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# Some Reactions of Triphenyltinlithium and Triphenylleadlithium

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Homogeneous solutions of triphenyltin- and triphenylleadlithium have been prepared from the corresponding chloride and lithium in tetrahydrofuran. Hexaphenylditin has been cleaved to give good yields of the tin-lithium derivative. This triphenyltinlithium reacted with water and carbon dioxide to give only hexaphenylditin. In contrast to the benzoic acid obtained from carbonation of the triphenylleadlithium prepared from lead dichloride and phenyllithium in ether, benzoic acid was not formed from carbonation of the lead-lithium compound prepared from triphenyllead chloride in tetrahydrofuran. Refluxing a tetrahydrofuran solution of triphenyltinlithium has been found to give tetraphenyltin.

In order to compare the reactions and reactivity of the lithium derivatives of the triaryl Group IV-B elements ($Ar_3MLi$, where M is Si, Ge, Sn, or Pb) under similar conditions,[1] it was essential that triphenyltin-[2] and triphenylleadlithium be prepared under similar conditions in tetrahydrofuran as triphenylsilyl-[3,4] and triphenylgermyllithium.[1,4] It was also of interest to investigate the existence of an equilibrium system with triphenylleadlithium in tetrahydrofuran, a condition which has been proposed to exist with triphenylleadlithium in diethyl ether.[5,6]

$$(C_6H_5)_3PbLi \rightleftharpoons (C_6H_5)_2Pb + C_6H_5Li$$

In this case the triphenylleadlithium, prepared from lead (II) chloride and phenyllithium, was postulated to be 20[5] and 50%[6] dissociated. A similar dissociation was proposed for triphenyltinlithium (22% dissociated),[6] but evidence for such an equilibrium could not be detected by carbonation[7] and other experiments.[8] However, tri-*n*-butyltinlithium was recently postulated to be dissociated.[9] Also, the presence of tetraphenyltin in many of the reactions of triphenyltinlithium, prepared from tin(II)chloride and phenyllithium,[7-10] led us to repeat some of these reactions using the triphenyltinlithium prepared directly from triphenyltin chloride.

Triphenyltinlithium has previously been prepared from phenyllithium and diphenyltin in an ether–benzene mixture,[11] from phenyllithium and tin(II) chloride in ether,[10] and from triphenyltin bromide and lithium in liquid ammonia.[11] Triphenylleadlithium was obtained in good yields from lead (II) chloride and phenyllithium in ether.[5] Since phenyllithium has been observed to be unstable in tetrahydrofuran,[12] the addition of a tetrahydrofuran solution of phenyllithium to tin(II) chloride or lead(II) chloride did not appear promising for the preparation of the tin- and lead-lithium derivatives, although this was not investigated. However, the recently reported[4] preparation of triphenylsilyl- and triphenylgermyllithium from chlorotriphenylsilane and bromotriphenylgermane, respectively, in tetrahydrofuran suggested the utilization of triphenyltin chloride and triphenyllead chloride in the same solvent. Subsequently, by allowing tetrahydrofuran (THF) solutions of these halogen compounds to react with lithium at room temperature, homogeneous solutions of the lithium derivatives were obtained. The triphenyltin- and triphenylleadlithium were characterized by reaction with benzyl chloride to give the known compounds benzyltriphenyltin and benzyltriphenyllead, in yields of approximately 75%.

$$(C_6H_5)_3MCl + Li \xrightarrow{THF} (C_6H_5)_3MLi \xrightarrow{C_6H_5CH_2Cl} (C_6H_5)_3MCH_2C_6H_5$$

$$M = Sn \text{ or } Pb$$

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[1] H. Gilman, O. L. Marrs, W. J. Trepka, and J. W. Diehl, *J. Org. Chem.*, **27**, 1260 (1962).

[2] The improved method of preparation of triphenyltinlithium was summarized in R. K. Ingham, S. D. Rosenberg, and H. Gilman, *Chem. Rev.*, **60**, 459 (1960). See C. Tamborski and E. J. Soloski, *J. Am. Chem. Soc.*, **83**, 3734 (1961), for an organotin-magnesium compound; and, particularly, C. Tamborski, F. E. Ford, W. L. Lehn, C. J. Moore, and E. J. Soloski, *J. Org. Chem.*, **27**, 619 (1962), for their excellent related studies.

[3] H. Gilman and G. D. Lichtenwalter, *J. Am. Chem. Soc.*, **80**, 608 (1958).

[4] M. V. George, D. J. Peterson, and H. Gilman, *ibid.*, **82**, 403 (1960).

[5] H. Gilman, L. Summers, and R. W. Leeper, *J. Org. Chem.*, **17**, 630 (1952). F. Glockling, K. Hooton, and D. Kingston, *ibid.*, 4405 (1961).

[6] J. d'Ans, H. Zimmer, E. Endrulat, and K. Lübke, *Naturwissenschaften*, **39**, 450 (1952).

[7] H. Gilman and S. D. Rosenberg, *J. Org. Chem.*, **18**, 680 (1953).

[8] H. Gilman and S. D. Rosenberg, *ibid.*, **18**, 1554 (1953).

[9] D. Blake, G. E. Coates, and J. M. Tate, *J. Chem. Soc.*, 618 (1961).

[10] H. Gilman and S. D. Rosenberg, *J. Am. Chem. Soc.*, **74**, 531 (1952).

[11] G. Wittig, F. J. Meyer, and G. Lange, *Ann.*, **571**, 167 (1951); G. Wittig, *Angew. Chem.*, **62**, 231 (1950).

[12] H. Gilman and B. J. Gaj, *J. Org. Chem.*, **22**, 1165 (1957).

The yields of other triphenyltin derivatives which were obtained when triphenyltinlithium was allowed to react with various organic halides and triphenyltin chloride are given in Table I.

TABLE I
REACTIONS OF TRIPHENYLTINLITHIUM

| Reactant, RX | Yield of $(C_6H_5)_3SnR$, % | Yield of $(C_6H_5)_6Sn_2$, % | Yield of $(C_6H_5)_4Sn$, % |
|---|---|---|---|
| Benzyl chloride | 68.7 | 2.9 | None |
| Allyl chloride | 70.0 | 4.4 | None |
| Allyl bromide | 27.4 | 8.1 | Trace |
| Ethyl bromide | 64 | | 6.3 |
| Triphenyltin chloride | | 59.7 | |

A small amount of hexaphenylditin (3–4%) was isolated from the reaction of triphenyltinlithium with organic chlorides. Tetraphenyltin could not be detected with the chlorides although the bromides do give some tetraphenyltin. This difference cannot be explained at present. More significant is the fact that when triphenyltinlithium, prepared from phenyllithium and tin(II) chloride in ether, was allowed to react with benzyl chloride a 60% yield of tetraphenyltin was obtained,[10] while the yield of benzyltriphenyltin was only 21.7%. When this triphenyltinlithium was hydrolyzed or carbonated, a mixture of tetraphenyltin and hexaphenylditin was produced,[7,8] although in a similar hydrolysis reaction a 61% yield of hexaphenylditin was reported.[11] But hydrolysis or carbonation of the triphenyltinlithium prepared from triphenyltin chloride gave no detectable amounts of tetraphenyltin—hexaphenylditin was the only product. The product was free of tetraphenyltin, as shown by the fact that the solid obtained was easily purified by one recrystallization, and, in some cases, even this was not necessary. Mixtures of tetraphenyltin and hexaphenylditin characteristically melt over a range of about 200–215° and are not easily purified by recrystallization.[7] Hexaphenylditin was the only organotin product when triphenyltinsodium was allowed to react with carbon dioxide.[9] Incidentally, benzoic acid could not be isolated from the carbonation experiments. Coates and coworkers[9] have shown in their splendid studies that the expected oxalate is formed.

The formation of hexaphenylditin in the hydrolysis and carbonation reactions is probably a result of the triphenyltinlithium acting as a reducing agent. This has been proposed by Blake, Coates, and Tate[9] for the formation of hexaphenylditin from triphenyltinsodium in carbonation and other reactions.

Since tetraphenyltin was not being formed in reactions of the triphenyltinlithium prepared directly from triphenyltin chloride—particularly in the benzyl chloride, hydrolysis, and carbonation reactions—it was postulated that tetraphenyltin was formed, at least in part, during the preparation of triphenyltinlithium from phenyllithium and tin(II) chloride in ether. Subsequently, an ether solution of triphenyltinlithium was prepared from phenyllithium and tin(II) chloride as described[10] and filtered. There was obtained a 4.1% yield of pure tetraphenyltin and a mixture of tetraphenyltin and hexaphenylditin. Apparently, some tetraphenyltin is present in the reaction mixture prior to any reaction with a substrate. The mode of formation of the tetraphenyltin is not clear, but since diphenyltin is an intermediate in the preparation of triphenyltinlithium by this method,[7,8] the diphenyltin may disproportionate.[13] However, diphenyltin has been proposed[14] to disproportionate to hexaphenylditin when heated with excess phenylmagnesium bromide. In one case[14b] tetraphenyltin and dodecaphenylpentatin were also isolated. Hexaphenylditin and dodecaphenylpentatin could be cleaved by phenyllithium. The cleavage of hexaphenylditin

$$\begin{tikzcd} 3(C_6H_5)_2Sn \arrow[r] & (C_6H_5)_3SnSn(C_6H_5)_3 + Sn \arrow[d, "C_6H_5Li"] \\ & (C_6H_5)_4Sn + (C_6H_5)_3SnLi \end{tikzcd}$$

has been observed to give an 88.6% yield of tetraphenyltin.[7]

It should be emphasized that these reactions may be occurring during the preparation of triphenyltinlithium from tin(II) chloride and phenyllithium. Since the direct preparation from triphenyltin chloride does not involve the intermediate diphenyltin, these reactions are not likely to occur. However, if the tetrahydrofuran solution of triphenyltinlithium is refluxed or shaken at room temperature for about a week, tetraphenyltin is formed.

Incidental to these studies, an attempt was made to form a derivative of the triphenyltin hydride formed in the metalation of fluorene by triphenyltinlithium[1] as tetraphenyltin by treating the triphenyltinlithium-fluorene reaction mixture with phenyllithium.[15] Therefore, triphenyltinlithium was prepared from triphenyltin chloride and divided into three portions. One portion was allowed to react with fluorene, followed by the addition of phenyllithium. The yield of tetraphenyltin was 75.2%. Since triphenyltinlithium has been found to metalate fluorene to the extent of about 20%,[1] a second portion of the triphenyltinlithium was treated with phenyllithium. The yield of tetraphenyltin was 65.8%. The final portion was allowed to react with benzyl chloride. Subsequently benzyltriphenyltin (54.7%) and hexaphenylditin (2.4%) were isolated.

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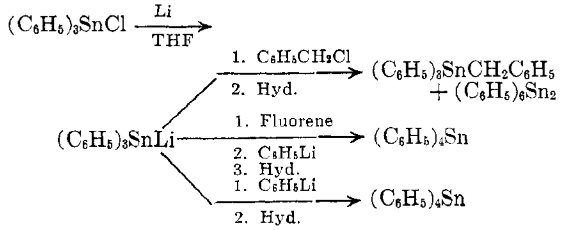
[13] H. Gilman and J. Eisch, *J. Org. Chem.*, **20**, 763 (1955).

[14] (a) E. Krause and R. Becker, *Ber.*, **53**, 173 (1920). (b) J. Boeseken and J. J. Rutgers, *Rec. trav. chim.*, **42**, 1017 (1923).

[15] Phenyllithium has been found to react with triphenyltin hydride to give tetraphenyltin. See H. Gilman and H. W. Melvin, *J. Am. Chem. Soc.*, **71**, 4050 (1949).



In separate experiments, triphenyltinlithium was allowed to react with phenyllithium in 1:1, 1:2, and 1:3 molar equivalents, respectively, followed by the addition of benzyl chloride to characterize any unchanged triphenyltinlithium. These results are shown in Table II.

TABLE II

REACTION OF PHENYLLITHIUM WITH TRIPHENYLTINLITHIUM

| $C_6H_5Li:(C_6H_5)_3SnLi$[a] ratio | Yield of $(C_6H_5)_4Sn$, % | Yield of $(C_6H_5)_3SnCH_2C_6H_5$,[c] % |
|---|---|---|
| 1:1 | 47.8 | 12.5 |
| 2:1 | 39.8[b] | |
| 3:1 | 73.6 | None |

[a] Prepared from hexaphenylditin. [b] A mixture of tetraphenyltin and hexaphenylditin was also isolated. [c] Unchanged triphenyltinlithium was characterized by the addition of benzyl chloride to the reaction mixture.

A satisfactory explanation for these results cannot be given at this time. The tetraphenyltin could arise, in part, by cleavage of hexaphenylditin present in the triphenyltinlithium preparation, and/or from the reaction of bromobenzene present in the phenyllithium solution with the tin-lithium derivative. However, these two sources should provide a maximum yield of about 25%.

The preparation of triphenyltinlithium (and probably triphenylleadlithium) from triphenyltin chloride and lithium appears to follow the same course as that proposed for the formation of triphenylsilyllithium from chlorotriphenylsilane.[4] Ar-

$$(C_6H_5)_3SnCl + 2Li \longrightarrow (C_6H_5)_3SnLi + LiCl$$

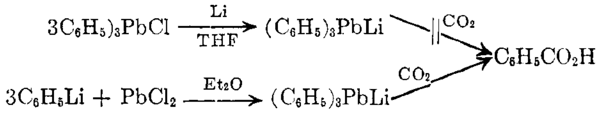
$$(C_6H_5)_3SnLi + (C_6H_5)_3SnCl \longrightarrow (C_6H_5)_3SnSn(C_6H_5)_3 + LiCl$$

$$(C_6H_5)_3SnSn(C_6H_5)_3 + 2Li \longrightarrow 2(C_6H_5)_3SnLi$$

resting of the reaction before the cleavage had begun gave hexaphenylditin. In a separate run hexaphenylditin was cleaved with lithium to give a good yield of triphenyltinlithium.

As discussed above, triphenyllead chloride reacted with lithium to give triphenylleadlithium. The reaction with benzyl chloride proceeded with ease to give a good yield of benzyltriphenyllead. When the triphenylleadlithium was carbonated, benzoic acid could not be detected. Hexaphenyldilead was isolated from the organic layer. These results are to be contrasted with the isolation of benzoic acid from carbonation of the triphenylleadlithium prepared from phenyllithium and lead(II) chloride.[5]

In the case of triphenylleadlithium prepared from triphenyllead chloride and lithium in tetrahydrofuran, the equilibrium system, if it exists at all, is displaced principally toward the triphenylleadlithium.



The triphenyltin- and triphenylleadlithium prepared directly from the chloride in tetrahydrofuran appear to be reasonably stable at room temperature, although some disproportionation may have occurred during their preparation as dark green to black solutions were produced. But, refluxing triphenyltinlithium for eight hours apparently caused complete disproportionation of the compound since derivatization of the refluxed mixture with benzyl chloride gave no benzyltriphenyltin. Tetraphenyltin was the only isolable product. Color Test I[16] of triphenyltinlithium was slightly positive, but with triphenylleadlithium it was negative.[2]

## Experimental

The starting materials were pure, dry commercial chemicals. The tetrahydrofuran was dried and purified by refluxing over sodium wire and then distilled from lithium aluminum hydride immediately before use. All reactions were carried out under dry nitrogen with oven-dried glassware.

Melting points are uncorrected.

**Preparation of Triphenyltinlithium. (A) From Triphenyltin Chloride.**—A solution of 11.56 g. (0.03 mole) of triphenyltin chloride in 30 ml. of tetrahydrofuran (THF) was stirred with 0.7 g. (0.1 g.-atom) of finely cut lithium wire until the reaction had begun as evidenced by the evolution of heat and the formation of a tan color. An additional 45 ml. of THF was added at a moderate rate. The mixture was stirred 8 hr. at room temperature and then allowed to stand 12 hr. (Subsequent studies indicate that the formation of the tin-lithium compound is complete in 3–4 hr.) The dark green solution was filtered through a glass-wool plug and added to 4.4 g. (0.035 mole) of benzyl chloride. After refluxing 1 hr., the mixture was poured into an ammonium chloride solution. The organic layer was separated, dried, and concentrated. Addition of ethanol to the residue gave 10.0 g. of benzyltriphenyltin,[10] m.p. 86–89°. Recrystallization from ethanol gave 9.07 g. (68.6%) of pure product, m.p. and mixed m.p. 89.5–90.5°. The ethanol-insoluble material weighed 0.3 g. (2.9%) and melted at 226–230°. This was identified as hexaphenylditin by a mixed melting-point determination.

**(B) From Hexaphenylditin.**—A mixture of hexaphenylditin (7.0 g., 0.01 mole) and cut lithium wire (0.7 g., 0.1 g.-atom) was treated with a small amount of tetrahydrofuran (THF) to form a paste. The mixture was stirred at room temperature until the cleavage had started (heat evolved and a dark brown color developed) at which time the remainder of 50 ml. of THF was added. After stirring 7 hr. at room temperature, the mixture was filtered into an addition funnel and added to 3.17 g. (0.025 mole) of benzyl chloride in 20 ml. of THF. Subsequent to refluxing 1 hr., hydrolysis was effected with an aqueous ammonium chloride solution and ether added. The organic layer was separated and dried. The concentrated oil was seeded with benzyltriphenyltin to give 6.27 g. of solid, m.p. 88–91°. Recrystallization from ethanol gave 5.72 g. (64.8%) of pure product,

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[16] H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

m.p. 89–91°, identified as the benzyl derivative by mixed melting point.

**Interrupted Triphenyltinlithium Preparation.**—Five grams (0.013 mole) of triphenyltin chloride and 0.7 g. (0.1 g.-atom) of cut lithium wire were dissolved in 10 ml. of tetrahydrofuran (THF) at which time the reaction began and a solid was formed. Before the cleavage began (formation of a dark brown), the mixture was diluted with 30 ml. of THF and the lithium removed by filtration through a loose glass-wool plug. The filtrate was filtered through a Büchner funnel to give a solid which was taken up in water to dissolve any lithium chloride. Subsequent filtration gave 3.7 g. (81.3%) of hexaphenylditin, m.p. and mixed m.p. 231–233° after recrystallization from a petroleum ether (b.p. 100–120°)–benzene mixture.

**Hydrolysis of Triphenyltinlithium.**—A tetrahydrofuran (THF) solution containing 0.026 mole of triphenyltinlithium, prepared from 10.0 g. (0.026 mole) of triphenyltin chloride and 0.7 g. (0.1 g.-atom) of cut lithium wire in 60 ml. of THF, was divided into two equal portions and one portion poured into an ammonium chloride solution. Ether was added and the layers separated. The combined organic layer was concentrated to give 1.68 g. of a solid, m.p. 229–231°. Recrystallization from petroleum ether (b.p. 100–120°) gave 1.58 g. (34.8%) of hexaphenylditin, m.p. and mixed m.p. 229–231°.

Treatment of the solid with carbon disulfide did not afford any tetraphenyltin.[7]

The second portion of the triphenyltinlithium solution was added to an excess of benzyl chloride. After the usual workup, 0.47 g. (10.3%) of hexaphenylditin, m.p. and mixed m.p. 225–228°, and 3.19 g. (55.6%) of pure benzyltriphenyltin (4.24 g. or 74% of crude material), m.p. and mixed m.p. 89–91°, were isolated.

Approximately the same yield (44%) of hexaphenylditin was isolated when the hydrolysis was carried out under nitrogen.

**Carbonation of Triphenyltinlithium.**—A solution of triphenyltinlithium, prepared from 5.0 g. (0.013 mole) of triphenyltin chloride and lithium wire in 30 ml. of tetrahydrofuran, was poured jet-wise onto a slurry of Dry Ice and ether. After hydrolysis with water, the layers were separated. The organic layer was filtered to give 1.5 g. of a solid, m.p. 224–228°, identified as hexaphenylditin by mixed melting point.

Acidification of the aqueous layer, which was basic, did not give any insoluble products.

The organic layer was dried over magnesium sulfate and distilled. Treatment of the residual solid with petroleum ether (b.p. 60–70°) afforded an additional 1.1 g. of hexaphenylditin. The combined fractions were recrystallized from a petroleum ether–benzene mixture to give 2.25 g. (49.6%) of pure product, m.p. 231–233°.

**Isolation of Tetraphenyltin from the Reaction of Phenyllithium with Tin(II) Chloride.**—Triphenyltinlithium was prepared in ether according to the reported procedure[10] from 0.135 mole of phenyllithium and 0.045 mole of tin(II) chloride at −10°. The suspension was then filtered under nitrogen through a sintered-glass filter. The insoluble material was treated with a small amount of tetrahydrofuran (THF) and filtered. There was obtained 0.95 g. (4.12%) of tetraphenyltin, m.p. 225–228°, identified by mixed melting point. The THF filtrate was hydrolyzed and ether added. The organic layer was separated, dried, and evaporated to give 0.3 g. of material melting with decomposition at 310°.

The original ether filtrate was added to 5.2 g. (0.045 mole) of benzyl chloride and worked up as described previously. A viscous oil and a mixture of tetraphenyltin and hexaphenylditin, m.p. 200–210°, were the only isolable products. Benzyltriphenyltin could not be detected.

In a second run, similar results were obtained.

**Reaction of Triphenyltinlithium with Fluorene Followed by Phenyllithium.**—Triphenyltinlithium was prepared from 15.42 g. (0.04 mole) of triphenyltin chloride and 0.7 g. (0.1 g.-atom) of lithium in 100 ml. of tetrahydrofuran and divided into three portions. One portion containing 0.01 mole of the tin-lithium derivative was added to 1.64 g. (0.04 mole) of fluorene and then stirred 18 hr. at room temperature. The reaction mixture was then treated with 0.025 mole of phenyllithium in ether. A solid was formed and a red color developed immediately. After stirring 6 hr., the solid was allowed to settle and the liquid was decanted. The residue was swirled with a small quantity of dry ether and filtered. There was obtained 3.21 g. (75.2%, based on 0.01 mole of triphenyltinlithium) of tetraphenyltin, m.p. 227–229°, identified by a mixture melting point determination. The melting point was depressed when admixed with hexaphenylditin.

The decantate and filtrate were hydrolyzed and the aqueous layer separated, extracted with ether, and discarded. The dried organic layer was evaporated to give 2.61 g. of a red solid melting over the range 95–100° (cloudy). Recrystallization from petroleum ether (b.p. 100–120°) gave 0.6 g. of a mixture of hexaphenylditin and tetraphenyltin. The filtrate gave 1.4 g. (85.4%) of crude fluorene, m.p. 98–107°.

Another portion containing 0.01 mole of triphenyltinlithium was allowed to react with 0.02 mole of phenyllithium for 6 hr. at room temperature. The solid was allowed to settle and the clear liquid decanted. The solid consisted of 2.81 g. (65.8%) of tetraphenyltin, m.p. 226–228°. From the hydrolyzed filtrate, there was obtained 1.33 g. of solid melting over the range 140–170°. Recrystallization from petroleum ether (b.p. 100–120°) gave 1.0 g. of a mixture of hexaphenylditin and tetraphenyltin, m.p. 188–200°.

The final portion containing 0.02 mole of triphenyltinlithium was added to 3.16 g. (0.025 mole) of benzyl chloride and worked up in the usual manner. There was obtained 4.83 g. (54.7%) of benzyltriphenyltin, m.p. and mixed m.p. 89–91°, and 0.33 g. (2.4%) of hexaphenylditin, m.p. 224–227°, identified by mixed melting point.

**Reaction of Triphenyltinlithium with Phenyllithium.**—To a tetrahydrofuran (THF) solution of triphenyltinlithium, prepared by the lithium cleavage of 7.0 g. (0.01 mole) of hexaphenylditin in 27 ml. of THF, was added 0.02 mole of phenyllithium in 100 ml. of ether. A solid was formed during the addition. The mixture was stirred overnight and then filtered under nitrogen. The insoluble material was recrystallized from a benzene–petroleum ether (b.p. 60–70°) mixture to give 0.23 g. of tetraphenyltin, m.p. and mixed m.p. 230–231°.

The filtrate was treated with 5.0 g. (0.04 mole) of benzyl chloride. After refluxing 3 hr., the reaction mixture was hydrolyzed with an ammonium chloride solution and filtered. The solid was recrystallized from a mixture of benzene and petroleum ether to afford 3.85 g. of tetraphenyltin, m.p. and mixed m.p. 229–230.5°. The total yield of tetraphenyltin was 47.8%.

The organic layer was separated and dried over sodium sulfate. The solvent was evaporated and ethanol added to the residue to give 1.1 g. (12.5%) of benzyltriphenyltin, m.p. 91.5–92.5° (mixed m.p.).

The results of two runs in which the ratios of phenyllithium to triphenyltinlithium were 2:1 and 3:1 are shown in Table II.

**Preparation of Triphenylleadlithium.**—Tetrahydrofuran (150 ml.) was added rapidly to 21.16 g. (0.04 mole) of triphenyllead chloride and 0.7 g. (0.1 g.-atom) of finely cut lithium wire. After a short induction period, heat was evolved and a dark colored suspension rapidly developed. The mixture was stirred 4 hr. at room temperature and filtered into an addition funnel. One-half of the dark solution (the remainder was used in the next experiment) was added to 3.42 g. (0.027 mole) of benzyl chloride. The color was partially discharged and, after 1 hr. at reflux, the reaction mixture was poured into an aqueous ammonium chloride solution. The aqueous layer was separated, extracted with ether and discarded. The organic layer was dried ($MgSO_4$) and distilled. The residual oil was treated with ethanol to give 10.3 g. (98.2%) of benzyltriphenyllead, m.p. 91–93°. A mixed melting point with an authentic sample[5] was not depressed.

In a run in which all the prepared triphenylleadlithium was added to benzyl chloride, the benzyl derivative was obtained in a 78% yield.

**Carbonation of Triphenylleadlithium.**—The second portion of the above triphenylleadlithium solution was poured onto a slurry of Dry Ice and ether. After acid hydrolysis, the layers were separated and filtered to give 3.9 g. of a solid which did not melt below 360°. The organic layer was extracted with dilute sodium hydroxide. Acidification of the basic extracts gave no products. The organic layer was dried over magnesium sulfate and the solvent was evaporated. The residue was treated with petroleum ether (b.p. 60–70°) to afford 2.95 g. (16.8%) of hexaphenyldilead. Recrystallization from chloroform gave 2.7 g. (15.4%) of the pure dilead compound which turned black at 153° and completely melted at 220°. There was no change in these properties when admixed with an authentic sample, which also showed these melting characteristics.

**Stability of Triphenyltinlithium.**—A tetrahydrofuran (THF) solution containing triphenyltinlithium was prepared from 11.5 g. (0.03 mole) of triphenyltin chloride and 0.7 g. (0.1 g.-atom) of cut lithium wire in 75 ml. of THF. After stirring the reaction mixture 3 hr. at room temperature, the excess lithium was removed by pouring the suspension through a glass-wool plug into a second flask. The solution was then refluxed 8 hr. After cooling, the solid was removed by filtration under nitrogen and recrystallized from petroleum ether (b.p. 60–70°)-benzene mixture to give 2.5 g. (19.5%) of tetraphenyltin, m.p. and mixed m.p. 229–230°.

The filtrate was added dropwise to 3.4 g. (0.03 mole) of benzyl chloride in 20 ml. of THF. The mixture was refluxed and hydrolyzed. The usual work-up afforded no benzyltriphenyltin.

In another test of the stability of the tin-lithium compound, the triphenyltinlithium solution was shaken in a sealed tube under nitrogen for 1 week at room temperature, and then was allowed to stand 8 hr. The solid that had formed was filtered and identified as tetraphenyltin (18.2%). The filtrate was added to benzyl chloride and treated as described above. A mixture of hexaphenylditin and tetraphenyltin were the only products isolated.

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# N(Im)-Carbobenzoxyhistidine Derivatives as Intermediates for the Synthesis of Histidine Peptides[1]

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When the esters of N($\alpha$),N(Im)-dicarbobenzoxy-L-histidine or -L-histidyl peptides are treated with hydrogen bromide in glacial acetic acid or in dioxane, the action of the acid reagent leads to selective decarbobenzoxylation at the $\alpha$-position under the ordinary conditions. The resulting N(Im)-carbobenzoxy-L-histidine derivatives can be smoothly coupled with the carboxyl functions by the carbodiimide method to give peptide bonds at the $\alpha$-position of histidine. The N(Im)-carbobenzoxy group can be easily removed by alkaline hydrolysis or catalytic hydrogenation. By this procedure a variety of histidine peptides, some of which have the sequences occurring in insulin, corticotropin, and hypertensin, have been synthesized with excellent yields without any difficulties.

Histidine occurs widely in biologically active proteins and peptides, such as ribonuclease, insulin, corticotropin (ACTH), melanocyte-stimulating hormone (MSH), hypertensin, and so on. Since it has recently been suggested that in some instances the histidine residue occupies the site of biological activity,[2] development of methods for the synthesis of histidine peptides is very desirable for biochemical studies on proteins and peptides.

In recent years, Akabori, *et al.*,[3,4] have reported that N($\alpha$),N(Im)-dicarbobenzoxy-L-histidine[4,5] is an excellent starting material in the synthesis of histidyl peptides. Thus, the peptide containing a histidine residue at the amino end of the molecule can be obtained in high yield without any difficulties. On the other hand, it is rather troublesome to prepare the peptide containing histidine at the carboxyl end or in the middle of the molecule. This is mainly due to the fact that there has been lacking a simple and satisfactory method to protect selectively the basic imidazole group of histidine. Although in this respect N(Im)-benzyl-L-histidine[6] and its derivative[7] are valuable intermediates,[7,8] they are not easily accessible enough to be used for practical purposes. Of late, Zervas, *et al.*,[9] have obtained N(Im)-trityl-L-histidine methyl ester hydrochloride by heating a methanolic solution of ditrityl-L-histidine methyl ester hydrochloride This compound may, however, be useless because of its labile nature.

It has now been found that the carbobenzoxy group linked at the imidazole nitrogen of histidine is unexpectedly resistant to treatment with hydrogen bromide in glacial acetic acid or in dioxane. Thus treatment of an N($\alpha$),N(Im)-dicarbobenz-

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[1] This investigation was presented in part at the Vth International Congress of Biochemistry, Moscow, August, 1961, and at the Japanese Symposium on Protein Structure, Kanazawa, November, 1961. K. Inouye and H. Otsuka, *J. Org. Chem.*, **26**, 2613 (1961).

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