197. *Organo-lead Compounds. Part I. Trialkyl-lead Salts possessing Sternutatory Properties.*

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This is the first of a series of papers giving an account of the preparation of organo-lead compounds having powerful sternutatory action. The present paper deals largely with the preparation of salts of the triethyl-, tri-*n*-propyl-, and tri-*n*-butyl-lead series. A definite peak of activity is reached in the tri-*n*-propyl series.

The work to be described in this series of papers was undertaken in 1939 for the Ministry of Supply, to whom detailed reports were submitted during 1940 and 1941. The original intention was to prepare volatile organic lead compounds of the type PbR_4 (*e.g.*, $R = CH_2{\cdot}CH_2Cl$) which might be toxic by inhalation. At that time, the supplies of arsenic in this country were low, whereas lead was readily available. Tetraethyl-lead was a convenient starting point for such compounds and we accordingly set out to prepare it in quantity from sodium–lead alloy and an ethyl halide. We found, however, that the method described in the patent literature gave poor yields on a laboratory scale. By carrying out a number of experiments, we finally effected the correct modification, which consisted in adding water extremely slowly during the reaction.

The next step was to prepare triethyl-lead chloride in quantity. While working with this compound, one of us (B. C. S.) developed the symptoms of influenza, which, however, wore off at night and returned during the day. The compound was accordingly tested for sternutatory properties and found to give a difficultly respirable atmosphere at a concentration of 1 part in a million. This then gave a great impetus to the preparation of other trialkyl-lead salts. The original intention of preparing substituted plumbanes of the type mentioned above was then dropped and the preparation and examination of trialkyl-lead salts were carried out. Many of these were new compounds and were tested as potential sternutators at Cambridge.

Passing reference had been made by Krause and Pohland (*Ber.*, 1922, **55**, 1282) to the irritant action of trialkyl-lead fluorides, and Gilman and Robinson (*Rec. Trav. chim.*, 1930, **49**, 766) had noted that sneezing was caused by dust containing traces of triethyl-lead salts. No systematic attempt, however, had been made to correlate potency with the nature of the constituent groupings. It was obviously desirable that this should be undertaken in the hope that it would serve as a guide to the type of compound likely to possess maximum sternutatory action. The work now described was carried out as part of a programme drawn up with this end in view, and attention was directed almost wholly to the preparation of new trialkyl-lead compounds. Emphasis was placed upon the production of substances which had the following characteristics : (i) ease of preparation, (ii) reasonable stability, (iii) strong sternutatory action. Each substance was submitted to physiological examination, the toxicity data being compiled chiefly from the results of human inhalation at known concentrations. The figures so obtained gave a clear indication of the directions in which toxicity increased, and compounds with an action more pronounced than any previously reported in this class were prepared. The most effective compounds did not fall far short of diphenylchloroarsine (D.A.) in potency.

Many of the compounds were easily obtained in a pure condition, were highly crystalline, and have not deteriorated on being stored for a number of years.

Physiological Examination.—Examination of the physiological action upon human beings of these compounds was carried out in a glass-walled chamber of 10 c. m. capacity. The substance was dissolved in a suitable solvent and dispersed in the chamber by means of a spray. Suitably placed fans ensured, as far as possible, an even distribution of the material in the atmosphere inside the chamber. The human observers, four in number, entered the chamber by an air-lock as soon as spraying was complete. The times which then elapsed before irritation occurred in the nose, throat, chest, and gums were noted. Unless the substance proved to be intolerable, the observers stayed in the chamber for 10 minutes. During this period, it was observed that, in spite of all precautions, the activities of some of the compounds decreased because of condensation on the walls of the chamber; hence, it was not always possible accurately to assess the maximum virulence of a compound, especially where this rate of condensation was particularly rapid. Nevertheless, a consistency was almost always obtained among the observations of the four subjects in any one test. From the data thus compiled, a toxicity rating for a given concentration was allotted to each compound on the following basis : Grade 0, not detectable or only slightly irritant; grade 1, unpleasant but tolerable indefinitely; grade 2, very unpleasant but just tolerable indefinitely; grade 3, distressing and not tolerable indefinitely.

The first concentration to be tried was 1 molecule of substance in 10,000,000 molecules of air; *i.e.*, about 20 mg. of organo-lead compound were actually dispersed in the chamber. The required amount was dissolved in about 15 c.c. of solvent (usually alcohol). For certain of the more potent substances, tests were also carried out at concentrations of 1 : 25,000,000.

A list of compounds, whose preparation is described later, is given in the accompanying table, together with their toxicity ratings. These results, taken in conjunction with others

Substance.	$1 : 10^7$.	$1 : 2{\cdot}5 \times 10^7$.	Substance.	$1 : 10^7$.	$1 : 2{\cdot}5 \times 10^7$.
Triethyl-lead salts.					
Chloride	1	0^+	*Anthranilate*	2	—
Acetate	2	1			
Tri-*n*-propyl-lead salts.					
Acetate	3	2^+	*Crotonate*	2^+	—
Acrylate	2^+	1	*Cyanide*	2^+	—
Anthranilate	3	2^+	*Iodoacetate*	2	—
Bromide	3	1^+	*Propionate*	2	—
Bromoacetate	2	—	*Toluene-*o*-sulphonate*	3	2
n-*Butyrate*	3	2^+	*Toluene-*p*-sulphonate*	3	1^+
Chloride	2^+	—	*Trichloroacetate*	2	—
Chloroacetate	3	2^+	iso*Valerate*	3	1^+
β-Chloropropionate	3	—	*Xanthate*	2	—
Tri-*n*-butyl-lead salts.					
Acetate	3	—	*Iodoacetate*	1^+	—
Bromoacetate	1^+	—	*Naphthalene-β-sulphonate*	2^+	—
Chloride	3	—	*Propionate*	2^+	—
Chloroacetate	1^+	—	*Toluene-*p*-sulphonate*	2	—
β-Chloropropionate	2^+	—	*Trichloroacetate*	2	—
Crotonate	2^+	—			

Diethyl-lead dichloride and *bis-*p*-nitrophenoxide*, *di-*n*-propyl-lead dichloride* and *diacetate*, and di-*n*-butyl-lead dichloride at $1 : 10^7$ were of grade 0.

obtained for trimethyl-, triethyl-, and tri*iso*butyl-lead compounds (to be described later), show that a definite peak of activity is reached in the tri-*n*-propyl-lead series. The difficulty of obtaining pure compounds prevented extensive work on the diethyl-*n*-butyl-lead series, and tetra*iso*propyl-lead was not sufficiently stable to be of service.

Methods of preparing Trialkyl-lead Salts.—The methods used were all ultimately dependent upon the tetra-alkyl-lead. A very useful method (1), due to Browne and Reid (*J. Amer. Chem. Soc.*, 1927, **49**, 830), consists in warming together a tetra-alkyl-lead and an acid in presence of silica gel. Owing to its directness, this method would no doubt be favoured on a manufacturing scale. We found, however, that it suffers from two main drawbacks : (*a*) it does not proceed easily (especially in the case of the higher alkyls) with weakly acidic substances ; (*b*) with too vigorous conditions there is a danger of the formation of the dialkyl-lead salt. This falls into line with Goddard and Goddard's observations (*J.*, 1922, **121**, 973) in the amyl series.

The second general method (2) of preparation consists of the double decomposition of the trialkyl-lead chloride with the appropriate sodium or potassium salt. The removal of any unchanged trialkyl-lead chloride often presents a difficulty here. A useful variation (3) is to use the silver salt, but this is unsuitable for large-scale work.

The method of widest application (4) depends upon the conversion of the tetra-alkyl- into the trialkyl-lead chloride and thence into the hydroxide (Pfeiffer, Truskier, and Disselkamp, *Ber.*, 1916, **49**, 2445 ; Krause and Pohland, *Ber.*, 1922, **55**, 1282), which on treatment with the appropriate acid gives the required salt. As an extension of this method we have found that, in certain instances, the trialkyl-lead hydroxide will react with the appropriate sodium or potassium salt (5). These methods may be summarised thus :

(1) $PbR_4 + HA \longrightarrow PbR_3A + RH$

(2) $PbR_3Cl + NaA \longrightarrow PbR_3A + NaCl$

(3) $PbR_3Cl + AgA \longrightarrow PbR_3A + AgCl$

(4) $PbR_3OH + HA \longrightarrow PbR_3A + H_2O$

(5) $PbR_3OH + NaA \longrightarrow PbR_3A + NaOH$

Tri-n-*propyl-lead Salts.*—With the discovery that tri-*n*-propyl-lead salts were more powerful sternutators than the corresponding triethyl-lead salts, it became necessary to prepare tetra-*n*-propyl-lead in quantity on a laboratory scale. For this purpose the method generally adopted was the action of sodium–lead alloy on *n*-propyl iodide.

The production of tri-*n*-propyl-lead chloride by the action of hydrogen chloride on tetra-*n*-propyl-lead brought to light several important points. In the first place, this chloride, unlike triethyl-lead chloride, is very soluble in organic solvents (*e.g.*, ether). Consequently, the progress of the reaction could not be judged by the quantity of white crystals formed, and it was necessary to find by trial and error the approximate amount of hydrogen chloride required. After the gas had been passed for some time, a faint white precipitate was formed. This was identified as di-*n*-propyl-lead dichloride, and from this observation a new method for preparing the latter compound was devised (see p. 925). This small amount of precipitate was filtered off, and the ethereal filtrate evaporated, leaving impure tri-*n*-propyl-lead chloride. It was thus found that over-treatment with the gas produced di-*n*-propyl-lead dichloride, and the precipitation of this compound continued even after the actual passage of hydrogen chloride was discontinued. This may have been due to two causes : (i) excess of hydrogen chloride may have reacted slowly with the tri-*n*-propyl-lead chloride first formed : $PbPr_3Cl + HCl = PbPr_2Cl_2 + PrH$; (ii) as shown by Calingaert *et al.* (*J. Amer. Chem. Soc.*, 1939, **61**, 2748, 3300), triethyl-lead halides can undergo spontaneous and reversible redistribution reactions. Austin (*ibid.*, 1932, **54**, 3287) had shown that this redistribution could be considerably facilitated by heating in benzene or toluene : $2PbEt_3Cl = PbEt_4 + PbEt_2Cl_2$. Similar behaviour will presumably be displayed by the *n*-propyl derivatives, and the direction in which the reaction proceeds will, after a time, be governed by the insolubility of the dichloride. Under the conditions considered above, it is probable that the first reaction is the major one, especially in view of its rapidity and of the good yields of the dichloride obtainable. Thus by passing hydrogen chloride until precipitation had begun, and then allowing the ethereal solution to stand, an almost pure specimen of di-*n*-propyl-lead dichloride was obtained. When preparing tri-*n*-propyl-lead chloride, however, it was found that the use of light petroleum (b. p. 40—60°) (in which the hydrogen chloride is almost insoluble) in place of ether reduced the yield of the dichloride to a minimum. In subsequent preparations, one volume of tetra-*n*-propyl-lead was dissolved in about 10 volumes of this petroleum and a stream of hydrogen chloride was passed through the ice-cooled solution for 2—3 hours. The solvent was rapidly distilled off, and pure tri-*n*-propyl-lead chloride obtained after recrystallisation from aqueous alcohol.

In preparing the tri-*n*-propyl-lead salts the reaction between the hydroxide and the acid in solution was the most convenient. The tri-*n*-propyl-lead hydroxide was not actually isolated in these preparations, but was prepared in aqueous solution as required. Krause and Pohland (*loc. cit.*) claim to have isolated the compound by treating an ethereal solution of tri-*n*-propyl-lead bromide with aqueous 30% potassium hydroxide. Unlike the ethyl analogue, the tri-*n*-propyl-lead hydroxide was not precipitated, so the ethereal layer had to be separated and the ether removed under reduced pressure, leaving an oily liquid which slowly deposited colourless crystals on standing over quick-lime. The yield was small and the product did not have the m. p. reported by Krause and Pohland. Experiments were then tried, using moist silver oxide as hydrolytic agent. The moist oxide (of known oxide content) was shaken with an aqueous suspension of tri-*n*-propyl-lead chloride in equivalent amount, the precipitate filtered off, and the aqueous solution of the tri-*n*-propyl-lead hydroxide used in further preparative work. The actual amount of hydroxide used was not accurately known, but was estimated on the assumption of a theoretical yield from the chloride. In any case, the amount used need not be accurately established because the procedure was to add sufficient acid to the solution to give a slightly acid reaction to litmus. In this way, the following salts were readily prepared: acetate, acrylate, anthranilate, bromoacetate, bromide, *n*-butyrate, chloroacetate, β-chloropropionate, crotonate, iodoacetate, *naphthalene*-2-*sulphonate*, propionate, toluene-*o*- and -*p*-sulphonates, trichloroacetate, and *iso*valerate. Some derivatives, on first being thrown out of solution, did not crystallise readily, but addition of more acid beyond the neutralisation point often facilitated crystallisation. With certain acids, such as acrylic and naphthalene-2-sulphonic, it was necessary to employ alcoholic instead of aqueous solutions. The product was then isolated by evaporation.

The action of an alkali metal on tri-*n*-propyl-lead chloride was used in a few instances where the free acid was not readily available. In this way, the xanthate was prepared and is of interest in that it is an organo-lead compound containing a Pb–S link. The reaction did not proceed to any appreciable extent with sodium or potassium cyanide. In preparing the cyanide, the action of free hydrogen cyanide on tri-*n*-propyl hydroxide was inconvenient, and it was in this connexion that the new method (5) was devised. An aqueous solution of potassium cyanide was added to an aqueous solution of tri-*n*-propyl-lead hydroxide, and tri-*n*-propyl-lead cyanide was readily precipitated.

Results obtained with Dialkyl-lead Salts.—These salts behaved differently from trialkyl compounds and, in particular, their sternutatory powers were negligible (see table).

n-*Butyl Derivatives.*—To determine whether increased physiological activity continued to be displayed as the series was ascended, an investigation of tri-*n*-butyl-lead compounds was undertaken. Tetra-*n*-butyl-lead, first prepared by Danser (*Monatsh.*, 1925, **46**, 241), served as the starting material for these compounds. The pure liquid was obtained by the method recommended by Jones, Evans, Gulwell, and Griffiths (*J.*, 1935, 41) from *n*-butyl magnesium bromide and lead chloride. The product was not distilled before use. It was converted into tri-*n*-butyl-lead chloride by passing hydrogen chloride through a solution of tetra-*n*-butyl-lead in ice-cold light petroleum (b. p. 40—60°) until a precipitate began to form. Pfeiffer, Truskier, and Disselkamp (*loc. cit.*) gave m. p. 109—110° but, in the present work, after three recrystallisations from aqueous alcohol, the m. p. remained at 106·5—108·5°. In general, the material was not recrystallised before use.

Without exception, derivatives were prepared by the interaction of an acid and tri-*n*-butyl-lead hydroxide. It was found that tetra-*n*-butyl-lead reacted much less readily with acids than did tetraethyl-lead.

*Results with Tri-*n*-butyl-lead Salts.*—The preparation of tri-*n*-butyl-lead hydroxide was attempted in the same manner as for the tri-*n*-propyl compound, but the former substance was not water-soluble, for the aqueous filtrate gave neither precipitates with acids nor an alkaline reaction towards litmus. It was therefore necessary to shake an alcoholic solution of tri-*n*-butyl-lead chloride with moist silver oxide in order to secure a solution of the hydroxide. On adding acids to this solution, the tri-*n*-butyl-lead salts were not, of course, precipitated. Two alternative procedures were available: (i) to evaporate the solution to dryness, leaving the required salt; (ii) to precipitate the salt by addition of excess of water. Except in the case of acetic acid, the second procedure was adopted and found to be satisfactory. In this way, the new tri-*n*-butyl-lead salts recorded in the table were readily obtained.

As several hundred organo-lead compounds were prepared in this series of investigations it was necessary to have a rapid and reliable method of determining lead. Details of the volumetric method employed are given on p. 925.

EXPERIMENTAL.

Sodium–Lead Alloy (22% Na).—Metallic lead (390 g.) was melted in an iron crucible by means of a gas-injector furnace. When the lead was completely molten, dry sodium (110 g., cut into pieces of about 5 g. each) was added, one piece at a time. The lid of the crucible was replaced immediately after each addition so as to keep the violent reaction under control. After all the sodium had been added, the mixture was stirred with an iron rod, the scum removed from the surface, and the molten alloy poured into cylindrical moulds of suitable size.

Tetraethyl-lead.—By following the directions given in *Chemical Reviews*, 1925, **2**, 47 (based on B.P. 216,083), we obtained only traces of tetraethyl-lead. We finally adopted the following conditions. The alloy (400 g.), in small quantities at a time, was ground in a mortar (heat was produced), and transferred as quickly as possible to a 1-l. 3-necked " Quickfit " flask fitted with condenser, dropping-funnel, and stirrer. Ethyl bromide (300 c.c.) was poured on the alloy, pyridine (32 c.c.) was added, and the mixture stirred and heated on a boiling water-bath, a stream of nitrogen being passed through the flask meanwhile. At hourly intervals 2 or 3 drops of water were added. At the end of 8 hours, water was added until no further action took place, and the mass was steam-distilled. The lower layer of the distillate was separated, washed with dilute sodium hydroxide solution, dilute sulphuric acid, and then with water, dried ($CaCl_2$), and distilled; b. p. 83°/13 mm., yield *ca.* 95 g.

Triethyl-lead Chloride.—This was readily obtained from tetraethyl-lead and hydrogen chloride by the method of Gilman and Robinson (*J. Amer. Chem. Soc.*, 1930, **52**, 1975). An improved method of preparation will be given in Part II of this series.

Triethyl-lead Hydroxide.—Triethyl-lead chloride (6·6 g., 0·02 mol.) was added to ether (30 c.c.) in a separating-funnel. Aqueous 30% sodium hydroxide (20 c.c.) was poured in and well shaken. The base was precipitated and rose into the ethereal layer, from which it was filtered off and washed well with ether. During drying, it was kept away from the air as much as possible to minimise reaction with carbon dioxide (cf. Krause and Pohland, *loc. cit.*).

Triethyl-lead Acetate.—Tetraethyl-lead (40 c.c.) and glacial acetic acid (12 c.c.) were heated together under reflux with several pieces of silica gel for 1 hour. The solid which separated was filtered off and washed with a small quantity of cold ether. It had m. p. 160° and was pure (Found : Pb, 58·8. Calc. for $C_8H_{18}O_2Pb$: Pb, 58·7%). It could be recrystallised from benzene, but this was usually unnecessary.

The above reaction is based on that of Browne and Reid (*J. Amer. Chem. Soc.*, 1927, **49**, 836) but we found it necessary to use more nearly molecular proportions (as above) in order to obtain a clean product. Our ratio (vol./vol.) of acetic acid to tetraethyl-lead was 3 : 10, whereas Browne and Reid used 3 : 9 (theoretical, 3 : 10·3).

Triethyl-lead Anthranilate.—To a dilute aqueous solution of triethyl-lead hydroxide was added a cool aqueous solution of anthranilic acid until crystals began to form. An alcoholic solution of anthranilic acid was then added, in small quantities at a time and with much stirring, until the mixture was slightly acid to litmus. The crystals thus obtained were filtered off, washed with water, and dried. The *anthranilate* was recrystallised from light petroleum (b. p. 60—80°) containing 10% of benzene; m. p. 96° (Found : Pb, 48·0. $C_{13}H_{21}O_2NPb$ requires Pb, 48·1%).

*Tetra-*n*-propyl-lead.*—Lead–sodium alloy containing 78% of lead (265 g., *i.e.*, 1 mol. of lead) was ground to powder and placed in a 1-l. round-bottomed flask fitted with a condenser, stirring rod, and dropping-funnel. *n*-Propyl iodide (453 g., 2·6 mol.) and pyridine (22 c.c.) were poured down the condenser and the whole was stirred on a water-bath, the reactants being kept in an atmosphere of nitrogen. The progress of the reaction was controlled by the addition of 2 c.c. of water every 15 minutes during 5—6 hours. Then more water (about 100 c.c.) was added to decompose the reaction complex. Steam-distillation gave some of the tetrapropyl-lead, which sank to the bottom of the aqueous distillate (about 1500 c.c.) and was separated off, washed with dilute sodium hydroxide solution then dilute sulphuric acid, dried ($CaCl_2$), and filtered. Extraction with ether of the liquid in the reaction flask, followed by washing, drying, and distillation under reduced pressure, gave more of the product of b. p. 80°/0·4 mm.; total yield 113 g. (45% calc. on the *n*-propyl iodide used). The relative amounts obtained by steam-distillation and by ether-extraction varied considerably from one experiment to another. The yield was not appreciably affected by leaving the mixture overnight just before the final addition of water. This compound was first obtained by Grüttner and Krause (*Ber.*, 1916, **49**, 1421) who used the Grignard method.

*Tri-*n*-propyl-lead Chloride.*—Tetra-*n*-propyl-lead (7·6 g., 0·02 mol.) was dissolved in light petroleum (b. p. 40—60°) (50 c.c.) and a stream of dry hydrogen chloride was passed through until a small quantity of a pinkish-white precipitate appeared. This was filtered off, and the petroleum filtrate quickly evaporated to dryness on the water-bath, and finally under reduced pressure. The product so obtained (6·6 g., 89%) was sufficiently pure for preparation of the hydroxide; it recrystallised from aqueous alcohol in colourless crystals, m. p. 133—134° (Found : Cl, 9·60. Calc. for $C_9H_{21}ClPb$: Cl, 9·54%).

The use of light petroleum (b. p. 40—60°) instead of ether as solvent gives a higher yield with less contamination with di-*n*-propyl-lead dichloride (cf. Pfeiffer *et al.*, *loc. cit.*).

*Tri-*n*-propyl-lead Hydroxide.*—Moist silver oxide (2·5 g., containing 1·4 g. of oxide, *i.e.*, 0·006 mol.) was mixed with tri-*n*-propyl-lead chloride (1·5 g., 0·004 mol.) in aqueous suspension and the whole was well shaken. The residual solid was removed, giving an aqueous solution of tri-*n*-propyl hydroxide, in which form the reagent was used (cf. *idem*, *ibid.*).

*Tri-*n*-propyl-lead Acetate.*—To an aqueous solution of tri-*n*-propyl-lead hydroxide was added dilute acetic acid until the liquid was just acid to litmus. A white crystalline precipitate appeared on standing and stirring. The acetate was filtered off, dried, and recrystallised from light petroleum (b. p. 40—60°); m. p. 126—127° (Found : Pb, 52·4. Calc. for $C_{11}H_{24}O_2Pb$: Pb, 52·4%).

*Tri-*n*-propyl-lead Acrylate.*—An alcoholic solution of tri-*n*-propyl-lead hydroxide was prepared by shaking the chloride in alcohol with freshly prepared moist silver oxide. To the filtrate, an alcoholic solution of acrylic acid was added until the mixture was just acid to litmus. The liquid was evaporated almost to dryness on the water-bath and the crystals which formed on cooling were filtered off. After thorough draining, the *acrylate* was recrystallised from light petroleum (b. p. 60—80°); m. p. 123° (Found: Pb, 50·5. $C_{12}H_{24}O_2Pb$ requires Pb, 50·8%).

*Tri-*n*-propyl-lead Bromide.*—An aqueous solution of tri-*n*-propyl-lead hydroxide was added to dilute hydrobromic acid until neutral. After standing for 30 minutes, the precipitate was filtered off, washed well with water, and drained. The sticky solid thus obtained was dried in a desiccator. The solubility in organic solvents was high but it could be recrystallised from a small quantity of light petroleum (b. p. 40—60°); m. p. 76—78° (Found: Pb, 50·1. Calc. for $C_9H_{21}BrPb$: Pb, 49·8%) (cf. Pfeiffer, Truskier, and Disselkamp, *loc. cit.*).

*Tri-*n*-propyl-lead Bromoacetate.*—Prepared like the acetate, the *bromoacetate* was filtered off after a few minutes' standing, dried, and recrystallised from light petroleum (b. p. 40—60°); m. p. 93—94° (Found: Pb, 42·8. $C_{11}H_{23}O_2BrPb$ requires Pb, 43·7%).

*Tri-*n*-propyl-lead Anthranilate.*—This *salt* was similarly prepared and recrystallised; m. p. 57—58° (Found: Pb, 43·1. $C_{16}H_{27}O_2NPb$ requires Pb, 43·9%).

By similar means were prepared the n-*butyrate*, m. p. 105—106° (Found: Pb, 48·5. $C_{13}H_{28}O_2Pb$ requires Pb, 48·9%); the *chloroacetate*, m. p. 109—110° (Found: Pb, 48·3. $C_{11}H_{23}O_2ClPb$ requires Pb, 48·2%); the *β-chloropropionate*, m. p. 99—100° (Found: Pb, 46·3. $C_{12}H_{25}O_2ClPb$ requires Pb, 46·7%); the *crotonate*, m. p. 135° (Found: Pb, 48·1. $C_{13}H_{26}O_2Pb$ requires Pb, 49·2%); the *propionate*, m. p. 121—122° (Found: Pb, 50·7. $C_{12}H_{26}O_2Pb$ requires Pb, 50·6%); and the iso*valerate*, m. p. 110—111° (Found: Pb, 47·3. $C_{14}H_{30}O_2Pb$ requires Pb, 47·4%).

*Tri-*n*-propyl-lead Iodoacetate.*—In this case, the white precipitate produced did not crystallise properly until excess of acid had been added. After standing for a few minutes, the *iodoacetate* was filtered off, dried, and recrystallised as above. The white needles thus obtained soon turned brown on standing; m. p. 88—89° (Found: Pb, 39·8. $C_{11}H_{23}O_2IPb$ requires Pb, 39·8%).

The *trichloroacetate* was prepared and crystallised similarly; m. p. 139—140° (Found: Pb, 41·2. $C_{11}H_{21}O_2Cl_3Pb$ requires Pb, 41·6%).

*Tri-*n*-propyl-lead Naphthalene-2-sulphonate.*—An alcoholic solution of the hydroxide was prepared from moist silver oxide (3 g.) and an alcoholic solution of tri-*n*-propyl-lead chloride (3·7 g., 0·01 mol.). To the filtrate was added an alcoholic solution of naphthalene-2-sulphonic acid (2·1 g., 0·01 mol.) and the mixture was heated on the water-bath for 10 minutes. It was then cooled and excess of water was added with stirring, giving a sticky white precipitate which was kept for a short time before filtration and drying. The *sulphonate* was recrystallised thrice from benzene; m. p. 126—127° (Found: Pb, 35·3. $C_{19}H_{28}O_3SPb$ requires Pb, 38·1%).

*Tri-*n*-propyl-lead Toluene-*o*-sulphonate.*—To an aqueous solution of tri-*n*-propyl-lead hydroxide, cooled in ice-water, was added, with stirring, an aqueous solution of toluene-*o*-sulphonic acid. At first, an oil separated and, in order to bring about crystallisation, it was necessary to add a slight excess of the acid and to scratch the sides of the vessel vigorously. After standing for a few minutes, the crystals were filtered off, washed with water, and dried. The *toluenesulphonate* was recrystallised from a fairly large quantity of light petroleum (b. p. 40—60°); m. p. 86—87° (Found: Pb, 40·96. $C_{16}H_{28}O_3Pb$ requires Pb, 40·85%).

The *toluene-*p*-sulphonate* was prepared in the same way and its behaviour was very similar; it recrystallised from a large quantity of light petroleum (b. p. 40—60°); crystallisation was slow; m. p. 82—83° (Found: Pb, 40·98%).

*Tri-*n*-propyl-lead Xanthate.*—To tri-*n*-propyl-lead chloride (3·7 g., 0·01 mol.), dissolved in alcohol, potassium xanthate (1·8 g., 0·011 mol.) was added. The mixture was gently heated under reflux for 20 minutes, cooled, and filtered. On adding water to the filtrate, a brownish, crystalline precipitate was formed. This was filtered off, washed with water and dried. Recrystallisation from light petroleum (b. p. 40—60°), in which it was rather soluble, afforded the *xanthate* as buff-coloured needles on cooling the solution in ice-water; m. p. 57·5° (Found: Pb, 44·7. $C_{12}H_{26}OS_2Pb$ requires Pb, 45·3%).

*Tri-*n*-propyl-lead Cyanide.*—An aqueous suspension of tri-*n*-propyl-lead chloride (3·7 g., 0·01 mol.) was shaken with moist silver oxide (2·8 g.). To the filtrate was added, with stirring, a dilute aqueous solution of potassium cyanide (1·0 g., 0·015 mol.). The white precipitate which separated was allowed to stand for a short time before being filtered off, drained, and dried. The *cyanide* recrystallised from aqueous alcohol as very fine white needles; m. p. 135° (decomp., after turning brown between 122° and 130°) (Found: Pb, 56·7; CN, 7·66. $C_{10}H_{21}NPb$ requires Pb, 57·2; CN, 7·18%).

*Tri-*n*-butyl-lead Chloride.*—Tetra-*n*-butyl-lead (Jones, Evans, Gulwell, and Griffiths, *loc. cit.*) (5·4 g., 0·0125 mol.) was dissolved in light petroleum (b. p. 40—60°) (50 c.c.) and dry hydrogen chloride was passed through the ice-cooled solution. A whitish precipitate began to settle out after about 30 minutes and the passage of gas was stopped. The solid was filtered off and the filtrate was evaporated to dryness, leaving a slightly sticky white solid (4·0 g., 77%). Owing to its high solubility in organic solvents, recrystallisation was difficult. Two methods were adopted. One was to dissolve the solid in light petroleum (b. p. 40—60°) and leave the liquid to evaporate slowly. The second, and easier, method was to use aqueous alcohol. After several recrystallisations with the latter solvent, poorly-developed crystals melting to a clear liquid at 106·5—108·5° were obtained (Found: Cl, 8·96. Calc. for $C_{12}H_{27}ClPb$: Cl, 8·57%). In general, the material was not recrystallised before further use.

*Tri-*n*-butyl-lead Hydroxide.*—Moist silver oxide (2 g., containing 1·2 g. of oxide, *i.e.*, 0·005 mol.) was thoroughly shaken with an alcoholic solution of tri-*n*-butyl-lead chloride (3·3 g., 0·008 mol.). The residual solid was filtered off, and the alcoholic solution of tri-*n*-butyl-lead hydroxide used for the preparation of tri-*n*-butyl-lead salts (cf. Pfeiffer *et al.*, *loc. cit.*).

*Tri-*n*-butyl-lead Acetate.*—To an alcoholic solution of tri-*n*-butyl-lead hydroxide was added, with stirring, dilute aqueous acetic acid until the mixture was distinctly acid to litmus. The solution was evaporated almost to dryness on the water-bath, and the crystals which formed were drained at the pump and washed with water. After drying, the *acetate* was recrystallised from light petroleum (b. p. 40—60°); m. p. 86° (Found: Pb, 47·4. $C_{14}H_{30}O_2Pb$ requires Pb, 47·4%).

*Tri-*n*-butyl-lead Bromoacetate.*—A solution was prepared as for the acetate, and addition of excess of water precipitated the *bromoacetate*. Crystallisation was facilitated by cooling in ice-water and scratching the walls of the vessel. The white solid, after filtration and drying, was extremely soluble in light petroleum and was therefore recrystallised from aqueous alcohol; m. p. 54—55° (Found : Pb, 39·0. $C_{14}H_{29}O_2BrPb$ requires Pb, 40·1%).

Similarly prepared and recrystallised, the *chloroacetate* had m. p. 60° (Found : Pb, 43·4. $C_{14}H_{29}O_2ClPb$ requires Pb, 43·9%) ; the *crotonate*, m. p. 119° (Found : Pb, 44·8. $C_{16}H_{32}O_2Pb$ requires Pb, 44·7%), and the *iodoacetate*, m. p. 83° (Found : Pb, 36·9. $C_{14}H_{29}O_2IPb$ requires Pb, 36·8%), were crystallised from light petroleum.

Tri-n-*butyl-lead β-Chloropropionate.*—An alcoholic solution of tri-*n*-butyl-lead hydroxide and dilute aqueous β-chloropropionic acid were mixed and cooled in ice-water ; addition of excess of water increased the amount of white precipitate, and after a few minutes this was filtered off and dried. The *β-chloropropionate* was recrystallised from a small volume of light petroleum (b. p. 40—60°), with cooling to 0° ; m. p. 65—66° (Found : Pb, 42·5. $C_{15}H_{31}O_2ClPb$ requires Pb, 42·6%).

Tri-n-*butyl-lead Naphthalene-2-sulphonate.*—Similarly prepared, this *salt* was recrystallised from light petroleum (b. p. 40—60°) containing 10% of benzene ; m. p. 68° (Found : Pb, 35·6. $C_{22}H_{34}O_3SPb$ requires Pb, 35·4%).

The toluene-p-*sulphonate*, similarly prepared and recrystallised, had m. p. 81—82° (Found : Pb, 37·2. $C_{19}H_{34}O_3SPb$ requires Pb, 37·7%).

By a similar method of preparation, the *propionate*, recrystallised from aqueous alcohol, had m. p. 79—80° (Found : Pb, 45·4. $C_{15}H_{32}O_2Pb$ requires Pb, 45·9%), and the *trichloroacetate*, recrystallised from light petroleum (b. p. 40—60°), had m. p. 119° (Found : Pb, 38·1. $C_{14}H_{27}O_2Cl_3Pb$ requires Pb, 38·3%).

Diethyl-lead Dichloride.—Tetraethyl-lead (40·4 g., 0·125 mol.) was dissolved in dry toluene (250 c.c.), and the solution heated on the steam-bath. A stream of dry hydrogen chloride was passed through the liquid, and after a few minutes, a white precipitate began to appear. The passage of gas was continued for twice as long again before the precipitate was filtered off, washed with hot toluene, and thoroughly drained. A further small quantity of solid was obtained by passing hydrogen chloride through the filtrate; yield 31·9 g. (76%). In their original preparation, Gilman and Robinson (*loc. cit.*) claimed a yield of 97% of pure substance. Yakubovich and Petrov (*J. pr. Chem.*, 1936, **144**, 67) stated that considerable quantities of lead chloride and triethyl-lead chloride were also produced, the yield of diethyl-lead dichloride being only 50%.

Diethyl-lead Bis-p-*nitrophenoxide.*—*p*-Nitrophenol (4·2 g., 0·03 mol.) and tetraethyl-lead (9·7 g., 0·03 mol.) were dissolved in warm xylene, a few pieces of silica gel added, and the whole was gently heated under reflux for 1 hour. A yellow solid separated and was filtered off. It could not be recrystallised from water, ether, benzene, carbon tetrachloride, chloroform, light petroleum, or toluene owing to its insolubility. It was therefore treated with boiling alcohol, filtered off hot, and dried. On heating, the *salt* did not melt, but burnt at a fairly high temperature (Found : Pb, 37·3. $C_{16}H_{18}O_6N_2Pb$ requires Pb, 38·2%).

Di-n-*propyl-lead Dichloride.*—A slow stream of dry hydrogen chloride was passed through a solution of tetra-*n*-propyl-lead (22·7 g., 0·06 mol.) in absolute ether (150 c.c.) cooled in ice-water. When a faint white precipitate began to appear, the passage of gas was stopped and the liquid was set aside for 24 hours, during which more precipitate slowly formed. This was filtered off and dried, yield, 18·0 g. (82%). The salt was recrystallised from a rather large volume of ethyl alcohol, giving a fine white powder which did not melt below 245° (Found : Cl, 19·5. Calc. for $C_6H_{14}Cl_2Pb$: Cl, 19·5%). (Grüttner and Krause, *Ber.*, 1916, **49**, 1415, used chlorine, instead of hydrogen chloride, in this preparation.)

Di-n-*propyl-lead Diacetate.*—Moist silver oxide (5·1 g., containing 50% of water) was shaken with an aqueous suspension of di-*n*-propyl-lead dichloride (3·6 g., 0·01 mol.). The solid was filtered off, and the aqueous solution of di-*n*-propyl-lead dihydroxide thus obtained was used in the following preparation. To this solution was added dilute aqueous acetic acid until the mixture was acid to litmus. The solution was allowed to evaporate over sulphuric acid in an evacuated desiccator. The sticky residue thus obtained was drained, dried, and recrystallised from light petroleum (b. p. 60—80°), giving the *diacetate*, m. p. 122° (decomp.) (Found : Pb, 49·7. $C_{10}H_{20}O_4Pb$ requires Pb, 50·4%) ; mixed m. p. with an equal quantity of tri-*n*-propyl-lead acetate, 104—114°.

Determination of Lead in an Organic Compound.—The compound (0·15—0·2 g.) was digested with concentrated nitric acid on a hot plate until all the oxides of nitrogen ceased to be evolved (complete removal of these oxides was essential). To the precipitated lead nitrate, water (100 c.c.) was added, followed by 4N-ammonia solution until all the plumbous hydroxide had been precipitated. Aqueous acetic acid (10%) was then added until a clear solution was obtained, and this was heated to 90°. Potassium dichromate solution (approx. 1%) was added from a burette, about 2 c.c. at a time, with shaking and reheating after each addition. When no more precipitate was formed and coagulation was complete, a 25% excess of the dichromate solution was added, and the mixture heated on a hot plate for 15 minutes with constant shaking. If the supernatant liquid was then not quite clear, a further 2 c.c. of dichromate was added, and the heating repeated.

The precipitate of lead chromate was collected on a Swedish filter-paper and washed with warm 5% ammonium acetate solution. The filter paper was pierced, and the precipitate washed with warm dilute hydrochloric acid into a conical flask. The solution was then cooled and titrated with approx. N/10-ferrous ammonium sulphate solution, ferrous phenanthroline being used as internal indicator. One minute was allowed for fading when determining the end-point. The ferrous ammonium sulphate solution was standardised against pure lead nitrate.

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