth iodide (?)		(17)
Diphenylbismuth chloride	185	(17, 18, 21, 23, 51)
Diphenylbismuth bromide	158	(14, 17, 51, 83)
Diphenylbismuth iodide	134	(7, 17, 43, 51)
Diphenylbismuth selenocyanate	Decomposes	(20)
Diphenylbismuth azide	168	(22)
Diphenylbismuth cyanide	210	(17, 20, 26)
Diphenylbismuth hydroxide		(83, 100)
Diphenylbismuth thiocyanate	123.5	(25, 26)
Di-*p*-tolylbismuth chloride	181.5	(15, 18, 51, 59)
Di-*p*-tolylbismuth selenocyanate		(20)
Di-*p*-tolylbismuth iodide	148	(51)
Di-*o*-carboethoxyphenylbismuth chloride	148	(53)
Di-*o*-carbomethoxyphenylbismuth chloride	181	(53)
Phenylbismuth chlorobromide		(16, 17)
Phenylbismuth dibromide	206	(14, 18, 51)
Phenylbismuth dichloride (?)	74	(74)
Phenylbismuth diiodide	194	(17)
Phenylbismuth dithiocyanate (?)	186	(25)
p-Chlorophenylbismuth dibromide	244	(23)
α-Naphthylbismuth dibromide	208	(13, 18, 51)
p-Tolylbismuth dichloride	207	(18)
o-Tolylbismuth dibromide	181	(51)
Phenylbismuth oxide (?)	233	(74)
o-Carbomethoxyphenylbismuth dichloride	221	(53)
o-Methoxyphenylbismuth dibromide	171	(55)
Diethylbismuth bromide		(80)
Diethylbismuth iodide (?)		(34)
Dimethylbismuth chloride	116	(80)
Dimethylbismuth bromide		(80)
Dimethylbismuth hydroxide		(80, 81)
Diisobutylbismuth bromide		(81)
Diisoamylbismuth bromide		(81)
Methylbismuth dichloride	242	(80)
Methylbismuth dibromide	214	(80, 114)
Methylbismuth diiodide		(80)
Methylbismuth oxide		(80, 81)
Methylbismuth sulfide (?)		(81)
Ethylbismuth dichloride		(34, 80)
Ethylbismuth sulfide (?)		(34)
Ethylbismuth dibromide		(34, 80)

TABLE 2—*Concluded*

COMPOUND	MELTING POINT	REFERENCES
	°C.	
Ethylbismuth oxide (?)		(34)
Ethylbismuth diiodide		(34, 80)
Ethylbismuth carbonate (?)		(34)
Isobutylbismuth dibromide	124	(81)
Isobutylbismuth diiodide		(81)
Isoamylbismuth dibromide	134	(81)
Amylbismuth dichloride		(90)
Cetylbismuth dibromide		(107)

* A question mark following any compound indicates that its composition as indicated is open to some criticism, owing either to the fact that the compound was not analyzed, or to the fact that the analyses given by the workers were not conclusive.

yielded phenylbismuth chlorobromide (16). Diphenylbismuth iodide and bromine gave phenylbismuth dibromide (16).

(*g*) *Cleavage of a tertiary bismuth compound during the preparation of the dichloride:* Challenger and Wilkinson (26) have obtained small quantities of diphenylbismuth chloride during the preparation of triphenylbismuth dichloride from triphenylbismuth and chlorine. Considerable quantities of this compound are formed if the chloroform solution of the tertiary compound is not cooled in ice prior to the introduction of the chlorine (55).

Table 2 lists all the known R_2BiX and $RBiX_2$ compounds.

6. Pentavalent bismuth compounds

The pentavalent bismuth derivatives are the most stable of the organobismuth compounds.[4] They are crystalline solids which are soluble in chloroform, dioxane, benzene, and acetone; they are insoluble in alcohol and ether.

Triarylbismuth dichlorides may be prepared by passing a stream of dry gaseous chlorine through the ice-cold solution of the tertiary compound in chloroform until an excess of the gas is present. The chloroform is then partially evaporated, and the addition of several volumes of methanol precipitates the dichloride in a high state of purity. The yields are generally better than 90 per cent. An alternative method is to pass a stream of dry chlorine over a petroleum ether solution of the tertiary compound. This method has the disadvantage that triarylbismuth compounds are not very soluble in this solvent and it is necessary to work with large volumes of solution. Its advantage, however, is that the dichloride which forms is insoluble in petroleum ether and separates out immediately. Thus, nuclear chlorination is not possible. Trimesitylbismuth forms a dichloride readily in this solvent (121), but if the preparation is carried out in benzene or chloroform nuclear or lateral substitution occurs (51). Sulfuryl chloride, sulfur monochloride, thionyl chloride (15, 18), and iodine trichloride

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[4] The only exceptions are the action of alkali and heat, which decompose R_3BiX_2 compounds more rapidly than R_3Bi compounds.

(19) also yield dichlorides when reacted with tertiary bismuth compounds, but some cleavage occurs simultaneously.

Triphenylbismuth difluoride is prepared by the interaction of triphenylbismuth dichloride and potassium fluoride.

Triarylbismuth dibromides are prepared by the dropwise addition of a solution of bromine in carbon tetrachloride to an ice-cold solution of the tertiary compound in chloroform or petroleum ether. The first slight excess of bromine is easily visible and can be used to indicate the end point of the reaction. From chloroform the dibromide is isolated by partial evaporation of the solvents and precipitation with methanol. The dibromide separates out of the petroleum ether directly. Yields are generally about 90 per cent.

The halogens in R_3BiX_2 compounds are quite labile and undergo double decomposition reactions readily.

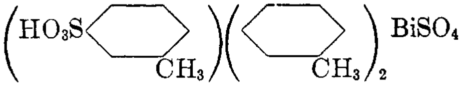
$$(C_6H_5)_3BiX_2 + \begin{cases} 2AgOCN \rightarrow (C_6H_5)_3Bi(OCN)_2 + 2AgX \\ 2C_6H_5COOAg \rightarrow (C_6H_5)_3Bi(OOCC_6H_5)_2 + 2AgX \\ 2\text{-}o\text{-}HOC_6H_4COONa \rightarrow (C_6H_5)_3Bi(OOCC_6H_4OH\text{-}o)_2 \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad + 2NaX \\ (CH_3COO)_2Pb \rightarrow (C_6H_5)_3Bi(OOCCH_3)_2 + PbX_2 \\ 2AgOH \rightarrow (C_6H_5)_3Bi(OH)_2 + 2AgX \end{cases}$$

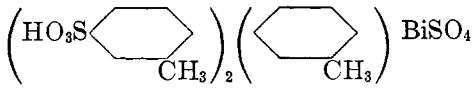
Supniewski and Adams (111) have reported that the side chains of tri-*o*- and tri-*p*-tolylbismuth dichlorides are oxidized by potassium permanganate, lead tetraacetate, or chromic acid. Yields range from 15 to 25 per cent.

$$(CH_3C_6H_4)_3BiCl_2 \rightarrow (HO_2CC_6H_4)_3BiCl_2$$

The compounds are soluble in alkali but upon reprecipitation by hydrochloric acid yield low-melting solids. Alkaline solutions of these compounds appear to be unstable and deposit a yellow solid on standing. The tri-1,3-xylylbismuth dichloride and the tri-*m*-tolylbismuth dichloride were oxidized also, but the products were not isolated. The permanganate oxidation appears difficult to repeat (55).

Supniewski (110) was the first to report the successful nuclear sulfonation of tri-*o*-tolylbismuth dichloride. He obtained two compounds, 4-sulfo-2-methylphenyldi-*o*-tolylbismuth sulfate and a corresponding di-4-sulfo-2-methylphenyl-*o*-tolylbismuth sulfate.





These compounds were soluble in alkali and were precipitated by acid. Once precipitated by acids, however, they did not redissolve readily in alkali.

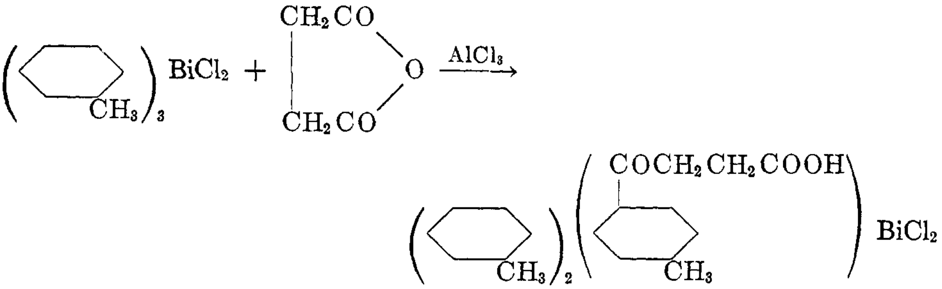
The nuclear nitration of aromatic bismuth compounds is carried out successfully only at comparatively low temperatures and with the triarylbismuth dinitrates. In order to form the corresponding trinitro derivative, triphenylbismuth dinitrate was nitrated at 0°C. for 12 hr. with fuming nitric acid, and tri-*p*-tolylbismuth dinitrate for 2 hr. at room temperature (111). Wilkinson and Challenger (118) have prepared a hexanitro derivative by nitration at −10°C. for 68 hr.

The orienting influence of bismuth in triarylbismuth compounds is not readily determined, since the compounds are decomposed easily by fuming nitric acid. A neutral nitrating agent, benzoyl nitrate, and triphenylbismuth yielded only triphenylbismuth dinitrate (118).

The nitration of triphenylbismuth dinitrate yields, on the average, 86 per cent of the meta, 12 per cent of the ortho, and 2 per cent of the para isomers (24, 115). Supniewski and Adams (111) and Supniewski (109, 110) have reported several nitro derivatives, but they have not presented any structural proof for their compounds.

Triarylbismuth dihydroxides are prepared by treating the dichloride or dibromide with moist ammonia or silver hydroxide. The reaction proceeds through two steps, so that it is possible to isolate the hydroxyhalide. The dihydroxide will oxidize ethyl alcohol to acetaldehyde, isopropyl alcohol to acetone, and *n*-propyl alcohol to propionaldehyde (22). With carbon dioxide the dihydroxide forms a carbonate, and with hydrochloric acid it forms a dichloride.

The attempted preparation of water-soluble organobismuth compounds by the reaction between maleic or succinic anhydride and a triarylbismuth dichloride has been generally unsuccessful (55).



If mild conditions were employed, the triarylbismuth dichloride was recovered unreacted. When more drastic conditions were employed, the bismuth compound was partially or wholly destroyed without any indication of the desired reaction having occurred.

Supniewski and Adams (111) attempted to cleave the ether linkage in tri-*p*-anisylbismuth dibromide with hydriodic acid and with aluminum chloride. These reactions resulted only in the complete decomposition or the recovery of unchanged bismuth compound. Similarly, an attempted lateral bromination, in the presence of ultraviolet light, of tri-*o*-tolylbismuth dibromide and tri-*p*-tolylbismuth dibromide resulted only in the cleavage of the carbon–bismuth linkage. When triphenylbismuth dichloride, ethyl chloroacetate, and copper bronze were refluxed in chloroform, only triphenylbismuth was obtained. There was no evidence that the pentavalent compound, $(C_6H_5)_3Bi(CH_2COOC_2H_5)_2$ had formed (55).

Triphenylbismuth hydroxychloride when treated with hydrobromic acid did not give triphenylbismuth chlorobromide. The products isolated were equimolecular quantities of triphenylbismuth dichloride and dibromide (17). No compounds of the type R_3BiXX' have been prepared, although phenylbismuth chlorobromide can be obtained in 77 per cent yield.

An unusual application of triarylbismuth dihalides has been their use in the color test described recently (56). The test is based on the observation made some years ago by Challenger and coworkers (14, 19, 26) that a transitory purple color developed when triphenylbismuth dibromide reacted with phenylmagnesium bromide incidental to an attempted preparation of tetraphenylbismuthonium bromide. The reaction apparently did not proceed as expected,

$$(C_6H_5)_3BiBr_2 + C_6H_5MgBr \rightarrow (C_6H_5)_4BiBr + MgBr_2$$

since the only products obtained were triphenylbismuth, diphenylbismuth bromide, phenylbismuth dibromide, and bromobenzene.

Two suggestions were offered to account for the transient purple color. One of these was the possible formation of tetraarylbismuthonium halides, and the other was the momentary formation of compounds of the type R_5Bi, analogous to the bright red triphenylmethyltetramethylammonium and benzyltetramethylammonium prepared by Schlenk and Holtz (103, 104). These are the only R_5 types reported in Group V. The purple color is probably not due to the formation of a bismuthonium halide, because R_4AsX and R_4SbX compounds are colorless. The explanation based on the formation of an R_5Bi compound is somewhat vitiated by the fact that triphenylantimony dichloride, tri-*p*-tolylantimony dichloride, tributylantimony dibromide, or triphenylarsenic dichloride and an arylmagnesium halide do not give a purple color. Although organoantimony and organobismuth compounds have some decidedly different chemical properties, it might be expected that an R_5Sb or R_5As compound, if formed, should also give a purple color.

The color test is carried out by adding 1 ml. of the RM solution to 1 ml. of an approximately 1 per cent solution of triphenylbismuth dichloride in dry benzene. With *aryl*lithium and *aryl*magnesium compounds a deep purple color forms instantaneously. To detect the presence of other aromatic RM compounds, which do not give this purple color, the test solution, obtained as described above, is heated to boiling, cooled, and hydrolyzed with 1 ml. of water. The benzene layer is then colored yellow, yellow-brown, or yellow-orange when the test is positive. These hydrolysis colors are obtained also by hydrolyzing the purple solutions obtained with RLi and RMgX compounds. No color is obtained before or after hydrolysis with *alkyl*metallic compounds like ethylmagnesium bromide, benzyllithium, or phenylethynyllithium.

A large number of triarylbismuth dihalides give the test. This applies to both symmetrical (R_3BiX_2) and unsymmetrical $(R_2R'BiX_2)$ types. Steric

TABLE 3

Pentavalent bismuth compounds

COMPOUND	MELTING POINT °C.	REFERENCES
Triarylbismuth difluorides:		
Triphenyl-	159	(26)
Triarylbismuth dichlorides:		
Tri-*o*-anisyl-	174	(108, 110)
Tri-*p*-anisyl-	133	(110)
Trichloro-*p*-anisyl-	133	(43)
Tribiphenyl-	200 d.*	(120)
Tri-*p*-bromophenyl-	155	(23)
Tri-*p*-chlorophenyl-	170	(23, 55)
Tri-*p*-cumyl-	208	(43)
Tri-2-*p*-cymyl-	164	(51) .
Trimesityl-	150	(121)
Dichlorotrimesityl-	150	(51)
Tri-α-naphthyl-	174	(18, 19, 55)
Triphenyl-	141.5	(15, 19, 26, 83, 84, 109, 121)
Tri-*o*-carboxyphenyl-	159	(110, 111)
Tri-*o*-carbomethoxyphenyl-	137	(110)
Tri-*p*-carboxyphenyl-	130	(109, 111)
Tri-*p*-carbomethoxyphenyl-	107	(110, 111)
Trinitrophenyl-	128	(118)
Tri-*p*-nitrophenyl	134	(109, 111)
Dinitrotriphenyl-	136	(43, 118)
Tetranitrotriphenyl-	146	(118)
Mononitrotriphenyl-	110	(118)
Hexanitrotriphenyl-	148	(118)
Tri-*p*-carbomethoxy-*o*-nitrophenyl-	260 d.	(110, 111)
Tri-α-thienyl-		(73)
Tri-*o*-tolyl-	162	(43, 108, 110)
Tri-*m*-tolyl-	133	(111)
Tri-*p*-tolyl-	147	(18, 83, 108, 109)
Tri-3-nitro-*o*-tolyl-	150	(110, 111)
Tri-2-nitro-*p*-tolyl-	156	(109, 111)
Tri-*m*-xylyl-	161	(83, 110)
Tri-*p*-xylyl-	167.5	(43)
Diphenyl-α-naphthyl-	142	(26)
Di-*p*-tolyl-α-naphthyl-	147	(51)
Di-*p*-chlorophenyl-α-naphthyl-	132	(51)
Di-*p*-chlorophenyl-*o*-tolyl-	133	(51)
Di-*o*-tolyl-α-naphthyl-	140	(51)
Diphenyl-*p*-tolyl-	110	(51)
Triarylbismuth dibromides:		
Tri-*o*-anisyl-	101	(108)
Tri-*p*-anisyl-	103	(43, 111)
Tribiphenyl-	Decomposes	(120)
Tri-*p*-bromophenyl-	107 d.	(23)
Tri-*p*-chlorophenyl-	105	(23)
Tri-*p*-cumyl-	150	(43)
Tri-2-*p*-cymyl-	103	(51)
Trimesityl-	Above 250	(121)
	93 d.	(51)

TABLE 3—*Concluded*

COMPOUND	MELTING POINT	REFERENCES
Triarylbismuth dibromides—*continued:*	°C.	
Tri-α-naphthyl-	124	(14, 108)
Tri-*o*-phenetyl-	128	(51)
Triphenyl-	124	(14, 83, 84)
Tri-*o*-tolyl-	127	(43, 108)
Tri-*m*-tolyl-	92	(21, 111)
Tri-*p*-tolyl-	114	(83, 108, 109)
Tri-*m*-xylyl-	117	(83)
Tri-*p*-xylyl-	130	(43)
Diphenyl-α-naphthyl-	140	(19, 26)
Di-*p*-tolyl-α-naphthyl	127	(51)
Di-*p*-chlorophenyl-α-naphthyl-	103	(51)
Di-*p*-chlorophenyl-*o*-tolyl-	110	(51)
Di-*o*-tolyl-α-naphthyl-	122	(51)
Triarylbismuth diiodides:		
Triphenyl-	Stable at −78	(118)
Triarylbismuth hydroxychlorides:		
Triphenyl-	161	(19, 22)
Tri-*p*-tolyl-	154 d.*	(108)
Trihydroxy-*o*-tolyl-	154	(111)
Triarylbismuth hydroxybromides:		
Triphenyl-	148	(19)
Tri-*p*-tolyl-	140	(108)
Tri-*m*-xylyl-	250 d.	(108)
Triarylbismuth dinitrates:		
Tribiphenyl-	162 d.	(120)
Triphenyl-	130 d.	(83, 109, 115, 118)
Tri-*p*-carbomethoxy-*x*-nitrophenyl-	160 d.	(111)
Tri-*m*-nitrophenyl-	145 d.	(24, 115)
Tri-*p*-nitrophenyl-	147 d.	(109, 111)
Dinitrotriphenyl-	150 d.	(43)
Tetranitrotriphenyl-		(118)
Mononitrotriphenyl-		(118)
Hexanitrotriphenyl-		(118)
Tri-*o*-tolyl-		(43)
Tri-*p*-tolyl-		(83, 109)
Tri-2-nitro-*p*-tolyl-	160 d.	(109, 111)
Miscellaneous pentavalent derivatives:		
Triphenylbismuth carbonate	Above 220	(19, 83)
Triphenylbismuth diazide	93	(22)
Triphenylbismuth dicyanate	129	(27)
Triphenylbismuth hydroxycyanide	135	(22)
Triphenylbismuth oxide	120 d.	(15, 22, 83)
Tri-*o*-tolylbismuth oxide	100 d.	(55)
Tri-*p*-tolylbismuth oxide	109 d.	(55)
Triphenylbismuth sulfate	Above 284	(15, 19)
4-Sulfo-2-methylphenyldi-*o*-tolylbismuth sulfate	167	(110)
Tetranitrotriphenylbismuth oxide	108 d.	(118)
Di-4-sulfo-2-methylphenyl-*o*-tolylbismuth sulfate	174	(110)

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* d. = decomposes.

factors either in the RM compound or in the R_3BiX_2 compound decrease the intensity of the purple color, or may in some instances prevent its formation. For example, triphenylbismuth dichloride or tri-*p*-tolylbismuth dichloride (or dibromide) and mesitylmagnesium bromide gave no purple color, whereas with *o*-tolylmagnesium bromide a very intense purple color was obtained. Tri-*o*-tolylbismuth dichloride gave a weak purple color with phenylmagnesium bromide and with *p*-tolylmagnesium bromide, but a negative test with α-naphthylmagnesium bromide. Trimesitylbismuth dichloride gave a negative test with these three Grignard reagents. Challenger and Allpress (18) have reported no purple color in the reaction between tri-α-naphthylbismuth dibromide and phenylmagnesium bromide.

Diarylbismuth halides (R_2BiX) and arylbismuth dihalides ($RBiX_2$) do not give the color test.

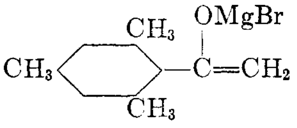
The color test is extremely sensitive. Five-hundredths of a milliliter of a 1.08 molar solution of *o*-tolylmagnesium bromide gave a positive test with 1 ml. of a 0.0078 molar solution of triphenylbismuth dichloride. This represents 0.004 g. of triphenylbismuth dichloride or 0.0016 g. of bismuth.

The color test has found application in studies on the rates and mechanisms of some metalation and halogen–metal interconversion reactions.

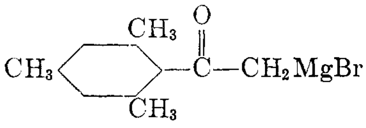
$$\text{Aryl—H} + n\text{-}C_4H_9Li \rightarrow \text{Aryl—Li} + n\text{-}C_4H_{10}$$

$$\alpha\text{-}C_{10}H_7Br + n\text{-}C_4H_9Li \rightarrow \alpha\text{-}C_{10}H_7Li + C_4H_9Br$$

A further application has to do with the bromomagnesium derivatives of sterically hindered ketones, like acetomesitylene, the enolates (A) of which behave like true organomagnesium compounds (B).



(A)



(B)

The bromomagnesium derivative of acetomesitylene, prepared from phenylmagnesium bromide and an excess of acetomesitylene, gave a positive color test with Michler's ketone (45b, 45c). Any uncertainty concerning the influence of phenylmagnesium bromide was ruled out, because the negative color test with triphenylbismuth dichloride showed that no *aryl*magnesium halide was present.

Table 3 lists all the known pentavalent organobismuth compounds.

7. Reactions in liquid ammonia

Diarylbismuth halides react smoothly with metals which dissolve in liquid ammonia to give deep red R_2BiM or $(R_2Bi)_2M$ compounds. The metals employed were lithium, sodium, potassium, calcium, and barium (52). The R_2BiM and $(R_2Bi)_2M$ compounds decompose slowly to the corresponding R_3Bi compound and inorganic bismuth, but they are sufficiently stable to react promptly with RX compounds. This provides an additional avenue of approach to the preparation of unsymmetrical organobismuth compounds.

$$R_2BiX + 2M \rightarrow R_2BiM + MX$$

$$R_2BiM + R'X \rightarrow R_2R'Bi + MX$$

The reactivity of the R_2BiM compounds is due in part to their solubility in liquid ammonia, for the insoluble sodium–bismuth alloy does not react with iodobenzene. Thus far it has not been possible to prepare these compounds directly from the R_3Bi compound and the metal.

$$R_3Bi + 2M \rightarrow R_2BiM + [RM]$$

The reaction between an arylbismuth dibromide and sodium does not lead to the expected $RBiNa_2$.

$$RBiBr_2 + 4Na \rightarrow RBiNa_2 + 2NaBr$$

Instead, a complex decomposition occurs and the only products are RH and inorganic bismuth.

Mention has been made (page 285) of the possible existence of the diarylbismuth radical in liquid ammonia.

A metal–halogen interconversion (46, 52) appears to take place in liquid ammonia between R_2BiM compounds and α-iodonaphthalene. In these reactions significant quantities of naphthalene are formed in addition to the diphenyl-α-naphthylbismuth. The naphthalene very probably does not come from the following reaction:

$$\alpha\text{-}C_{10}H_7I + 2Na \xrightarrow{NH_3} \alpha\text{-}C_{10}H_7Na \xrightarrow{NH_3} C_{10}H_8$$

since there is no free sodium in the R_2BiNa solutions. It appears, therefore, that the naphthalene may owe its formation to a new type of halogen–metal interconversion.

$$R_2BiNa + \alpha\text{-}C_{10}H_7I \rightarrow R_2BiI + \alpha\text{-}C_{10}H_7Na$$

$$\alpha\text{-}C_{10}H_7Na \xrightarrow{NH_3} C_{10}H_8 + NaNH_2$$

The liquid ammonia reactions make possible the preparation of water-soluble organobismuth compounds.

$$R_2BiM + p\text{-}BrC_6H_4OH \rightarrow R_2BiC_6H_4OH\text{-}p + MBr$$

$$R_2BiM + o\text{-}IC_6H_4COONa \rightarrow R_2BiC_6H_4COONa\text{-}o + MI$$

The phenolic compound was rather unstable, as might have been predicted, because of the lability of a hydroxyphenyl radical attached to a metal. The carboxylic derivative could not be obtained pure, owing primarily to the relative inertness of halogens ortho and para to the functional group in benzoic acid and benzoates towards R_2BiM compounds in liquid ammonia. Such halogens are much less reactive in this medium than the halogens in a simple halogenated benzene or naphthalene. There was evidence, however, of the presence of a water-soluble bismuth compound.

8. Organobismuth salts of organic acids

(a) Trivalent compounds

In studying the cleavage of tertiary bismuth compounds by thiophenol (page 297), the reaction products were isolated in order to determine their composition and possible therapeutic properties. It was of importance to determine what effect a $C_6H_5S—$ group instead of a $C_6H_5—$ group would have on the toxicity of bismuth in an organometallic molecule (55).

Early observations with triphenylbismuth and thiophenol showed that the only product obtained was the secondary cleavage product, even though an equimolecular ratio of the two compounds was used.

$$(C_6H_5)_3Bi + 2C_6H_5SH \rightarrow C_6H_5Bi(SC_6H_5)_2 + 2C_6H_6$$

This would indicate either of two possibilities: (*1*) that $(C_6H_5)_2BiSC_6H_5$ is unstable, or (*2*) that the second phenyl group was cleaved with greater ease apparently than was the first. The latter presumption is in contradiction with the general rule that a second R group is cleaved with greater difficulty than the first. Furthermore, while Catlin (12) found that primary cleavage of various RM compounds by means of hydrogen chloride is aided by chloroform as the solvent, secondary cleavage of triphenylbismuth by thiophenol occurred preferentially in the absence of a solvent or in chloroform, benzene, or toluene.

Further work with tri-*p*-chlorophenylbismuth and tri-*p*-tolylbismuth indicated that here, too, the secondary cleavage was preferential, since the products obtained were p-$ClC_6H_4Bi(SC_6H_5)_2$ and p-$CH_3C_6H_4Bi(SC_6H_5)_2$, respectively. Triphenylbismuth and methyl thiosalicylate also gave the corresponding secondary cleavage product, $C_6H_5Bi(SC_6H_4COOCH_3\text{-}o)_2$. If the experimental conditions were made quite drastic, e. g., by using a large excess of RSH compound and a high temperature, all three R groups were cleaved. The anomalous behavior of tri-α-naphthylbismuth towards thiophenol has been noted before (page 297).

Kharasch (69a) has reported a method for the preparation of water-soluble organobismuth compounds of the general formula $RBi(SeC_6H_4COOH\text{-}o)_2$ by cleavage of R_3Bi compounds by selenosalicylic acid. This again demonstrates the unusual tendency to cleave two R groups.

In the course of a related study, triphenylbismuth was cleaved with several aliphatic and aromatic carboxylic acids (55). With benzoic and cinnamic acids the products were $C_6H_5Bi(OOCC_6H_5)_2$ and $C_6H_5Bi(OOCCH{=}CHC_6H_5)_2$, respectively, indicating again preferential cleavage of two R groups. With acetic, trichloroacetic, propionic, butyric, thioglycolic, lactic, salicylic, and thiosalicylic acids the cleavage products were mixtures which could not be resolved because of the insolubility of these salts in water and organic solvents. Koton (71) has described the complex products obtained by the cleavage of triphenylbismuth by formic and acetic acids when a large excess of these acids was employed.

It is of interest to point out that every compound possessing a carbon–bismuth-sulfur linkage which has been prepared is deep yellow in color. The products obtained with the carboxylic acids were always white powders.

(b) Pentavalent compounds

Pentavalent bismuth salts of the general formula $R_3Bi(OOCR)_2$ have been prepared by various methods (15, 19, 27, 111, 121).

TABLE 4

Organobismuth salts of organic acids

COMPOUND	MELTING POINT	REFERENCES
	°C.	
Trivalent compounds:		
$C_6H_5Bi(SC_6H_5)_2$	170 d.*	(55)
p-$ClC_6H_4Bi(SC_6H_5)_2$	170 d.	(55)
p-$CH_3C_6H_4Bi(SC_6H_5)_2$	155 d.	(55)
$C_6H_5Bi(SC_6H_4COOCH_3$-$o)_2$	102	(55)
Pentavalent compounds:		
Triphenylbismuth diacetate	162	(15, 19, 111, 121)
Triphenylbismuth diacetate·$0.5CH_3COOH$	137	(19)
Tri-*m*-tolylbismuth diacetate	149	(111)
Tri-*p*-tolylbismuth diacetate	162	(111)
Triphenylbismuth dibenzoate	173	(27)
Tri-*p*-tolylbismuth dibenzoate	169 d.	(55)
Tri-*o*-tolylbismuth disalicylate·C_6H_6	165 d.	(55)
Diphenylbiphenylbismuth dibenzoate	147	(52)
Diphenyl-β-naphthylbismuth dibenzoate	140	(52)
Triphenylbismuth dicinnamate	178	(55)
Triphenylbismuth disalicylate	185 d.	(55)
Triphenylbismuth di-*o*-carboxybenzoate	169 d.	(55)
Triphenylbismuth di-*p*-hydroxybenzoate	Above 250	(55)
Triphenylbismuth di-*p*-aminobenzoate	148 d.	(55)
Triphenylbismuth di-*p*-aminobenzoate·$2CH_3COCH_3$	148 d.	(55)
Triphenylbismuth dianthranilate·C_6H_6	102 d.	(55)
Triphenylbismuth dichloroacetate	156	(55)
Tri-*p*-chlorophenylbismuth disalicylate	187 d.	(55)
Triphenylbismuth dilactate		(19)
Triphenylbismuth dicamphorsulfonate		(19)
Triphenylbismuth ditartrate		(15)
Triphenylbismuth dipicrate		(15)

* d. = decomposes.

$$(1)\quad R_3Bi(OH)_2 + 2RCOOH \rightarrow R_3Bi(OOCR)_2 + 2H_2O$$

$$(2)\quad R_3Bi(OH)Cl + 2RCOOH \rightarrow R_3Bi(OOCR)_2 + H_2O + HCl$$

$$(3)\quad R_3BiCO_3 + 2RCOOH \rightarrow R_3Bi(OOCR)_2 + H_2O + CO_2$$

$$(4)\quad R_3BiX_2 + 2RCOOM \rightarrow R_3Bi(OOCR)_2 + 2MX$$

$$(5)\quad R_3Bi + (C_6H_5CO)_2O_2 \rightarrow R_3Bi(OOCC_6H_5)_2 + O_2$$

Reaction 3 has been employed to prepare a large number of pentavalent derivatives in which the benzoyl radical possessed potential water-solubilizing groups.

In an attempt to prepare amine hydrochlorides of triphenylbismuth dianthranilate or triphenylbismuth di-*p*-aminobenzoate the only products obtained were triphenylbismuth dichloride and the hydrochloride of the corresponding acid. With the disalicylate, di-*p*-hydroxybenzoate, and di-*o*-carboxybenzoate there occurred complete dissociation into triphenylbismuth dihydroxide and the potassium salt of the acid when the compounds were treated with dilute potassium hydroxide solution.

Proof of the structure of these pentavalent compounds was achieved by cleavage with hydrochloric acid and the identification of the R_3BiCl_2 and organic acid formed.

A rather interesting observation made during the course of this work was that when these derivatives were crystallized from acetone or benzene there was a general tendency to add molecules of solvent of crystallization. In several instances, as with tri-*o*-tolylbismuth disalicylate and triphenylbismuth dianthranilate, any attempts to remove the solvent resulted in the decomposition of the compound.

TABLE 5

Inorganic halide double salts of organobismuth compounds

COMPOUND	MELTING POINT	REFERENCES
	°C.	
(p-$CH_3C_6H_4)_3Bi \cdot HgCl_2$	234	(108)
(o-$CH_3C_6H_4)_3Bi \cdot HgCl_2$	148	(108)
(m-$(CH_3)_2C_6H_3)_3Bi \cdot HgCl_2$	160	(108)
(α-$C_{10}H_7)_3Bi \cdot HgCl_2$	193	(108)
$(CH_3)_2BiBr \cdot ZnBr_2$		(80)

Table 4 lists all the known organobismuth salts of organic acids, both tertiary and pentavalent types. Table 5 lists the comparatively few inorganic halide double salts of organobismuth compounds.

D. ANALYTICAL PROCEDURES

1. *Qualitative*

A very convenient test for bismuth in an organobismuth compound is to burn a small portion of the compound on a clean spatula. The yellow-brown residue of bismuth oxide is easily recognized. Another method involves cleaving 0.05 g. of the compound with 5 ml. of concentrated nitric acid and heating the solution to dryness. After allowing the residue to cool, it is taken up in 5 ml. of concentrated hydrochloric acid, concentrated to 1 ml., and then treated with a freshly prepared solution of sodium stannite. A heavy black precipitate of metallic bismuth forms, if bismuth is present in the compound.

The color test described on page 306 also possesses possible utilization as a qualitative test for the presence of some organobismuth compounds.

2. Quantitative

Michaelis and Polis (84) have described the determination of bismuth in organobismuth compounds as bismuth trioxide and Challenger and Goddard (19) as bismuth trisulfide. The analysis as the phosphate appears to be superior to both these methods (53).

III. THE PHYSICAL PROPERTIES OF ORGANOBISMUTH COMPOUNDS

A. MOLECULAR STRUCTURE

Bergmann and Schütz (4) have found the dipole moment of triphenylbismuth to be zero. From this they have concluded that its structure is that of a plane triangle with the bismuth atom situated at the center of gravity. The triphenylphosphines, -amines, -arsines, and -stibines appear to be triangular pyramids. Pai (91) and Rosenbaum, Rubin, and Sandberg (99a), from studies of the Raman spectra of trimethylbismuth, have concluded that this compound possesses a pyramidal structure, the three methyl groups forming the triangular base and the bismuth atom the apex.

B. CRYSTAL STRUCTURE

The crystal structures of triphenylbismuth (2), triphenylbismuth difluoride (26), and diphenylbismuth thiocyanate (26) have been studied. Michaelis and Marquardt (83) have reported two crystal forms of triphenylbismuth, one melting at 75°C. and the other at 78°C. This has not been substantiated by other workers in this field. Drew and Landquist (33) and Pascal (95) have studied the triphenyl compounds of the elements of Group V for possible isomorphism. They have observed compatibility only with triphenylphosphorus and triphenylarsenic. No close relationship such as can be found in the organometallic compounds of the elements of Group IV exists among the organometallic compounds containing Group V elements.

Greenwood (60, 61) and Bryant (9) have studied the rotatory polarization of light by crystals of triphenylbismuth dichloride.

From x-ray studies, Greenwood (61) has data which would indicate that triphenylbismuth dichloride has eight molecules in a unit cell.

C. PHENOMENA WITH LIGHT

Schaefer and Hein (101) have studied the absorption of light by trimethylbismuth, triphenylbismuth, and triphenylbismuth dichloride, and have observed that the first two compounds show normal curves and obey Beer's law. The dichloride absorbs light much more strongly than the tertiary compounds, owing to the two chlorine atoms and the higher valence of bismuth.

IV. THE BIOLOGICAL APPLICATIONS OF ORGANOBISMUTH COMPOUNDS

A. ORGANOBISMUTH THERAPY

The therapeutic properties of bismuth were recognized as early as 1660. By 1750 it had been used in the treatment of gonorrhea and by 1779 in syphilis therapy. It was not until 1921, however, that research in the field of bismuth therapy became intense. With the pioneer work of Levaditi and his coworkers there began what may be called "The French School of Bismuth Therapy." In the six years immediately following Levaditi's first publication, nineteen hundred and sixteen articles on bismuth therapy were published, and by 1935, a conservative estimate would have placed this number close to five thousand. By 1932 about two hundred and fifty organic and inorganic bismuth compounds had been prepared and investigated for possible therapeutic utilization.

One result of this intensive research has been the large number of contradictory reports to be found with regards to the effectiveness of bismuth therapy. The actual value of organic bismuth compounds in spirochetosis has long been the subject of debate, although their value in the intermittent treatment of syphilis by arsenicals is acknowledged. Bismuth is much more toxic than arsenic and acts more slowly. Its compounds can be injected intramuscularly only, since intravenously their therapeutic index is about 1:3. This is true even for those compounds accepted as new and non-official remedies by the Council on Pharmacy and Chemistry of the American Medical Association. According to Dr. R. A. Vonderlehr, Assistant Surgeon General, Division of Venereal Diseases of the United States Public Health Service (116), " . . . It is the general consensus of opinion of experts in this country and particularly of the Coöperative Clinical Group that when all factors are taken into consideration, bismuth subsalicylate suspended in oil is probably the most practical bismuth preparation (for the treatment of syphilis)."

When injected intramuscularly, bismuth compounds form "depots" which slowly release bismuth into the blood. In some instances absorption is so slow that there is still evidence of bismuth at the point of injection after 400 days.

Kolle (70) has found that such a depot in the ear of a rabbit will prevent the appearance of scrotal lesions following intratesticular injections of the syphilis virus. When the ear was amputated after 3 months, however, scrotal lesions developed after an interval of several weeks. This can mean perhaps that the virulent organisms were not destroyed by the bismuth but that their multiplication was inhibited. It is to be noted, however, that *complete* cures of syphilis by the exclusive use of organic bismuth compounds have been reported also.

Of the more than five thousand papers published in the field of bismuth therapy between 1921 and 1935, only a very few have been concerned with the use of organobismuth compounds. Giemsa (39, 40, 41, 42) reported the remarkable healing properties of triphenylbismuth in experimental canine syphilis, relapsing fever, and nagana. He proposed its use in the later stages of syphilis because of its lipoid solubility, which enables it to penetrate undecomposed into the central nervous system. Albrecht and Evers (1) and Schlossberger (102) were unable to confirm these favorable reports. Rothermundt and Wichmann (99) have reported that triphenylbismuth had no therapeutic activity in the treatment of mice infected with *S. crocidurae* or *S. hispanica.* Sollman and Seifter (107) have ingeniously tested some alkylbismuth compounds for their antisyphilitic activity. They found that trimethylbismuth could be handled safely and was sufficiently soluble in water to produce marked effects in experimental animals when treatment was by vein, inhalation, or skin. It had a definite healing effect in rabbit syphilis, but it demonstrated no extraordinary therapeutic activity. The higher alkyls, trilaurylbismuth, tricetylbismuth. and cetylbismuth dibromide, were poorly absorbed and inactive.

Walker (117) has determined the least concentration of four organobismuth compounds which would destroy *Colpidum colpoda* in 3 min. His results are as follows:

Triphenylbismuth	mole/11,000
Diphenylbismuth bromide	mole/270,000
Tri-*p*-tolylbismuth	mole/2000
Triphenylbismuth dibromide	mole/7100

From this, one may observe that the secondary derivative, diphenylbismuth bromide, possesses the highest effectiveness. This holds true generally, inasmuch as $(C_6H_5)_2SbX$ and $(C_6H_5)_2AsX$ (where X is any halogen) are more effective than the primary or tertiary derivatives of the same elements. Lecoq (74) has found $C_6H_5AsCl_2$ to be more toxic than either $C_6H_5SbCl_2$ or $C_6H_5BiCl_2$. Pentavalent derivatives in this family are weakly toxic, and it has been suggested that whatever toxic effects they possess is due to their first being reduced to the trivalent form.

It is apparent that little work has been done in bismuth therapy with organobismuth compounds. The principal objection seems to be their high toxicity. If organobismuth compounds of low toxicity could be synthesized, a more accurate estimation of their effectiveness would be possible.

B. ABSORPTION OF BISMUTH BY THE ORGANISM

If massage of the muscle follows an intramuscular injection of a bismuth compound, bismuth appears in the blood 2 hr. after the injection. Without massage, the appearance is delayed for 24 hr. The concentration of bismuth appears to be highest in the kidneys, and less in the liver, spleen, and lungs. The blood and bile show varying content. Some of the bismuth may be stored in the liver and other organs, but the greater part is eliminated by the kidneys, liver, and intestinal mucosa. It appears in the urine from 18 to 24 hr. after the injection.

C. PHYSIOLOGICAL ACTION OF BISMUTH

Following an intramuscular injection of a bismuth compound there occurs a local necrosis of the muscle fibre which is slowly absorbed and replaced by scar tissue. Sometimes sterile abscesses are formed. The gluteal muscle mass is large enough to tolerate from fifty to a hundred or more injections without serious difficulty.

In the bismuth poisoning of animals by a single large dose, the chief pathological changes occur in the kidney and liver, other organs being affected little or not at all. In the kidneys there are marked tubular nephritis and degenerative changes similar to those produced by mercury poisoning. Intravenous injections produce these alterations more frequently than do intramuscular administrations. Of the local reactions, pain is the most frequent and this is due, in part, to the vehicle. A compound in olive oil may be extremely painful; in peanut oil it is bland and non-irritating.

The administration of bismuth compounds in therapeutic doses at weekly intervals is, however, remarkably free from toxic effects. The one exception appears in the bluish-gray pigment line which forms on the gum margins of the mouth after a half-dozen injections. In rare instances (thirty-five in the period from 1922 to 1935) death may result from bismuth therapy, but these cases have been reported as due to accidental intravenous injection.

V. Summary

An attempt has been made in the preceding review to survey the literature on organobismuth compounds up to April, 1942. Those properties which are characteristic of organobismuth compounds have been stressed, and some attention has been directed towards correlating the organometallic compounds of arsenic, antimony, and bismuth, in order to show gradations of stability, reactivity, and compound formation.

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