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# Reactions of organolithium compounds with some organic phosphorus and nitrogen compounds

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REACTIONS OF ORGANOLITHIUM COMPOUNDS WITH SOME ORGANIC  
PHOSPHORUS AND NITROGEN COMPOUNDS

by

George Earl Brown

A Thesis Submitted to the Graduate Faculty  
for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

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## INTRODUCTION

The first organometallic compound to be identified, diethylzinc, was prepared by Frankland<sup>1</sup> in 1849. A series of alkylzinc compounds was soon prepared and studies were extended to include organometallic compounds of metals other than zinc. Organometallic compounds of several metals were successfully prepared; however, the zinc and mercury compounds were the only ones that were used extensively in the synthesis of organic compounds before the discovery of the Grignard reagent.

The early attempts to prepare organomagnesium compounds were not encouraging. Hallwachs and Schafarik<sup>2</sup>, in 1859, and Cahours<sup>3</sup>, in 1860, heated ethyl iodide and magnesium powder in a sealed tube and obtained some impure diethylmagnesium. Then, in 1891, Lohr<sup>4</sup> prepared dimethylmagnesium powder, and two years later Fleck<sup>5</sup> used this reaction for the preparation of diphenylmagnesium. However, no successful application to synthesis was made with organomagnesium compounds until 1899, when Barbier<sup>6</sup> obtained dimethylheptenol from the interaction of a mixture of methylheptenone, methyl iodide and magnesium.

1. Frankland, Ann., 71, 213 (1849).
2. Hallwachs and Schafarik, ibid., 109, 206 (1859).
3. Cahours, ibid., 114, 240 (1860).
4. Lohr, ibid., 261, 48 (1891).
5. Fleck, ibid., 276, 129 (1893).
6. Barbier, Compt. rend., 128, 110 (1899).

The following year, Victor Grignard<sup>7</sup> resolved this synthesis into two distinct reactions, first preparing the RMgX compound in ether solution, then treating the organomagnesium halide with the reactant. He vigorously extended his investigation of this new reaction and soon had laid the foundation for much of our present knowledge of the reactions of the reagent that now bears his name. The Grignard reagent, because of the ease with which it could be prepared, and the variety of reagent types with which it would react, has been an important intermediate in the synthesis of organic compounds.

A series of organolithium compounds, similar in many respects to the corresponding Grignard reagents, has recently been prepared. Spencer and Wallace<sup>8</sup>, in 1908, were the first to attempt to prepare an organolithium compound. They failed to prepare  $\alpha$ -naphthyllithium from an ether solution of  $\alpha$ -bromonaphthalene and lithium metal; then Spencer and Price<sup>9</sup> obtained only biphenyl from the interaction of lithium with an ether solution of iodobenzene. Upon hydrolysis of the mixture formed by heating lithium metal and the organic halide without a solvent, Spencer and Price did obtain evidence for the formation of a number of organolithium compounds. An indirect method was developed by Schlenk and Holtz<sup>10</sup>, who

7. Grignard, Compt. rend., 130, 1323 (1900).
8. Spencer and Wallace, J. Chem. Soc., 1827 (1908).
9. Spencer and Price, ibid., 385 (1910).
10. Schlenk and Holtz, Ber., 50, 262 (1917).

treated organomercury compounds in an inert solvent with lithium metal. Ziegler and Colonius<sup>11</sup>, in 1930, reported a series of elegant studies in which they prepared organolithium compounds directly from the organic halogen compounds and lithium metal in ether, benzene, cyclohexane, and analogous solvents. This represented a great advance in the investigation of these compounds, but the reactions were carried out in the unhandy Schlenk tubes. Gilman and co-workers<sup>12</sup>, recognizing the importance of the organolithium compounds, successfully applied the simple technique and the conventional apparatus used in the preparation of the Grignard reagent to the preparation of the lithium reagents. They determined the optimum conditions<sup>13</sup> for the reaction of a large number of organic halogen compounds with lithium metal and found that the yields compared quite favorably with the yields of the corresponding Grignard reagents.

There is a marked similarity in the reactions of organolithium and organomagnesium compounds<sup>14</sup> with the unsaturated groups C=O, C=S, S=O, and N=O and inorganic salts; however,

11. Ziegler and Colonius, Ann., 479, 135 (1930); German Patent 512,882 [Chem. Zentr., (1931) I, 1165].
12. Gilman, Zoellner and Selby, J. Am. Chem. Soc., 54, 1957 (1932).
13. Gilman, Zoellner and Selby, ibid., 55, 1252 (1933); Gilman, Zoellner, Selby and Boatner, Rec. trav. chim., 54, 584 (1935).
14. Gilman, "Organic Chemistry", John Wiley and Sons, New York, (1936), p. 440.

some reactants form different products when they are treated with like members of these organometallic compounds. Also, under similar experimental conditions, the lithium reagent reacts with some compounds with which the Grignard reagent does not react.

The Grignard reagent reacts with those compounds having the type of conjugated system found in benzophenone-anil to give 1,4- addition products<sup>15</sup>. The organolithium compounds under the same conditions give 1,2- addition products.

The Grignard reagent does not add to a simple olefinic system while the alkyllithium compounds add smoothly to some ethylenic double bonds<sup>16</sup>. This addition, however, has been observed only in those cases in which the unsaturated carbon atoms are directly linked or conjugated with a benzene ring or other unsaturated system.

The alkyllithium compounds cleave ethers. The reaction, however, is slow with the normal compounds such as n-butyllithium, several hours being required for an appreciable change in the concentration of the RLi compound. The secondary and tertiary alkyllithium compounds<sup>17</sup> react with ether so rapidly that they are without value as a reagent in ether solution. It has recently been demonstrated that

15. Gilman and Kirby, J. Am. Chem. Soc., 55, 1265 (1933).

16. Wooster, Chem. Rev., 11, 46 (1932).

17. F. W. Moore, Doctoral Dissertation, Iowa State College (1941).

organolithium compounds can be prepared in satisfactory yields in low boiling fractions of petroleum in which they are quite stable<sup>18</sup>.

The Grignard reagent reacts with the so-called active hydrogen as follows:



The hydrogen atom in a hydrocarbon molecule is seldom active enough to react with the organomagnesium compounds. The true acetylenes, indene, fluorene, and triphenylmethane are exceptions<sup>19</sup>. Houben and co-workers<sup>20</sup> treated dialkyl-anilines with the Grignard reagent and carbonated the reaction mixtures at high temperatures to obtain acids having the carboxyl group para to the amino group. Oddo<sup>21</sup> also obtained acids by treating diphenylamine and carbazole with the Grignard reagent under the conditions used by Houben. Recently Challenger and co-workers<sup>22</sup> found that ethyl- and propylmagnesium bromides reacted with phenyl ethers and thiophenes, at 180-220°, to give products in which the magnesium was shown to have attached itself to the nucleus

18. Gilman and Moore, J. Am. Chem. Soc., 62, 1843 (1940).
19. See reference (14), p. 416.
20. Houben and co-workers, Ber., 37, 3978 (1904); 42, 3729, 4488, 4815 (1909); 46, 3833 (1913).
21. Oddo, Gazz. chim. ital., 41, I, 255 (1911) [C. A., 5, 2638 (1911)]/; Briscoe and Plant, J. Chem. Soc., 1990 (1928).
22. Challenger and Miller, J. Chem. Soc. 894 (1938); Challenger and Gibson, Ibid., 305 (1940).

in the position ortho to the hetero element. These are the only reported cases in which the Grignard reagent has replaced a hydrogen atom on an aromatic nucleus, and in these reactions the conditions were quite drastic.

The organolithium compounds react smoothly with many aromatic compounds to replace a hydrogen atom with a lithium atom<sup>23</sup>. The hydrogen-lithium interconversions are of particular value because the lithium often enters the nucleus in a different position from that ordinarily taken by the common substitution reagents. Dibenzofuran, for example, is substituted in the 2- position by halogenation, sulfonation, and the Friedel-Crafts reaction, in the 3- position by nitration and in the 4- position by metalation<sup>24</sup>. As a rule only one lithium atom is introduced into the molecule, but triphenylcarbinol<sup>25</sup> and diphenylmethylcarbinol<sup>26</sup> react to give the dilithio compounds.

Organolithium compounds and Grignard reagents react with the free halogens to form the metal halide and an RX compound. The Grignard reagent does not react with aromatic halogen compounds, but the organolithium compounds react very readily to give a halogen-metal interconversion<sup>27</sup> as represented by

23. Gilman and Bebb, J. Am. Chem. Soc., 61, 109 (1939).
24. Gilman and Young, ibid., 56, 1415 (1934).
25. Gilman, Brown, Webb and Spatz, ibid., 62, 977 (1940).
26. Gilman and Brown, ibid., 62, 3208 (1940).
27. Gilman, Langham and Jacoby, ibid., 61, 106 (1939).

the equation:



That this is one of the smoothest of organic reactions has been demonstrated by carrying out the halogen-metal interconversion at low temperatures with halogen compounds containing the anil linkage or the carboxyl group without disturbing those functional groups<sup>28</sup>. The halogen-metal interconversion reaction opens a number of interesting possibilities in the field of organic synthesis. 1-Bromo-3,4-dimethoxydibenzofuran has resisted all attempts to convert it into a Grignard reagent or an organolithium compound in the conventional manner, but it reacts readily with *n*-butyllithium to give the desired organometallic compound<sup>29</sup>.

The value of the Grignard reagent has been fully recognized and its reactions and limitations have been extensively investigated. The low cost of magnesium will insure its continued use in those reactions for which it is adapted.

Lithium is expensive but the cost is not great enough to prohibit its use in special reactions. Some of the contributions of organolithium compounds to organic synthesis have

28. Gilman and Spatz, J. Am. Chem. Soc., 62, 446 (1940);  
C. E. Arntzen, Unpublished results.  
29. Gilman, Swiss and Brown, ibid., 62, 348 (1940).



been pointed out. The fruitful studies in this field have been few and recent. Therefore, this investigation was undertaken in an attempt to contribute to the knowledge of this valuable reagent in those reactions for which the Grignard reagent cannot be used.

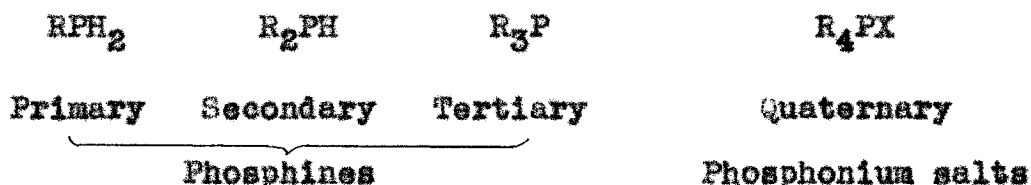
The metalation of carbazole by organolithium compounds<sup>30</sup> and by the Grignard reagent<sup>21</sup> resulted in substitution taking place ortho to the nitrogen atom. This was not in agreement with the results obtained by Houben<sup>20</sup> from the reaction of the Grignard reagent with the alkylanilines; and since there was little information available pertaining to the orientation of organic phosphorus and nitrogen compounds, the phosphines and amines were selected as the reactants.

30. Gilman and Kirby, J. Org. Chem., 1, 146 (1936).

## DISCUSSION

### Preparation of Arylphosphorus Compounds

The first organophosphorus compounds were prepared in 1846 by Thenard<sup>31</sup>. The organic phosphines may be considered as derivatives of the gas phosphine,  $\text{PH}_3$ , and are formally comparable with the amines. As in the case of the latter, primary, secondary and tertiary phosphines and the quaternary phosphonium salts are recognized.



Phosphine and primary phosphines are only slightly basic in character. They form salts but these salts are quickly hydrolyzed by water. The salts of the secondary phosphines are stable in water. The tertiary phosphines are fully as alkaline as the corresponding amines<sup>32</sup>.

The symmetrical triarylphosphines are conveniently prepared by treating phosphorus trichloride with an excess of the proper Grignard reagent<sup>33</sup>;

31. For a summary of the early work on organophosphorus compounds the reader is referred to the review by Michaelis, Ann., 181, 274 (1876).
32. Davies and Addis, J. Chem. Soc., 1622 (1937).
33. Pfeiffer, Ber., 37, 4620 (1904).



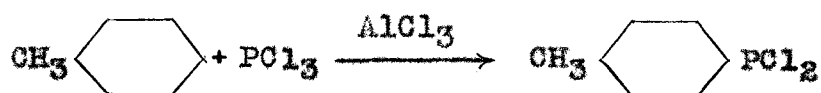
The unsymmetrical phosphines are not prepared in this way for no satisfactory method has been found for isolating the arylchlorophosphines from the molecular complex formed with the magnesium halide. There are, however, two general methods of preparing arylchlorophosphines.

When an organomercury compound is heated with phosphorus trichloride the following reaction occurs:



This reaction gives rather poor yields but is useful for the preparation of meta and ortho substituted arylchlorophosphines that cannot be prepared by other methods. The temperature required for this reaction is much higher than for the corresponding reaction with arsenic trichloride, and it may be noted that arsenic trichloride converts the organomercury compound completely to mercuric chloride<sup>34</sup>.

The Friedel-Crafts reaction is a method of choice for the preparation of a number of para substituted arylchlorophosphines<sup>35</sup>:



34. Michaelis, Ber., 9, 1566 (1876).

35. Michaelis, ibid., 12, 1009 (1879).

The compounds that have been prepared by this method are phenyl-, p-tolyl-, o-chlorotolyl-<sup>36</sup>, p-phenoxyphenyl-<sup>37</sup>, p-chlorophenyl-, p-bromophenyl-, p-anisyl-, p-phenethyl-, p-ethylphenyl-, o-(m- and p-)xylyl-, pseudocumyl-, mesityl-, cumyl-, p-benzylphenyl, biphenyl-,  $\alpha$ -naphthyl- and dibenzofuryldichlorophosphine<sup>38</sup>. These compounds were identified either by synthesis from the organomercury compound or by heating the compound in a sealed tube with bromine. In this latter reaction the phosphorus is replaced by the bromine and the resulting bromo derivative is isolated:



The dibenzofuryldichlorophosphine<sup>39</sup> has not been characterized; however, other groups, including the-AsCl<sub>2</sub> group, are introduced into the 2-position and by analogy the compound is 2-dibenzofuryldichlorophosphine.

The first member of this series, phenyldichlorophosphine, can also be prepared by passing a vaporized mixture of benzene and phosphorus trichloride through a red hot porcelain

36. Melchiker, Ber., 31, 2915 (1898).
37. Davies and Morris, J. Chem. Soc., 2880 (1932).
38. The reader is referred to the following review for individual references. Goddard, "Text-book of Inorganic Chemistry", edited by J. Newton Friend, Volume 11, part 3 (1936), Griffin and Co. Ltd., London.
39. Davies and Othen, J. Chem. Soc., 1236 (1936).

tube<sup>40</sup>. There are also a number of modifications<sup>41</sup> of this method designed to improve the yield. The yield by this method is much better than that obtained by use of the Friedel-Crafts<sup>35,42,43</sup> synthesis but the product is likely to be contaminated with free phosphorus. When only small quantities of phenyldichlorophosphine are required the Friedel-Crafts reaction is preferable, because of the purity of the product isolated and the simplicity of the apparatus required for the reaction. The vapor phase reaction has not been found successful for preparation of any of the analogs of phenyldichlorophosphine.

Michaelis and Schlenk<sup>44</sup> prepared p-dimethylaminophenyldichlorophosphine from dimethylaniline and phosphorus trichloride, using aluminum chloride as the condensing agent. Bourneul<sup>45</sup> found that dimethylaniline would react with either phosphorus trichloride or phosphorus oxychloride without a condensing agent, if the amine were used in excess so that

40. Michaelis, Ber., 6, 601 (1873); Ann., 181, 265 (1876); Köhler, Ber., 13, 1623 (1880).
41. Arbuzov, J. Russ. Phys. Chem., 42, 395 (1910) [C.A., 5, 1397 (1911)]/; Pope and Gibson, J. Chem. Soc., 101, 735 (1912); Bowles and James, J. Am. Chem. Soc., 51, 1406 (1929); Linder, Wirth and Zaunbauer, Monatsh., 70, 1 (1937).
42. This Thesis.
43. Kamai, J. Gen. Chem. (U.S.S.R.), 2, 524 (1932) [C.A., 27, 967 (1933)]/.
44. Michaelis and Schlenk, Ber., 21, 1497 (1888); Ann., 260, 2 (1890).
45. Bourneul, Bull. soc. chim., 33, 1808 (1923) [C.A., 18, 977 (1924)]/.

the hydrogen chloride was tied up as soon as it was formed:



All of the aryldichlorophosphines are liquids at room temperature except dibenzofuryldichlorophosphine. They combine with halogens<sup>35</sup> or halogenating agents to form tetrahalides, these being crystalline products that are decomposed by moisture into oxychlorides,  $\text{RPOCl}_2$ , and finally into phosphonic acids,  $\text{RPO}(\text{OH})_2$ . The aryldichlorophosphines combine with oxygen to form oxychlorides, but these are best obtained by the action of sulfur dioxide or acetic acid on the tetrahalides. Similarly sulphur and aryldichlorophosphines react to give the sulfur analog of the oxychloride,  $\text{RPSCl}_2$ , a quantitative yield being obtained if the ice-cold phosphine is treated with sulfur chloride. Hydrogen sulfide reacts to form the normal sulfide,  $\text{RPS}$ . The chlorine may be removed from aryldichlorophosphines by silver cyanide or thiocyanate, a dicyanide or dithiocyanate resulting from the reaction. Condensation takes place between aryldichlorophosphines and arylhydrazines, piperidine and tetrahydroquinoline, while the oxychlorides combine with aniline, hydrazines and ammonia. Phenyldichlorophosphine combines with phenylphosphine to give phosphorobenzene<sup>46</sup>:

46. Köhler and Michaelis, Ber., 10, 807 (1877).



This reaction can be reversed by the addition of concentrated hydrochloric acid. Phenylidichlorophosphine will react with benzenediazonium chloride to form a complex that is decomposed by copper powder to give nitrogen and diphenylphosphorus trichloride,  $(\text{C}_6\text{H}_5)_2\text{PCl}_3$ .<sup>47</sup>

The diarylechlorophosphines may be prepared by the interaction of arylidichlorophosphines and diarylmercury compounds or arylmercuric halides:



The diphenyl-, di-*p*-tolyl- and dipseudocumylchlorophosphine and the mixed diarylechlorophosphines of these radicals appear to be the only diarylechlorophosphines known<sup>38</sup>. The dipseudocumylchlorophosphine is formed, together with the primary phosphine when aluminum chloride is used as the catalyst in the interaction of phosphorus trichloride and pseudocumene, but the product is difficult to isolate in the pure state. Michaelis and Soden<sup>48</sup> have obtained diphenylchlorophosphine by heating triphenylphosphine dichloride and they suggest that this might prove a convenient method of

47. Pletz, Uspekhi Khim., **4**, 573 (1935) [J.C.A., **30**, 429 (1936)].

48. Michaelis and Soden, Ann., **229**, 295 (1885).

preparation for this compound:



Diphenylchlorophosphine<sup>42</sup> has also been prepared by heating a mixture of phenyldichlorophosphine and triphenylphosphine for several hours at 310°. All of these compounds are high-boiling viscous liquids, which may be oxidized to the corresponding phosphinic acids,  $\text{R}_2\text{PO}(\text{OH})$ . Treatment with chlorine yields the trichlorides,  $\text{R}_2\text{PCl}_3$ , which are readily hydrolyzed by water to the phosphinic acids.

A number of interesting condensation products may be prepared from the diarylchlorophosphines. An example is the reaction of diphenylchlorophosphine with sodium ethoxide to form ethyl diphenylphosphinite, with some ethyl diphenylphosphinate as a by-product. In the presence of ethyl iodide the ethyl diphenylphosphinite is completely converted to diphenylethylphosphine oxide<sup>41</sup>:



When sodium mercaptides are substituted for the sodium ethoxide, the reaction occurs in an analogous manner.

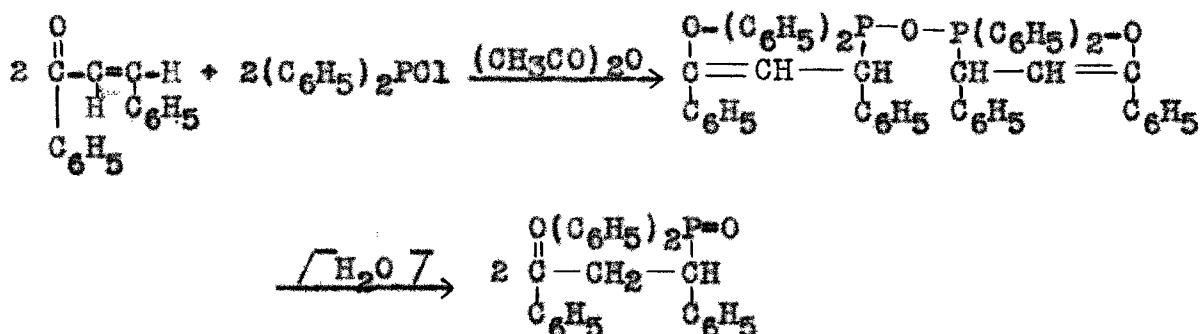
Diphenylchlorophosphine reacts with benzaldehyde<sup>49a</sup> to produce a 1,2-addition product:

49a. Conant, Braverman and Hussey, J. Am. Chem. Soc., 45, 165 (1923).





The reaction with  $\alpha,\beta$ -unsaturated ketones, such as benzal-acetophenone results in the formation of a 1,4-addition product:



A comparison of these results with earlier work<sup>49b</sup> shows that the three halides,  $\text{PCl}_3$ ,  $\text{C}_6\text{H}_5\text{PCl}_2$  and  $(\text{C}_6\text{H}_5)_2\text{PCl}$ , behave in a similar way. This is an unusual reaction, for a single atom, P, adds to an unsaturated system by an increase of valence. The reaction is reversible but acetic acid or acetic anhydride will cause the reaction to go to completion.

The primary arylphosphines are prepared by the reduction of the corresponding phosphinous acids or their esters. Most of the aryl-dichlorophosphines have been converted to the corresponding primary phosphines. The reaction with phenyldi-chlorophosphine may be taken as a typical example<sup>46</sup>:

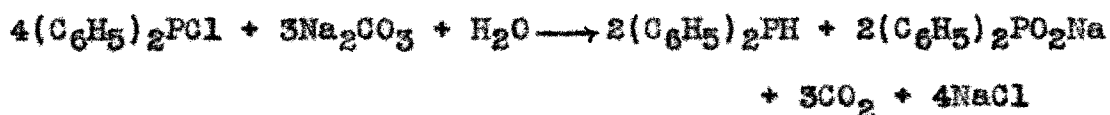
49b. Conant, J. Am. Chem. Soc., 43, 1705 (1921).



The yield of the phosphine from this reaction is about 60% of the theoretical quantity.

The primary arylphosphines are all liquids with the exception of the mesityl-, p-biphenylmethyl-, and p-dibenzylphosphines, which are low melting solids. They are rapidly oxidized in air to oxides and finally to acids. When hydrochloric acid solutions of the phosphines are treated with platinum chloride, crystalline platinichlorides are formed,  $(\text{RPH}_2\cdot\text{HCl})_2\text{PtCl}_4$  or  $(\text{RPH}_2)_2\text{H}_2\text{PtCl}_6$ . Hydriodic acid converts the phosphines to the yellow crystalline hydriodides,  $\text{RPH}_2\cdot\text{HI}$ . The phosphines possess vile odors, and phenylphosphine is reported to cause nosebleed<sup>50</sup>.

Only one aryl compound of the type  $\text{R}_2\text{PH}$  is known. It is diphenylphosphine<sup>51</sup> and may be prepared by treating diphenylchlorophosphine with an excess of sodium carbonate in a hydrogen atmosphere:



It can also be obtained by heating a mixture of diphenylchlorophosphine and zinc in a sealed tube to 230°, followed by decomposition of the product with water.

50. Michaelis, Ann., 181, 344 (1876).

51. Michaelis and Gleichmann, Ber., 15, 801 (1882).

Diphenylphosphine is a colorless, viscous, pungent liquid that oxidizes upon exposure to air or when heated with nitric acid. It acts as a weak base, its salts being decomposed by water. It combines with methyl iodide, acetyl chloride, hydrogen iodide, and dry hydrogen chloride. This hydrochloride is not stable in air, but it forms a platinumchloride,  $[(C_6H_5)_2PH]_2 \cdot H_2PtCl_6$ , that exists in the form of a yellow powder. Diphenylphosphine reacts with diphenylchlorophosphine to give tetraphenyldiphosphine:

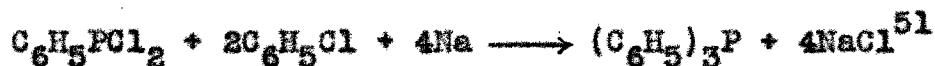


There are five types of tertiary aromatic phosphines known. They are  $Ar_3P$ ,  $ArAr'_2P$ ,  $AlkAr_2P$ ,  $Alk_2ArP$ , and  $AlkArAr'P$ .

As in the case of the corresponding arsenical compounds, the principal methods of preparing the aromatic tertiary phosphines are the application of the Fittig and the Grignard reactions. The Fittig reaction is a time-consuming reaction and the yields are not high.



or



When the aryldichlorophosphine is used the unsymmetrical phosphines of the type  $RR'_2P$  can be prepared. The Grignard reagent<sup>33,42,52</sup> when dropped into a cold, agitated ether

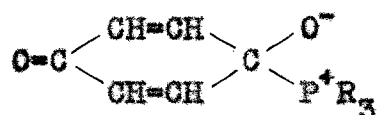
52. Dodonow and Medox, Ber., 61, 907 (1928).

solution of  $\text{PCl}_3$ ,  $\text{R}_2\text{PCl}_2$ , or  $\text{R}_2\text{PCl}$  reacts to give as high as eighty per cent yields of the corresponding phosphines. Also, according to Kollitowska<sup>53</sup>, phenylmagnesium bromide reacts with phosphorus pentachloride to give a mixture of biphenyl, triphenylphosphine, triphenylphosphine dichloride, and tetraphenylphosphonium bromide. No yields were reported in the abstract.

The properties of triphenylphosphine may be taken as representative of the properties of this group of compounds. It crystallizes in large transparent prisms and is readily soluble in most organic solvents, with the exception of alcohol. It distills unchanged in an inert atmosphere above  $360^\circ$  and has only feebly basic properties. The solution of triphenylphosphine in fuming hydrochloric acid yields the phosphine unchanged upon the addition of water. Triphenylphosphine forms triphenylphosphonium iodide which is insoluble in cold hydroiodic acid but is decomposed by water. Triphenylphosphine reacts violently with dry chlorine to form a greenish-yellow syrup, which is transformed by sodium hydroxide to the dihydroxide. The syrup, when heated, is transformed into chlorobenzene and diphenylchlorophosphine. Triphenylphosphine does not react with carbon disulfide but treatment of triphenylphosphine with a solution of sulfur in carbon disulfide gives triphenylphosphine sulfide. Triphenylphosphine readily

53. Kollitowska, Roczniki Chem., 9, 568 (1928) [C. A., 23, 2158 (1929)]<sup>7</sup>.

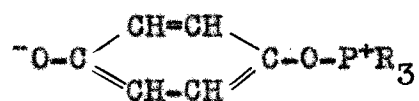
reacts with alkyl halides to give the corresponding phosphonium salts. It forms additive compound with mercuric chloride, platonic chloride, and antimony, arsenic, and bismuth trichlorides. The formation of the double salt with mercuric chloride has been suggested as a quantitative method for the determination of triphenylphosphine<sup>53</sup>. Phosphorus trichloride does not appear to form a double compound. Triphenylphosphine reacts with hydrogen persulfide,  $H_2S_2$ , to form triphenylphosphine sulfide<sup>52</sup>. This indicates that triphenylphosphine will not form a stable compound having the phosphorus attached to two -SH groups. Benzoquinone reacts readily with tertiary phosphines to form stable compounds. On the basis of analysis and molecular weight determinations, Davies and Walters<sup>54</sup> assigned to them the following structure:



Later, Schönberg and Michaelis<sup>55</sup> found that these compounds were easily broken down upon treatment with aqueous alkali. Since a phosphorus-carbon bond would probably not undergo cleavage under the conditions used, it is suggested that a phosphorus-oxygen bond is involved:

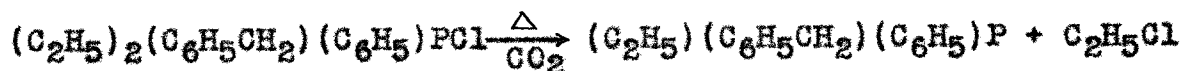
54. Davies and Walters, J. Chem. Soc., 1786 (1935).

55. Schönberg and Michaelis, Ber., 69, 1080 (1936).



The three known compounds of the type  $\text{AlkAr}_2\text{P}$ , methyldiphenyl-, ethyldiphenyl-, and methylditolylphosphine, were prepared by Michaelis and Link<sup>56</sup> from the corresponding diarylchlorophosphines and organozinc compounds. The Grignard reagent would be an excellent reagent for the synthesis of this type of compound; however, its use for this purpose has not been reported. These compounds are oils having pungent odors. Their chemical properties are not unlike those of triphenylphosphine.

Because of the ease of preparation of the aryldichlorophosphines a large number of compounds of the type  $\text{Alk}_2\text{ArP}$ <sup>46,57,58</sup> have been prepared. A number of them were prepared using alkylzinc<sup>46,54,55</sup> compounds and later Davies and co-workers<sup>59,60,61</sup> prepared them using the Grignard reagent as the Reactant. An unsymmetrical phosphine was prepared by heating diethylbenzylphenylphosphonium chloride<sup>43</sup> to produce ethylbenzylphenylphosphine:



56. Michaelis and Link, Ann., 207, 193 (1881).
57. Michaelis and Annanoff, Ber., 8, 493 (1875).
58. Michaelis, Ann., 181, 265 (1876).
59. Davies, Pearse and Jones, J. Chem. Soc., 1262 (1929).
60. Davies and Jones, ibid., 33 (1929).
61. Jackson, Davies and Jones, ibid., 2298 (1930).

An unsuccessful attempt was made to resolve the compound. These tertiary phosphines, in addition to the characteristic reactions previously described, form addition compounds with carbon disulfide,  $R_2R'P \cdot CS_2$ . Dry hydrogen chloride or methyl iodide causes the elimination of the carbon disulfide and the formation of phosphonium compounds. Dimethylphenylphosphine is equally as basic as dimethylaniline.

Compounds of the type  $AlkArAr'P$  are formed when dialkylzinc<sup>62</sup> compounds or alkylmagnesium halides<sup>63</sup> react with phenyl-p-tolyl- or phenylpseudocumylchlorophosphines. Radcliffe and Brindley<sup>63</sup> attempted to resolve methylphenyl-p-tolylphosphine, but were unable to obtain the product in crystalline form.

The phosphonium halides containing from one to three aromatic groups are readily prepared by treating the phosphine with an alkyl halide:



These are all crystalline compounds that form double salts with platinic chloride.

When arylphosphines are treated with monochloroacetic acid or ethyl monochloroacetate, phosphonium compounds are formed

62. Michaelis, Ann., 315, 60 (1901); Wedekind, Ber., 45, 2933 (1912).  
63. Radcliffe and Brindley, Chemistry and Industry, 42, 64 (1923) [C.A., 17, 1621 (1923)].



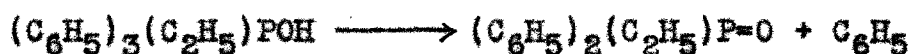


The tertiary arylphosphine oxides may be prepared as indicated above or by oxidation of the phosphine. Triphenylphosphine is resistant to oxidation with oxygen when it is suspended in water; however, if diphenyl disulfide is added the complex formed is readily oxidized by oxygen<sup>67</sup>.



Peracetic acid<sup>68</sup> reacts with triphenylphosphine to give a 93% yield of the oxide. Selenium oxide<sup>69</sup> is reported to convert a solution of triphenylphosphine in dry benzene to the oxide; however, no yields were indicated. The oxidation with bromonitromethane<sup>70</sup> gives almost a quantitative yield of the oxide and the same is true of alkaline permanganate<sup>42</sup>.

The mixed phosphine oxides of the type  $\text{AlkAr}_2\text{PO}$  can be prepared by the action of heat on the alkyltriarylphosphonium hydroxide:

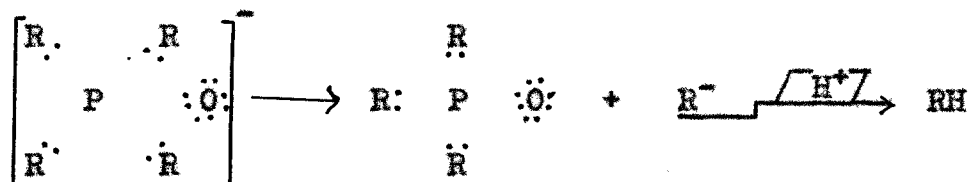
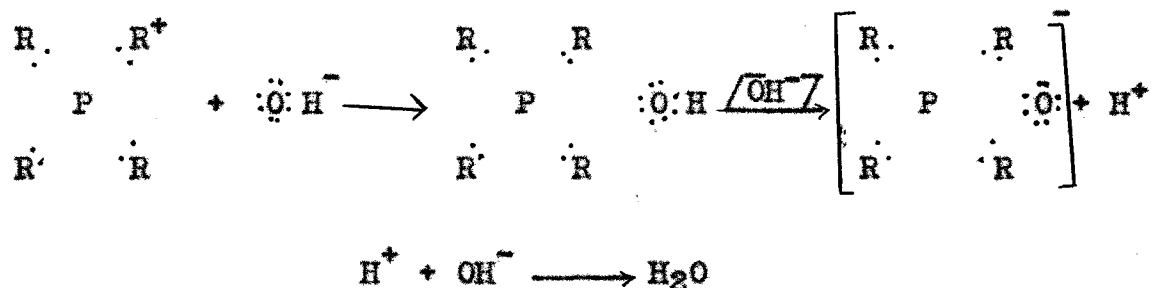


It is interesting to note in connection with this reaction that the ease of cleavage of a series of radicals appears to be in the following order:  $\alpha\text{-C}_{10}\text{H}_7\text{-}^{66} > \text{C}_6\text{H}_5\text{CH}_2\text{-}^{71} > \text{C}_6\text{H}_5\text{-}$

67. Schonberg, Ber., 68, 163 (1935).  
 68. Arbuzov, J. prakt. Chem., 131, 357 (1931) [C.A., 26, 104 (1932)].  
 69. Mel'nikov and Rokitskaya, J. Gen. Chem. (U.S.S.R.), 8, 834 (1938).  
 70. Mel'nikov, ibid., 7, 1546 (1937).  
 71. Fenton and Ingold, J. Chem. Soc., 2342 (1929).

$\text{CH}_3^- \text{ > } \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2^- \text{ > } \text{CH}_3\text{CH}_2^- \text{ > } \text{higher alkyls.}$

Substituted ammonium hydroxides, having an alkyl group containing two or more carbon atoms, are degraded in a similar manner, but the radical removed becomes an ethylenic compound. Renton and Ingold<sup>71</sup> have suggested a reaction mechanism to explain the fact that the radical removed from the phosphonium compound becomes a saturated hydrocarbon. Since nitrogen is the first member in the family group, it is impossible for more than an octet of electrons to be contained in its valence shell. The tertiary amine hydroxides should, therefore, be completely ionized in solution. The phosphorus atom, having a larger atomic radius, can add two, or sometimes four, electrons in addition to its normal octet. Naturally a highly basic anion such as the hydroxyl ion would favor this tendency. In this form the base could ionize as a weak acid, the high concentration of the hydroxyl ion also favoring this reaction. This new negative ion can, in a single step, recover both its neutrality and its octet by the ejection of an alkyl radical as an anion and forming the highly stable phosphine oxide. The anion, of course, is at once converted to the hydrocarbon:

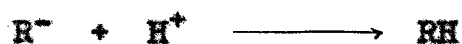
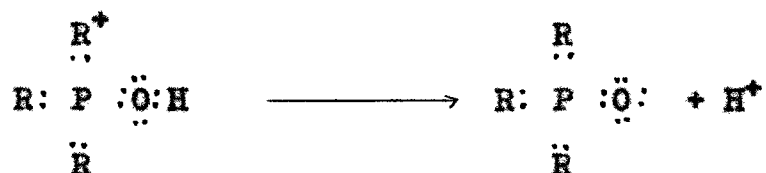
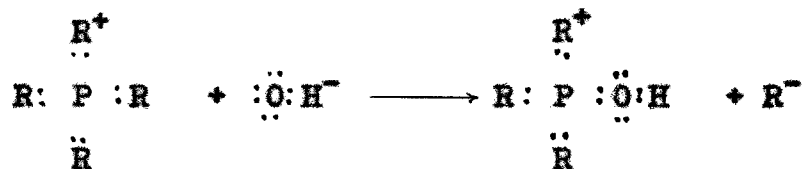


If the four radicals, here represented as R, are different, the radical having the greatest tolerance for a negative charge, or, according to the terminology suggested by Kharasch, the more negative radical, will be ejected. When there is a considerable difference in the negativity of the radicals involved, the more negative radical is ejected to the exclusion of the others. However, when the radicals are of about the same order of negativity, as is the case with n-propyl- and n-butyl-, the ejection occurs almost at random. The relative ease of ejection, as would be expected from the above mentioned mechanism, is in agreement with Kharasch's<sup>72</sup> series, with the exception of C<sub>2</sub>H<sub>5</sub>CH<sub>2</sub>-.

If the phosphorus atom, under the conditions used in the reaction, does not admit the decet of electrons to its outer electron shell, the reaction probably takes the following course. There is first a radical-hydroxyl exchange of the

72. Karasch and Flenner, J. Am. Chem. Soc., 54, 642 (1932).

type observed by Calingaert and co-workers<sup>73</sup> for the random distribution reaction and by Gilman and co-workers<sup>23</sup> in the halogen-metal interconversion reaction, then the  $R_3P^+OH$  compound, by loss of a hydrogen ion, would be converted to the neutral phosphine oxide:



This reaction would be favored by the high concentration of the hydroxyl ion and would be irreversible because of the ease of formation of the unreactive phosphine oxide. The phosphorus, in phosphonium compounds, is a negative atom. Therefore, a highly negative radical should undergo this reaction with greater ease than the relatively positive radicals, and experimental evidence substantiates this conclusion. The  $\alpha$ -naphthyl and phenyl groups are ejected at low temperatures while some

73. Calingaert and Beatty, *J. Am. Chem. Soc.*, **61**, 2748 (1939); Calingaert, Beatty and Neal, *ibid.*, **61**, 2755 (1939); Calingaert and Seroos, *ibid.*, **61**, 2758 (1939).

of the more positive aliphatic groups are not ejected until the temperature is high enough that some ethylenic degradation occurs. To explain the exclusive ethylenic degradation of the ammonium compounds, it is necessary to make the assumption that the temperature necessary for the paraffin decomposition with the more negative nitrogen atom is higher than that at which the ethylenic degradation occurs.

Another important method of preparing these diarylalkylphosphine oxides is the previously mentioned reaction in which the diarylphosphinites are caused to rearrange to give the oxide<sup>41</sup>.

The dialkylarylphosphine oxides are prepared by the oxidation of the phosphines or by the decomposition of the phosphonium hydroxides by heat<sup>74</sup>. There are no important reactions of this type of compound. These compounds are of interest because it was through the resolution<sup>74</sup> of the unsymmetrical phosphine oxide that the tetrahedral distribution of the valences of the phosphorus atom was demonstrated.

The oxides,  $\text{RPO}_2$ , corresponding to the nitro compounds, have no parallel in the arsenical compounds. They are prepared by heating the dried arylphosphonic acids with the

74. Meisenheimer and Lichtenstadt, Ber., 44, 356 (1911); Meisenheimer, Casper, Hüring, Lauter, Lichtenstadt and Samuel, Ann., 449, 213 (1926).

corresponding oxychlorides<sup>46,75,76.</sup>



They may also be prepared by dehydrating the phosphonic acids with phosphorus pentachloride, but the resulting products are not so crystalline as those formed by the former method.

These oxides differ from the nitro compounds, in that they are true acid anhydrides and are readily converted by water to the corresponding phosphonic acids.

There are three types of acids in the arylphosphorus series, namely  $\text{RP}(\text{OH})_2$ ,  $\text{RPO}(\text{OH})_2$ , and  $\text{R}_2\text{POOH}$ . The phenyl derivatives of these acids were known before the corresponding arsenical compounds were prepared, the method of preparation of the phosphorus compounds being adapted to the preparation of the arsenic derivatives. However, the diazonium reaction, that has been so successful in the preparation of the arsenic compounds, has not been so fruitful in the phosphorus series.

The phosphinous acids,  $\text{RP}(\text{OH})_2$ , are generally prepared by hydrolysis of the corresponding dichlorophosphines with water<sup>58,46,48,77</sup> or alcohol:

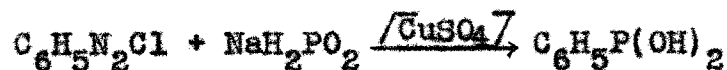


75. Michaelis and Rothe, Ber., 25, 1747 (1892).

76. Michaelis, Ann., 315, 43 (1901).

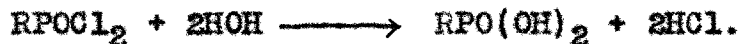
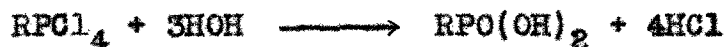
77. Michaelis and Ananoff, Ber., 7, 1688 (1874).

Sodium hypophosphite,  $\text{NaH}_2\text{PO}_2$ , reacts with diazonium compounds to give the phosphinous acid<sup>78</sup>:



The acids of this type are all solids that readily form metal salts and double salts with hydrazines. No nitro or amino substituted acids are known and the halogenated-acids are not obtained by halogenation. The esters are obtained by treating the aryldichlorophosphines with sodium alkoxides.

The phosphonic acids,  $\text{RPO}(\text{OH})_2$ , are prepared by the hydrolysis of the corresponding tetrachloride or oxychloride<sup>79,80</sup>:



These acids are solid, stable compounds that can be nitrated or halogenated. Some carboxylic acids are known, these being prepared by mild oxidation of the tolylphosphonic acids<sup>81</sup>.

The phosphonic acids lose water when heated to form the pyrophosphonic acids, and they may be decomposed by heating in a sealed tube with bromine<sup>82</sup>. When heated with soda-lime<sup>82</sup>, they are decomposed to form a hydrocarbon and phosphoric acid.

78. Pletz, J. Gen. Chem., 7, 84 (1937) [C.A., 31, 4965 (1937)].

79. Michaelis and Mathais, Ber., 7, 1070 (1874).

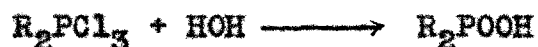
80. Michaelis and Köhler, ibid., 9, 519 (1876).

81. Michaelis, Ann., 293, 261 (1896).

82. Michaelis and Benzinger, Ber., 9, 517 (1876).

The diethyl esters<sup>83</sup> may be prepared by heating the silver salt of the acid with ethyl iodide, while decomposition of the tetrachloride,  $\text{RPCl}_4$ , with ethyl alcohol gives rise to a mono-ethyl ester,  $\text{RPO}(\text{OH})(\text{OC}_2\text{H}_5)$ . If the tetrachloride is heated with phenol, hydrogen chloride is evolved and the diphenyl ester is formed.

The phosphinic acids,  $\text{R}_2\text{PO}(\text{OH})$ , are also prepared by hydrolysis of the phosphorus halide<sup>62</sup>:



These acids undergo the same transformations as those described for the phosphonic acids.

#### Substitution in Arylphosphorus Compounds

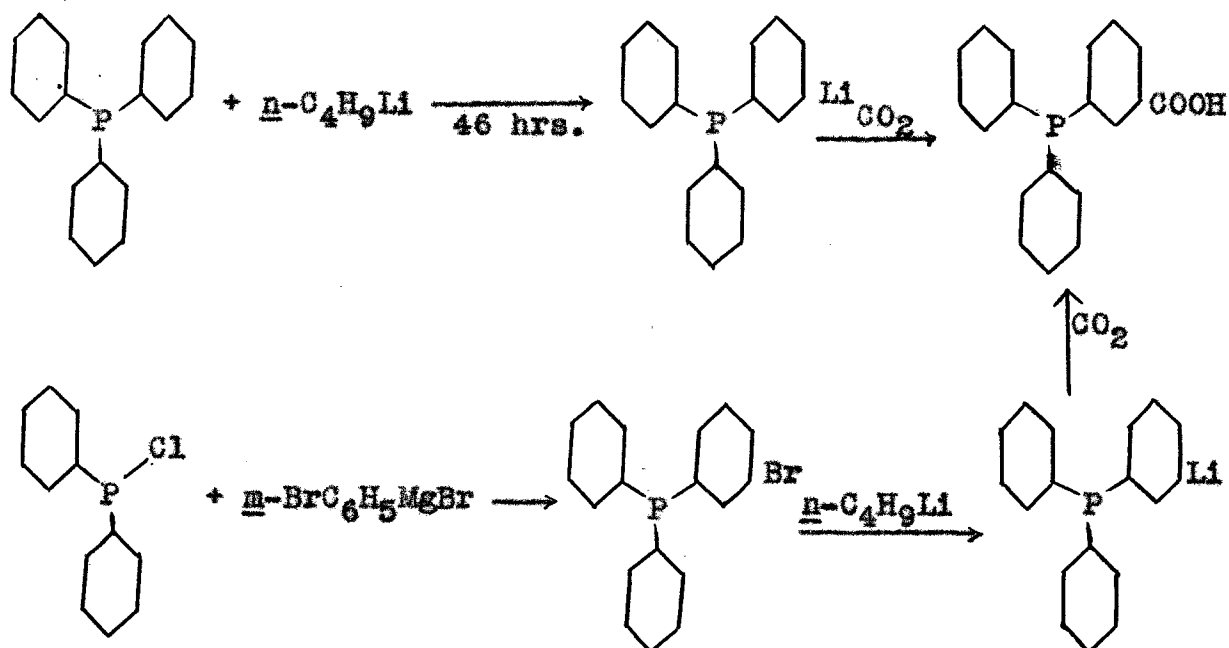
The phosphines are quite sensitive to oxidation reagents. The halogens add to them to form the pentavalent dihalide. Likewise, nitric acid and sulfuric acid react with them to form, respectively, the dinitrate and the disulfate. Consequently no nuclear substitution reactions have been reported that could have taken place with the trivalent phosphorus compounds.

*n*-Butyllithium has been found to metalate triphenylphosphine<sup>42</sup> to give, upon carbonation and hydrolysis, a mono-carboxytriphenylphosphine. The acid was synthesized in the

83. Michaelis and Kammerer, Ber., 8, 1306 (1875).



following manner: Diphenylchlorophosphine was treated with an excess of m-bromophenylmagnesium bromide to obtain m-bromophenyldiphenylphosphine. The latter compound was not isolated, but was subjected to steam distillation to remove bromobenzene. The ether solution was then treated for a short time with n-butyllithium and the product was carbonated. The resulting m-carboxyphenyldiphenylphosphine was identical with the product obtained by metalation of triphenylphosphine:



The validity of the halogen-metal interconversion reaction, with this type of compound, was tested by reacting n-butyllithium with p-bromophenyldiphenylphosphine. The melting point of a mixture of the resulting para acid and the meta acid was decidedly lower than the melting points of either of the pure compounds. It is of interest to note that triphenylamine also

undergoes hydrogen-metal interconversion to form a meta substitution product.

Michaelis and Soden<sup>48</sup> treated triphenylphosphine oxide with a mixture of fuming nitric and concentrated sulfuric acids to obtain a product that they believed to be the tri-p-nitrophenylphosphine oxide. However, Challenger and Wilkinson<sup>84</sup> have reduced the trinitro compound to the tri-amino derivative, then converted it, by means of the Sandmeyer reaction, to the same trichlorophenylphosphine oxide as the one prepared by treating phosphorus oxychloride with m-chlorophenylmagnesium bromide. The nitro group, therefore, is oriented to the meta position when triphenylphosphine oxide is nitrated. Nitration of triphenylphosphine dihydroxide<sup>48</sup> also results in the formation of tri-m-nitrophenylphosphine oxide.

Attempted halogenation of the triarylphosphines and oxides results in decomposition of the molecule.

Diphenylphosphinic<sup>85</sup> acid was nitrated by a mixture of fuming nitric and sulfuric acids to give a dinitro compound that, by analogy with the orientation of triphenylphosphine oxide, is di-m-nitrophenylphosphinic acid.

Michaelis and Benzinger<sup>86</sup> have obtained a mononitrophenylphosphonic acid by nitration of phenylphosphonic

84. Challenger and Wilkinson, J. Chem. Soc., 2675 (1924).

85. Dorken, Ber., 21, 1513 (1888).

86. Michaelis and Benzinger, ibid., 8, 1311 (1875); Ann., 188, 276 (1877).

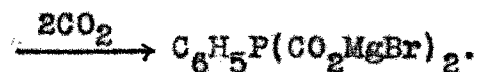
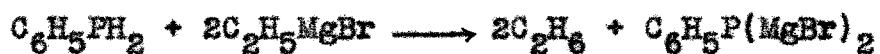
acid. The sulfonic group is a meta directing group and the phosphonic group bears a greater resemblance to this group than to the P=O group in triphenylphosphine oxide, which is also a meta directing group; therefore, there is little doubt that the nitration product is m-nitrophenylphosphonic acid.

The o-, m-, and p-tolylphosphonic acids<sup>81</sup> are more easily substituted than is phenylphosphonic acid. These acids can be halogenated without cleavage if the reaction mixture is kept quite cold. Chlorination of o-tolylphosphonic acid gives 2-methyl-5-chlorophenylphosphonic acid, and similar treatment of m-tolylphosphonic acid results in the formation of 2-chloro-3-methylphenylphosphonic acid. Nitration of p-tolylphosphonic acid gives 3-nitro-4-methylphenylphosphonic acid. In these three reactions the entering group has been directed ortho, meta, and para to the phosphonic group, while in no instance has it been directed meta to the methyl group; therefore, the phosphonic group has a weaker directive influence than the methyl group.

#### Reaction of Organometallic Compounds with Arylphosphines

Phenylphosphine, as would be expected from its similarity to aniline, reacts with ethylmagnesium bromide to liberate two molecular equivalents of ethane. The resulting dimagnesium bromide was not isolated, but its existence in

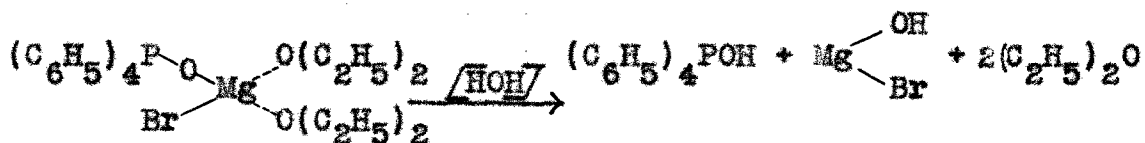
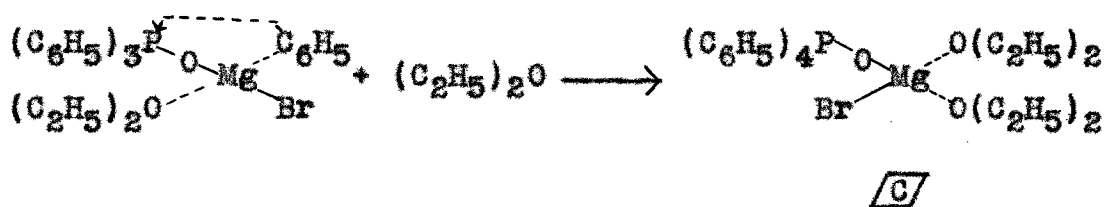
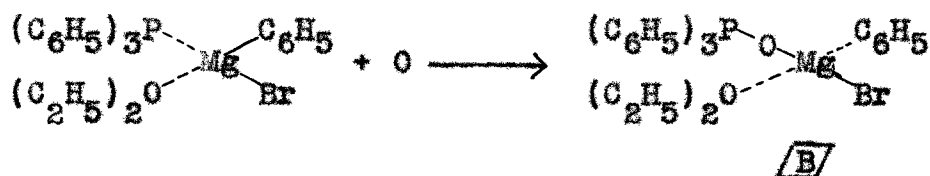
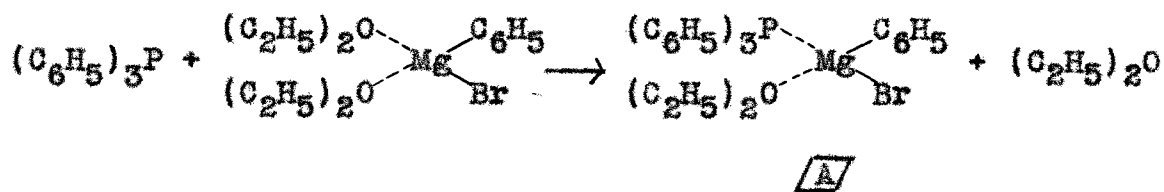
the brownish-green solution was shown by the isolation of the dimagnesium bromide salt of the acid corresponding to a substituted carbanic acid in the nitrogen series<sup>87</sup>:



Diphenylphosphine,  $(\text{C}_6\text{H}_5)_2\text{PH}$ , was shown to react with the Grignard reagent in accordance with the above reaction to give a monomagnesium bromide.

Triphenylphosphine has no active hydrogen, consequently it does not react with the Grignard reagent under ordinary circumstances. However, in the preparation of triphenylphosphine from phosphorus trichloride and phenylmagnesium bromide some tetraphenylphosphonium bromide was usually isolated. Further investigation showed that when oxygen was passed into a mixture of triphenylphosphine and phenylmagnesium bromide, and the resulting product was hydrolyzed with hydrobromic acid, a high yield of tetraphenylphosphonium bromide was obtained. Dodonow and Medox<sup>52</sup> have suggested the following mechanism for the reaction:

87. Job and Dusollier, Compt. rend., 184, 1454 (1927).



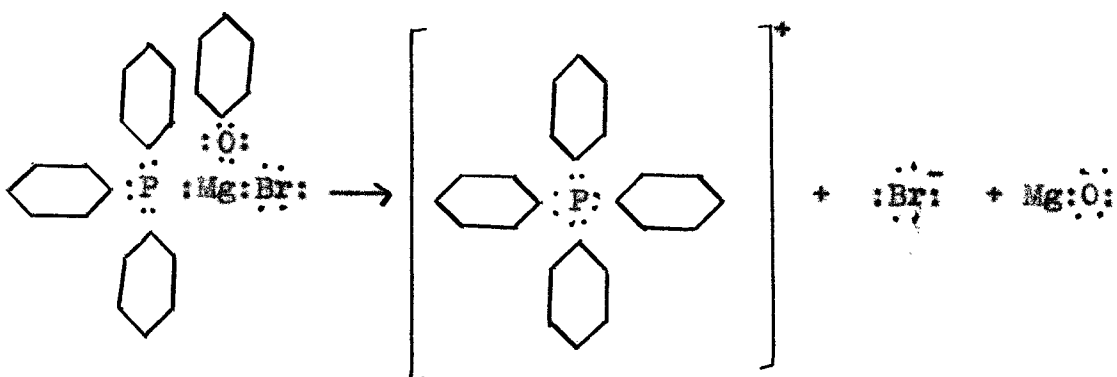
The coordination complexes **A** and **B** were assumed to explain the formation of the tetraphenylphosphonium bromide, which was obtained from the complex **C**. There were other possible courses that the reaction might take to give the same final products. Therefore, a series of experiments was planned and carried out for the purpose of establishing the true mechanism of this reaction.

It, at first, appeared highly improbable that a complex compound, such as compound **A**, would be oxidized at the

coördinate bond when an organometallic bond was present, or that triphenylphosphine would be oxidized in preference to the organometallic compound. Since the yields of phenol obtained by the oxidation of phenylmagnesium bromide<sup>88</sup> and phenyllithium<sup>42,89</sup> were much lower than the yields of tetraphenylphosphonium bromide obtained from these compounds, the organometallic compound was either not involved in the oxidation, or the triphenylphosphine acted as a catalyst for the reaction. Proof that the oxidation of the organometallic compound was not a step in this mechanism was obtained when lithium phenoxide failed to react with triphenylphosphine. The failure of the phenoxide to react also eliminated the proposed oxidation of complex  $\boxed{A}$  at the organometallic bond, for the phenoxide should react with triphenylphosphine to form the oxidized complex. A consideration of the electronic structure of the suggested oxidation complex supports the above evidence, for a rearrangement of this compound should give tetraphenylphosphonium bromide and magnesium oxide:

88. Gilman and Wood, J. Am. Chem. Soc., 48, 806 (1926).

89. Müller and Töpel, Ber., 72, 273 (1939).



No evidence for these products has been noted prior to hydrolysis of the reaction mixture with hydrobromic acid.

Triphenylphosphine, suspended in water, was not oxidized by oxygen gas unless a catalyst was present<sup>67</sup>. Since triphenylphosphine was soluble in ether, there was a possibility that the oxide was first formed and then reacted with the organometallic compound to give the phosphonium hydroxide. As a check on this mechanism, oxygen gas was passed into a cold ether solution of triphenylphosphine, but no appreciable oxidation occurred. This did not preclude the possibility that the organometallic compound acted as a catalyst in the conversion of the phosphine to the oxide, which then reacted as suggested above. That this was not the course of the reaction was shown by treating triphenylphosphine oxide with both phenyllithium and phenylmagnesium bromide<sup>52,90</sup>. In neither

90. Gilman and Vernon, J. Am. Chem. Soc., 48, 1063 (1926).

case was there any tetraphenylphosphonium bromide isolated, although the conditions for its preparation were closely parallel. These results were surprising because of the apparent similarity of the phosphine oxides and the carbonyl compounds:



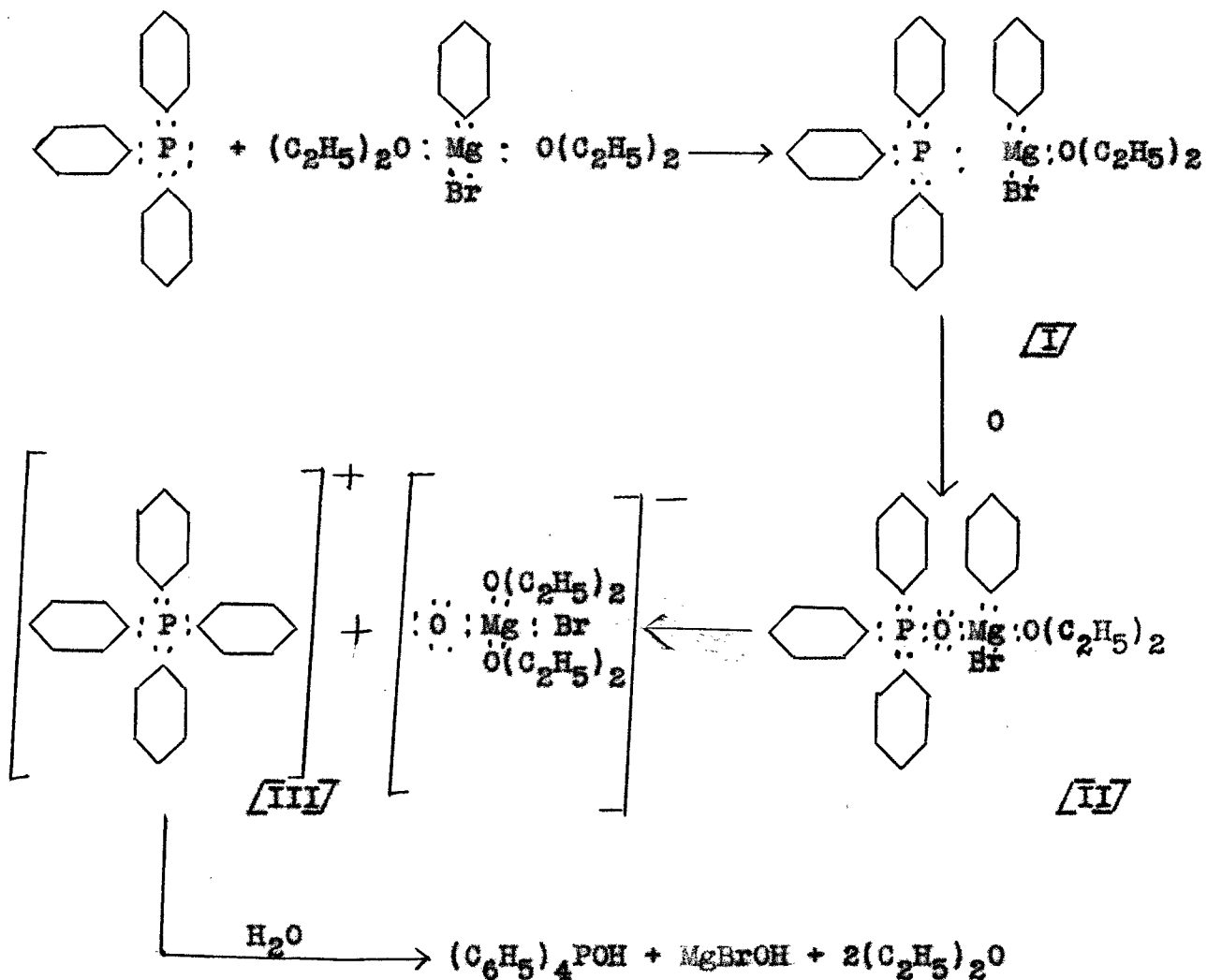
However, when these compounds are represented by their electronic structures a marked difference is at once evident. The oxygen of the carbonyl group is attached to the carbon atom by an active double bond while the oxygen in the phosphine oxide is held by a coordinate bond:



Since it has been shown that the reaction depended on neither the oxidation of triphenylphosphine, nor the oxidation of the organometallic compound, a reaction between triphenylphosphine and the organometallic compound was indicated. The quantitative recovery of triphenylphosphine, following the hydrolysis of a mixture of triphenylphosphine and phenyllithium, that had been refluxed for 1/2 hour, showed that the product of such a reaction was an unstable complex molecule. The yields of tetraphenylphosphonium bromide obtained from the corresponding organomagnesium, -lithium, and -sodium compounds (82%, 30%, and 0% respectively) furnished additional evidence for this mechanism. Magnesium compounds readily form complex



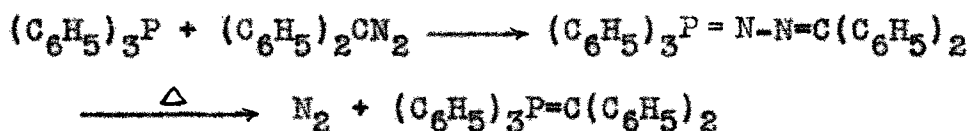
molecules and when the Grignard reagent was used the yield was high. The alkaline metals are strongly electropositive and have little tendency to form complex molecules or chelate compounds. The lower yield when phenyllithium was used indicated that the coordinate complex, if formed to as large an extent as with the Grignard reagent, was less stable and more likely to undergo side reactions. Since phenylsodium was insoluble in benzene, the nonpolar solvent used with it, complex formation appeared unlikely to occur, and no evidence for the formation of tetraphenylphosphonium bromide was found. These results indicate that the reaction takes place only when the coordinate complex is present and they may best be interpreted by the following mechanism, which is essentially that proposed by Dodonow and Medox:



According to this scheme, the complex compound **[I]** is oxidized to compound **[II]** which rearranges, with a 1,3- shift of the phenyl group attached to the magnesium to the more stable ion.

Triphenylphosphine is metalated by n-butyllithium to give a meta substitution product, as discussed in the preceding section.

Staudinger and Meyer<sup>91</sup> have prepared triphenylphosphinediphenylmethane by the interaction of triphenylphosphine with diphenyldiazomethane to produce a phosphazine which loses nitrogen when heated:

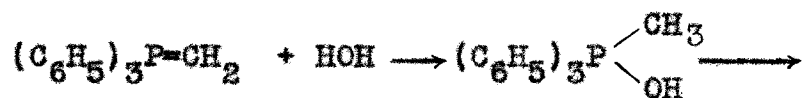
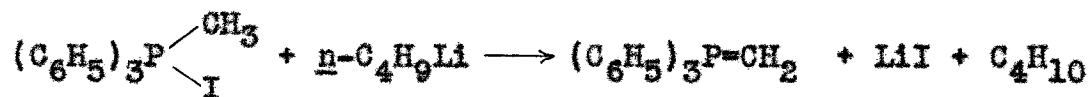


This compound was remarkable because of the fact that all five valences of the phosphorus atom were attached to carbon. However, since the properties of the compound resembled those of the tetramethyltriphenylmethylammonium prepared by Schlenk and Holtz<sup>92</sup> there was a question as to whether or not the five valences were equivalent. In the hope of gaining further knowledge concerning the valence of phosphorus, Coffman and Marvel<sup>93</sup> have investigated the reactions of alkali metal alkyls with phosphonium salts.

Triphenyldiphenylmethylphosphonium bromide reacts with *n*-butyllithium or triphenylmethylsodium to produce a good yield of triphenylphosphinediphenylmethylene. The other phosphonium salts that were used were methyl- and ethyltriphenylphosphonium iodides and isopropyltriphenylphosphonium bromide. These compounds reacted with an ether solution of

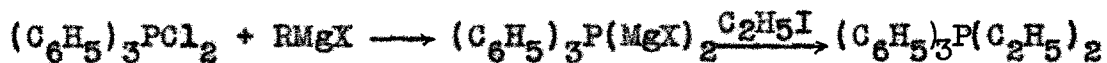
91. Staudinger and Meyer, Helv. Chim. Acta., 2, 635 (1919).
92. Schlenk and Holtz, Ber., 49, 603 (1916).
93. Coffman and Marvel, J. Am. Chem. Soc., 51, 3496 (1929).

n-butyllithium or triphenylmethylsodium to produce a colored solution, which was decolorized on exposure to moist air. The products isolated after decomposition were, respectively, diphenylmethyl-, diphenylethyl-, and diphenylisopropylphosphine oxides. To account for the formation of both triphenylphosphinediphenylethylene and the phosphine oxides, the assumption was made that the first product of the reaction was a phosphinemethylene that reacted with the moisture in the air to form a phosphonium hydroxide which decomposed to give the phosphine oxide and benzene<sup>48</sup>:



There was no indication in any of these reactions of the formation of a phosphorus compound in which five equivalent valences were combined with organic radicals.

Grignard and Savard<sup>94</sup> have reported the formation of a triphenyldiethylphosphine by the following sequence of reactions:



94. Grignard and Savard, Compt. rend., 192, 529 (1931).

However, Blount<sup>95</sup> has shown that the compound prepared by Grignard and Savard was triphenylethylphosphonium iodide. The melting point of this compound changes upon exposure to air, which probably accounts for the observation of Grignard and Savard that the melting point of a mixture of their compound and some authentic triphenylethylphosphonium iodide was depressed.

### Preparation of Arylamines

Aniline, the simplest of the aromatic amines, was isolated by Unverdorben<sup>96</sup>, in 1828, by the distillation of indigo. It was isolated from coal tar by Runge<sup>97</sup>, in 1834, and was synthesized by Zinin<sup>98</sup>, in 1842, by the reduction of nitrobenzene. In 1843 Hofmann<sup>99</sup> showed that the bases from these three sources were identical. The basis of our knowledge of aniline and its allies was laid down in 1846-51 by A. W. Hofmann in his "Contributions to our knowledge of the volatile organic bases."<sup>100</sup> The primary aromatic amines are either solids or high-boiling liquids, and are easily accessible by reduction of the nitro compounds that are

95. Blount, J. Chem. Soc., 337 (1932); 1891 (1931).
96. Unverdorben, Annalen der physik und chemie, 8, 397 (1828).
97. Runge, ibid., 31, 65 (1834).
98. Zinin, Ann., 44, 286 (1842).
99. Hofmann, ibid., 47, 37 (1843).
100. Hofmann, ibid., 79, 11 (1851) and earlier papers.

obtained by direct nitration. They are the starting material for the preparation of a large number of compounds of great technical importance. Consequently, there is scarcely any class of substances which has been investigated more thoroughly and with more success.

There are a number of methods of preparing primary aromatic amines<sup>101</sup> but they are generally prepared by the reduction of the nitro compounds.

A halogen atom can be replaced by an amino group if a mixture of the aromatic halide and ammonium hydroxide are heated in a pressure bomb. The halogen atom is usually replaced with difficulty, hence the reaction is used only in special cases, such as the preparation of 4-aminodibenzofuran<sup>102</sup>, where a nitro group cannot be introduced.

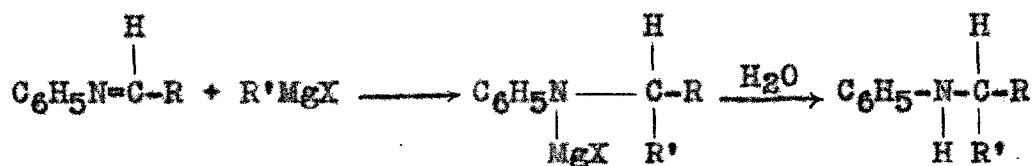
A hydroxyl group can be replaced by an amino group in certain aromatic compounds if the hydroxy compound is heated under pressure with a solution of ammonium sulfite and ammonia.

The Hofmann rearrangement may be used in special cases for the preparation of primary amines. The primary aromatic amines may be converted to secondary and tertiary amines.

101. For references to original literature the reader is referred to Hickinbottom, "Reactions of Organic Compounds", Longmans, Green and Co., New York, (1936) pp. 313-318.

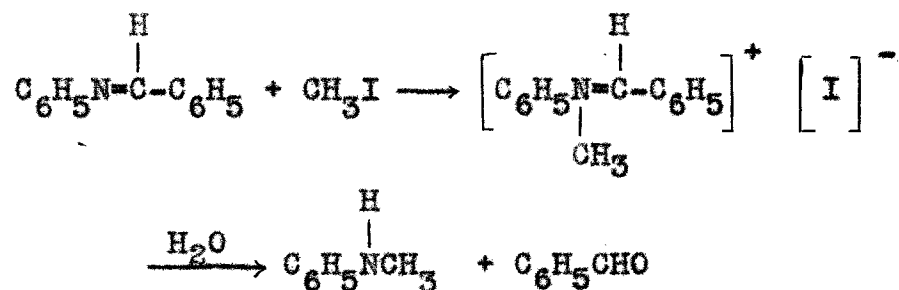
102. Gilman and Van Ess, J. Am. Chem. Soc., 61, 1365 (1939).

They can be alkylated<sup>103</sup> by heating with alkyl halides or alkyl sulfates, such as dimethyl sulfate. In these alkylation reactions, a mixture of the secondary and tertiary amines is usually obtained. These may be separated by treating the mixture with acetic anhydride or benzenesulfonyl chloride, with which only the secondary base reacts to give an amide. The amide is nonbasic while the tertiary base is soluble in dilute mineral acids. The secondary base can be recovered from the amide by hydrolysis. Several methods are known by which monoalkyl anilines can be obtained unaccompanied by the tertiary bases. For example, acetanilide forms a sodium derivative which reacts readily with alkyl halides to give N-alkylacetanilides that can be hydrolyzed to give the secondary amine. Also aniline condenses with aldehydes and with some ketones to form the so-called Schiff's bases. These bases can be reduced to secondary amines by sodium and alcohol. Treatment of a Schiff's base with a Grignard reagent forms an addition complex that is hydrolyzed by water to give a secondary amine:

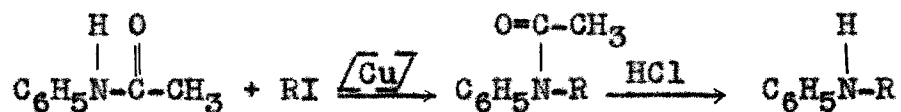


103. Sidgwick, Taylor and Baker, "Organic Chemistry of Nitrogen", Oxford University Press, New York (1937) pp. 57-61.

Another method consists in treating the Schiff's base with methyl iodide or dimethyl sulfate. A quaternary salt is formed which is easily hydrolyzed by water to give an N-methylamine:



Since the aromatic halogen compounds are more stable than the aliphatic halides, the secondary and tertiary aromatic amines are more difficult to prepare. The reaction, however, is facilitated by the use of copper bronze or of cuprous iodide, potassium carbonate<sup>104</sup>, and higher temperatures. The introduction of one or two groups is usually governed, more or less, by the quantity of aryl halide present. However, if a diarylamine is desired, it is best to use the acetyl derivative of the amine as starting material:



Goldberg and Nimerovsky<sup>105</sup> treated a solution of

104. Goldberg, Ber., 39, 1691 (1906); 40, 4541 (1907); German Patent 185,663; 187,870.

105. Goldberg and Nimerovsky, Ber., 40, 2448 (1907).



anthranilic acid in nitrobenzene with iodobenzene and obtained a high yield of N,N-diphenylanthranilic acid. Copper powder and potassium carbonate were used as catalysts, and the reaction was carried out at the boiling point of nitrobenzene. Goldberg later attempted to duplicate this reaction using *p*-aminobenzoic acid in place of the anthranilic acid but obtained no condensation product<sup>106</sup>. An attempt has been made to condense *p*-iodobenzoic acid with diphenylamine, using these conditions, but the acid was decarboxylated before condensation had taken place<sup>42</sup>.

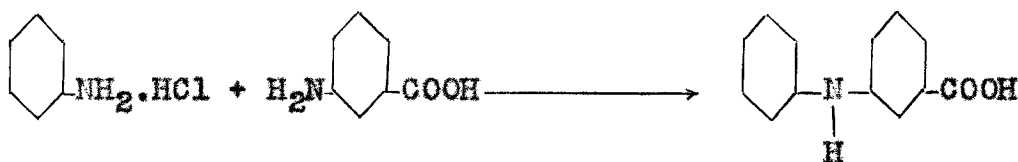
In an attempt to stabilize the carboxyl group, the methyl ester of *p*-aminobenzoic acid was prepared. This was treated with a large excess of iodobenzene; however, on the basis of the analysis, only one phenyl group was introduced to give methyl N-phenyl-*p*-aminobenzoate. Since the above reaction failed to give the desired tertiary amine, but did indicate that the methyl ester was a satisfactory reagent for this type of synthesis, methyl *p*-iodobenzoate was prepared. It condensed readily with diphenylamine to give methyl N,N-diphenyl-*p*-aminobenzoate. In this latter reaction a modification of the conditions used by Kawai<sup>107</sup>, in the preparation of *p*-nitrophenyldiphenylamine, was employed. The

106. Goldberg, Ber., 40, 4551 (1907).

107. Kawai, J. Chem. Soc. Japan, 49, 235 (1928) [C. A., 24, 80 (1930)].

only essential difference being that the reaction mass was mechanically stirred and the solvent, nitrobenzene, was replaced by a small quantity of xylene. Methyl *N,N*-diphenyl-*m*-aminobenzoate was prepared in the same manner. These esters were quantitatively hydrolyzed by boiling alkali to the corresponding acids.

Diphenylamine can also be obtained by heating equimolecular amounts of aniline and aniline hydrochloride<sup>108</sup> in an autoclave to 200-230°. Claus and Nicolaysen<sup>109</sup> treated *m*-aminobenzoic acid with aniline hydrochloride to obtain an acid which undoubtedly was *N*-phenyl-*m*-aminobenzoic acid:



#### Substitution in Arylamines

The primary amino group has a powerful activating influence on the ortho and para positions. Aniline chlorinates with great ease, the 2,4,6-trichloroaniline being formed. If chlorine is passed into a solution of aniline in hydrochloric acid the trichloro-derivative is formed but

108. DeLaire, Girard and Chapoteaut, Compt. rend., 63, 93 (1866).

109. Claus and Nicolaysen, Ber., 18, 2711 (1885).

most of it is hydrolyzed to 2,4,6-trichlorophenol<sup>110</sup>. Better yields of the chlorinated aniline are obtained by using acetic acid, chloroform, or benzene as the solvent. By carefully adding bromine to a solution of aniline in benzene, 4-bromoaniline, 2,4-dibromoaniline, and 2,4,6-tribromoaniline are obtained<sup>111</sup>. Aniline may be nitrated by nitrogen dioxide to give small quantities of o- and p-nitroaniline<sup>112</sup>. If a mixture of aniline and concentrated nitric acid is warmed picric acid is formed<sup>113</sup>. When aniline is dissolved in a large quantity of cold concentrated sulfuric acid and the calculated amount of nitric acid, diluted with concentrated sulfuric acid, is slowly dropped into the solution m- and p-nitroaniline are obtained with some o-nitroaniline as a by-product<sup>114</sup>. With concentrated sulfuric acid, aniline first forms benzenesulfamic acid, which when heated rearranges to give p-aminobenzenesulfonic acid or sulfanilic acid<sup>115</sup>.

Diphenylamine is brominated in alcohol solution to produce 2,4,2',4'-tetrabromodiphenylamine<sup>116</sup> which will, when

110. Hofmann, Ann., 53, 8, 35 (1895).  
111. Kekule, Zeitschrift für Chemie, 688 (1866).  
112. Bamberger, Ber., 27, 671 (1894).  
113. Muspratt and Hofmann, Ann., 57, 210 (1846).  
114. Hübner and Frerichs, Ber., 10, 1716 (1877); Hübner, Ann., 206, 299 (1881).  
115. Schmidt, ibid., 120, 132 (1831).  
116. Hofmann, ibid., 132, 166 (1864).

heated to 250° with bromine in the presence of iodine, form the decabromo compound<sup>117</sup>. When diphenylamine is warmed with fuming nitric acid 2,4,6,2',4',6'-hexanitrodiphenylamine is formed<sup>118</sup>. Fuming sulfuric acid reacts with diphenylamine to form N,N-diphenylbenzidine as the principal product<sup>119</sup>. No doubt the diphenylamine was first sulfonated in the para position followed by coupling.

Triphenylamine is halogenated<sup>120</sup> and nitrated<sup>121</sup> in the para positions.

Carbazole is a heterocyclic compound; however, it is closely related structurally to diphenyl amine.



It reacts with halogens and nitric acid to give 2- or 2,8-substituted compounds and when those positions are blocked the entering groups go to the 4- and 4,6- positions<sup>122</sup>.

117. Gessner, Ber., 9, 1511 (1876).  
118. Guehm, ibid., 7, 1401 (1874).  
119. Kadiere, ibid., 38, 3576 (1905).  
120. Wieland, ibid., 40, 4278 (1907).  
121. Herz, ibid., 23, 2537 (1890); Piccard and Larsen, J. Am. Chem. Soc., 39, 2006 (1917).  
122. Mazzara and Lamberti-Zanardi, Gazz. chim. ital., 22, 238 (1892); 26, 238 (1896); Tucker, J. Chem. Soc., 549 (1926); 1144 (1924).

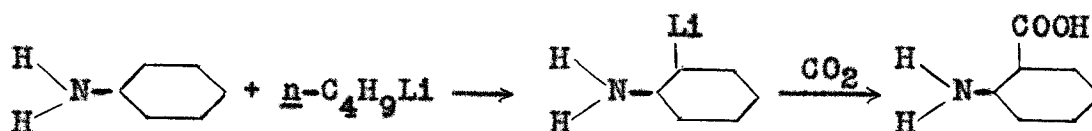
### Reaction of Organometallic Compounds with Arylamines

The investigations in this field have not been extensive. As previously mentioned, Houben and co-workers<sup>20</sup> have treated a number of mono- and dialkylated anilines with a Grignard reagent, carbonating the mixtures at high temperatures. In each instance they isolated the corresponding *p*-carboxylic acid. Then Oddo<sup>21</sup> treated diphenylamine with a Grignard reagent under similar conditions and isolated a monobasic carboxylic acid melting at 152°. Since the acid prepared by Claus and Nicolaysen<sup>109</sup> from aniline hydrochloride and *m*-aminobenzoic acid melts at 220°, *N*-phenylanthranilic acid melts at 186°, and *N*-phenyl-*p*-aminobenzoic acid melts at 156°, there is little doubt that Oddo's acid is *N*-phenyl-*p*-aminobenzoic acid. Oddo also found that carbazole will react with the Grignard reagent to give, upon carbonation at high temperatures, an acid that was later shown to be carbazole-4-carboxylic acid.

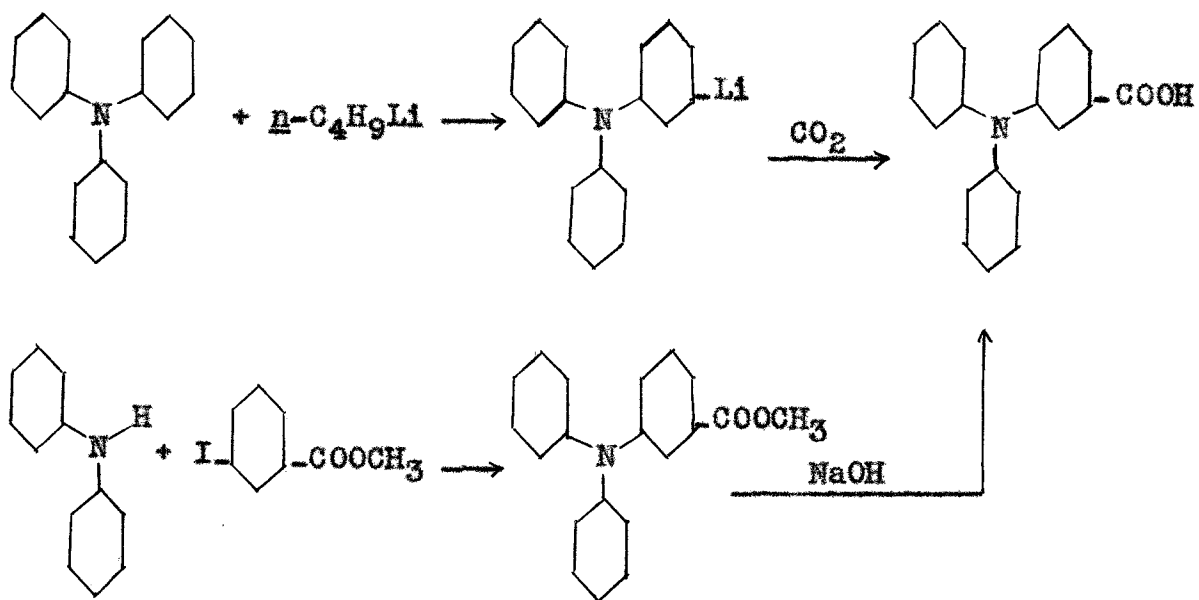
Gilman and Kirby<sup>30</sup> have found that carbazole and *N*-ethylcarbazole undergo a hydrogen-metal interconversion when treated with an ether solution of *n*-butyllithium to give carbazole-4-carboxylic acid and 5-ethylcarbazole-4-carboxylic acid, respectively. Mercuration of 5-ethylcarbazole, however, took place in the 2-position or *para* to the nitrogen atom.

Aniline<sup>25,42</sup> was treated with slightly more than one

equivalent of n-butyllithium in excess of that required to react with the two active hydrogen atoms of the amino group. After refluxing for two days the reaction mixture was carbonated and anthranilic acid was isolated:



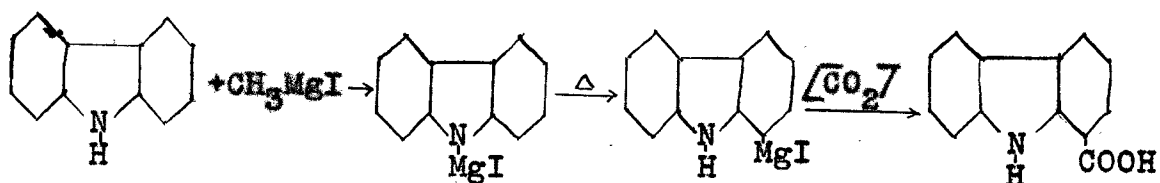
The yield was quite low as was the case with carbazole. The yield of N-phenylanthranilic acid obtained from diphenylamine<sup>25</sup> was slightly higher, but the yield was less than 15% of the theoretical amount. n-Butylaniline reacted with n-butyllithium under similar conditions to give a 2% yield of N-butylanthranilic acid. Since in all previous reactions of this type with compounds containing nitrogen, oxygen, or sulfur directly attached to the nucleus, the lithium atom was substituted in the position ortho to the hetero atom, it was expected that triphenylamine would also be substituted in the ortho position. However, the compound isolated was shown to be the meta substitution product by the following sequence of reactions:



Triphenylamine and triphenylphosphine have undergone hydrogen-metal interconversion in the meta position, while ortho substitution has been observed when primary or secondary amines are reacted under similar conditions. Because of the similarity of the chemical properties of other phosphorus and nitrogen compounds, it may be assumed that the hydrogen-metal interconversion reaction will take the same course with phenylphosphine and diphenylphosphine as it has taken with aniline and diphenylamine.

The reaction of n-butyllithium with triphenylamine and triphenylphosphine must take place by direct substitution. The primary and secondary compounds react with the active organometallic compounds to form a salt which may form an organometallic compound either by undergoing a rearrangement

or by direct substitution. The metal attached to the hetero element may rearrange by a 1,3- shift to give an ortho substituted product under the mild conditions used by hydrogen-metal interconversion reactions with organolithium compounds; or by a double 1,3- shift to give a para substitution product under the more severe conditions required for metalation with the Grignard reagent. Since the organometallic compounds are commonly characterized by converting them to carboxylic acids with carbon dioxide, the question may be asked as to whether the rearrangement takes place prior to, or during the carbonation. Mr. C. G. Stuckwisch<sup>123</sup> has shown that carbazole reacts with methylmagnesium iodide to give a product that does not give a color test<sup>124</sup>. When this product was heated prior to carbonation a positive color test was obtained. It is, therefore, quite probable that the reaction takes place in the way indicated in the following equation:



The high temperature required for this reaction would favor the rearrangement mechanism. It remains to be seen whether

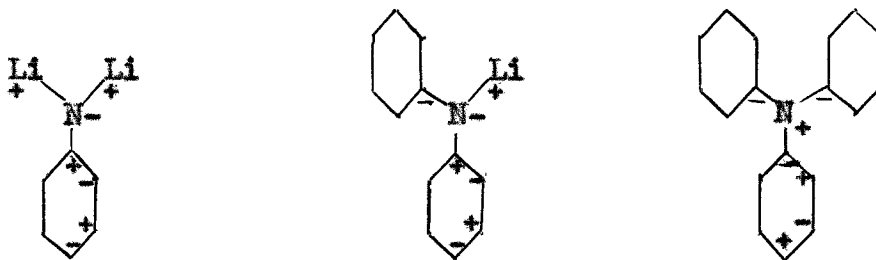
123. Gilman and Yablunsky, J. Am. Chem. Soc., **63**, 839 (1941).

124. Gilman and Schulze, ibid., **47**, 2002 (1925).



carbazole, diphenylamine, or aniline will form an organo-metallic compound when they are treated with n-butyllithium, equivalent in amount to the active hydrogen present and under the mild conditions employed for the hydrogen-metal inter-conversion reaction with organolithium compounds.

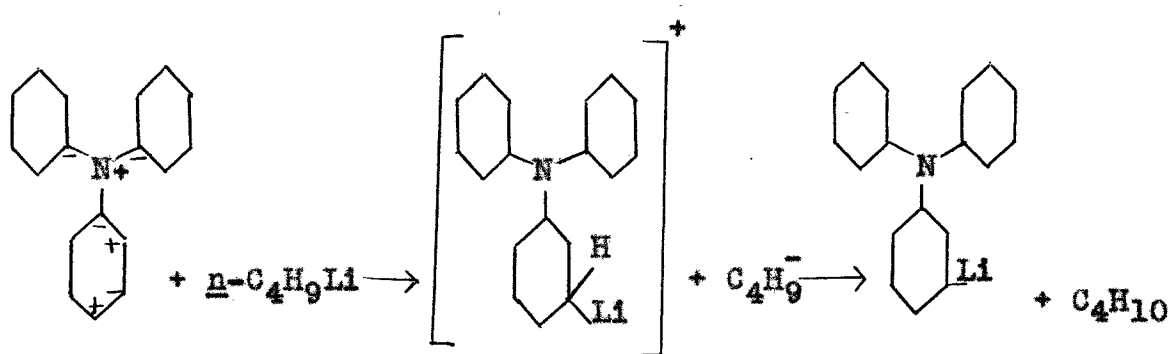
By making the assumption that the phenyl group is negative with respect to the nitrogen atom, a mechanism can be constructed that explains equally well the ortho substitution of the primary and secondary compounds and the meta substitution of the tertiary compounds. The lithium salt of the primary and the secondary compounds would differ in polarity<sup>125</sup> from the tertiary compounds:



Then according to the substitution mechanism proposed by Pfeiffer and Wizinger<sup>126</sup>, when the RLi compound comes in contact with the aromatic molecule at the point of strongest negative polarity it may dissociate to form a complex ion which may form a neutral molecule by the expulsion of a proton:

125. Ingold, Chem. Rev., 15, 225 (1934).

126. Pfeiffer and Wizinger, Ann., 461, 132 (1928).



Since there is a difference in the orientation when the Grignard reagent and organolithium compounds are used, it is probable that the rearrangement mechanism is followed by the  $\text{RMgX}$  compounds while the more active  $\text{RLi}$  compounds undergo hydrogen-metal interconversion reactions as described above.

## EXPERIMENTAL

### Preparation of Triphenylphosphine

Triphenylphosphine was prepared in general accordance with a method reported in the literature<sup>33,52</sup>. The Grignard reagent, prepared from 15.6 g. (0.64 g. atom) of magnesium and 94.2 g. (0.6 mole) of bromobenzene, was slowly added to an ether solution of 18 g. (0.13 mole) of phosphorus trichloride. The reaction was carried out in a nitrogen atmosphere and the flask was cooled with an ice bath. Agitation of the reaction mixture was secured with a motor driven stirrer. The reaction product was decomposed with dilute hydrochloric acid (33 cc. of concentrated hydrochloric acid and 240 cc. of water). The ether layer was withdrawn and distilled. The triphenylphosphine came over a 175-8°/3 mm. and melted at 78° without additional purification. The yield was 70 - 75% of the theoretical, based on the phosphorus trichloride used.

### Reaction of Triphenylphosphine with n-Butyllithium

The n-butyllithium solutions used in this and the following reactions with compounds containing phosphorus were

prepared<sup>13</sup>, filtered<sup>127</sup>, and standardized<sup>128</sup> in the customary manner.

An ether solution of 0.16 mole of n-butyllithium was transferred to a nitrogen-filled three-necked flask which contained 12.1 g. (0.05 mole) of triphenylphosphine and the volume was made up to 250 cc. with ether. The solution was refluxed with stirring for forty-six hours. It was then carbonated by pouring small portions at a time into a liter flask containing one pound of crushed solid carbon dioxide moistened with ether. The reaction mixture was decomposed with dilute hydrochloric acid. The ether extract was shaken with an excess of 5% potassium hydroxide solution; the alkaline layer was treated with Norit and acidified by pouring it into a beaker containing ice and an excess of concentrated hydrochloric acid. A 6 g. yield of a semi-solid acid was secured. This acid was dissolved in glacial acetic acid and placed in the refrigerator. The crystals formed, when recrystallized from alcohol, melted at 157°. The purified product weighed 0.9 g. which represents a 5.9% yield. A mixed melting point with an authentic sample showed the compound to be m-carboxyphenyl-diphenylphosphine.

127. Gilman, Langham and Moore, J. Am. Chem. Soc., 62, 2327 (1940).

128. Gilman, Wilkinson, Fishel and Meyers, ibid., 45, 150 (1923).

Anal. Calcd. for  $C_{19}H_{15}O_2P$ : P, 10.12; Neut. Eq., 306.1. Found<sup>129</sup>: P, 10.38 and 10.46; Neut. Eq., 307.5

A small quantity of benzoic acid was isolated from the acid filtrate.

Attempted Short Time Reaction of Triphenylphosphine  
With n-Butyllithium

An ether solution of 0.25 mole of triphenylphosphine and 0.25 mole of n-butyllithium was stirred in a nitrogen-filled flask for 1/2 hour before it was carbonated in the customary manner. The solution was acidified with dilute hydrochloric acid, then the ether layer was extracted with dilute potassium hydroxide. The extract, when acidified, became slightly cloudy but no acid material precipitated out. The recovery of triphenylphosphine was practically quantitative.

Preparation of p-Bromophenyldiphenylphosphine

An ether solution of 25.7 g. (0.1 mole) of p-bromophenyldichlorophosphine was slowly added to a vigorously

129. The sample was digested with sulfuric acid and the phosphorus was determined by the gravimetric method. Pregel, "Quantitative Organic Microanalysis", P. Blakiston's Son and Co., Philadelphia, 3rd. English edition, (1937) pp. 128-30.

stirred solution of 0.22 mole of phenylmagnesium bromide in ether. After refluxing for two hours the reaction mixture was hydrolyzed with dilute hydrochloric acid. The ether extract was dried over anhydrous calcium chloride and the ether was removed by distillation. The *p*-bromophenyldiphenylphosphine was distilled under reduced pressure (b.p. 205 - 210°/4 mm.). The yield was 23 g. (67% of theoretical). Also, 4.2 g. of biphenyl was isolated from the reaction.

Anal. Calcd. for  $C_{18}H_{14}PBr$ : C, 63.3; H, 4.11; P, 9.09. Found: C, 63.6; H, 4.20; P, 9.23.

#### Preparation of *p*-Carboxyphenyldiphenylphosphine

A solution of 6.82 g. (0.02 mole) of *p*-bromophenyldiphenylphosphine in a mixture of 30 cc. of ether and 20 cc. of benzene was added to 60 cc. of ether containing 0.02 mole of *n*-butyllithium. The solution was stirred for 30 minutes in a nitrogen atmosphere before it was carbonated with solid carbon dioxide. The reaction mixture was hydrolyzed with dilute hydrobromic acid solution, then the ether layer was extracted with dilute potassium hydroxide solution. The alkaline solution was warmed with Norit and the acid was obtained by pouring the solution into a mixture of concentrated hydrochloric acid and ice. The white precipitate weighed 3.5 g. and represented a 57% yield. Three

recrystallizations from glacial acetic acid gave a pure product melting at 156°.

Anal. Calcd. for  $C_{19}H_{15}O_2P$ : P, 10.13. Found: P, 10.24 and 10.32.

#### Preparation of Phenylidichlorophosphine

A mixture of 30 g. of aluminum chloride, 150 g. of benzene and 200 g. of phosphorus trichloride<sup>43</sup> was refluxed in a round-bottomed flask having a condenser unit sealed to the neck. The top of the condenser was attached to a U-tube which in turn was attached to a calcium chloride tube. After 30 hours of heating, the evolution of HCl fumes was not noticeable. The solution was poured into 400 cc. of petroleum ether (b.p. 60 - 68°). The mixture was shaken at short intervals for two hours, then the two layers were separated. The heavy syrupy layer containing most of the aluminum chloride was discarded. The lighter petroleum ether solution was transferred to a distilling flask and was heated until no more distillate could be collected with the heating bath at 150°. The residue was once more poured into petroleum ether and the mixture was allowed to stand in a separatory funnel for 12 hours. A few grams of viscous liquid collected at the bottom. This was removed and the petroleum ether solution was distilled with a slow stream of carbon dioxide. The fraction boiling at 218 - 225° was

collected. The average yield for several runs was 32.6., or about 13% of the theoretical yield based on the phosphorus trichloride used.

#### Preparation of Diphenylchlorophosphine

A mixture of 26.2 g. (0.1 mole) of triphenylphosphine and 17.9 g. (0.1 mole) of phenyldichlorophosphine was placed in a round-bottomed flask sealed to an air condenser. The condenser was closed with a calcium chloride tube and the flask was heated in a metal bath at 280° for 4 hours, then at 300° for 6 hours. The dark colored oil was distilled in a carbon dioxide atmosphere. The yield was 6.5 g., or 29.5 per cent of the theoretical amount of a viscous liquid boiling at 316 - 320° 56.

#### Preparation of *m*-Carboxyphenyldiphenylphosphine

A benzene-ether solution containing 0.03 mole of *m*-bromophenylmagnesium bromide was slowly dropped into a rapidly stirred ether solution of 6.6 g. (0.03 mole) of diphenylchlorophosphine. The reaction vessel was filled with nitrogen and cooled with an ice bath. When the calculated quantity of Grignard solution was added, a color test<sup>134</sup> indicated a slight excess (previous color tests were negative). The solution was hydrolyzed with dilute



hydrochloric acid and was subjected to steam distillation to remove the bromobenzene. No attempt was made to isolate the m-bromophenyldiphenylphosphine, but the ether extract was dried over anhydrous sodium sulfate, and was added to 0.06 mole of n-butyllithium. The solution was stirred in a nitrogen atmosphere for 30 minutes before it was carbonated with dry ice. After hydrolysis with hydrochloric acid the ether layer was extracted with dilute potassium hydroxide. The alkaline solution was warmed with Norit and acidified with cold hydrochloric acid. A yield of 1 g. (10.9% of theoretical based upon diphenylchlorophosphine used) of acid was obtained which after recrystallizing from dilute acetic acid melted at 157°. A mixed melting point determination with the acid obtained by metalation of triphenylphosphine showed no depression.

#### Oxidation of m-Carboxyphenyldiphenylphosphine

An alkaline solution of 0.2 g. (0.00065 mole) of m-carboxyphenyldiphenylphosphine was stirred for one hour with enough potassium permanganate to maintain a pink color. The manganese dioxide was filtered out and washed free of soluble salts. The alkaline solution was treated with Norit and the solution was acidified with hydrochloric acid. The m-carboxyphenyldiphenylphosphine oxide gradually crystallized from the aqueous solution. The pure acid melted at 232°

after crystallization from alcohol. The yield was 0.12 g. or 57% of the theoretical amount.

Anal. Calcd. for  $C_{19}H_{15}O_3P$ : P, 9.63. Found: P, 10.12 and 10.09.

Preparation of Tetraphenylphosphonium Bromide  
from Triphenylphosphine

With phenylmagnesium bromide

According to the procedure outlined by Dodonov and Medox<sup>52</sup>, the filtered<sup>127</sup> solution of the Grignard reagent, prepared from 9.56 g. of bromobenzene and 1.5 g. of magnesium, was added to 4 g. of triphenylphosphine. The total volume of the solution was 75 cc. It was allowed to stand at room temperature for 10 minutes, then dry oxygen gas was passed over the surface of the vigorously stirred solution for 90 minutes. A solid soon began to form in the flask. At the end of the oxidation period a solution of hydrobromic acid (9.5 cc. 48% HBr to 20.5 cc.  $H_2O$ ) was added and the solid was broken up and washed, in a separatory funnel, three times with ether. The aqueous suspension was warmed and the salt was allowed to crystallize. The 5.75 g. of crystals, melting at  $282-3^\circ$ , corresponded to an 82.6% yield of tetraphenylphosphonium bromide dihydrate. One crystallization from alcohol sufficed to raise the melting point to  $287^\circ$  52.

With phenyllithium

The phenyllithium prepared from 9.56 g. of bromobenzene and 0.9 g. of lithium was filtered and added to 4 g. of triphenylphosphine. The reaction was carried out exactly as described above for phenylmagnesium bromide and 2.15 g. or a 31% yield of the dihydrate of tetraphenylphosphonium bromide was obtained. A duplicate run gave a 30% yield of the dihydrate of tetraphenylphosphonium bromide.

With phenylsodium

The phenylsodium was prepared by pressing 9 g. of sodium wire into a 500 cc. three-necked flask containing 100 cc. of dry benzene. Mechanical stirring was provided and 10 g. of diphenylmercury was added in small portions against a counter current of dry nitrogen. After stirring for three hours, the suspension of phenylsodium was decanted under a strong stream of nitrogen into a duplicate flask. The amalgam was washed several times with dry benzene and the washings were added to the phenylsodium suspension. Four grams of triphenylphosphine were added and the suspension was stirred for 30 minutes. Oxygen was passed into the flask for 90 minutes. Since a color test<sup>124</sup> indicated the presence of unreacted phenylsodium, the oxygen was passed into the flask for an additional 4 1/2 hours before it was treated with hydrobromic acid. No tetraphenylphosphonium bromide was obtained. This reaction was not checked.

No record was made of the quantity of triphenylphosphine recovered from these reactions.

Attempted Reaction of Phenyllithium with  
Triphenylphosphine Oxide

A suspension of 5.56 g. (0.02 mole) of triphenylphosphine oxide was added to a solution of phenyllithium prepared in the customary way from 4.91 g. (0.03 mole) of bromobenzene and 0.5 g. (0.06 g. atom) of lithium. After refluxing for 4 hours a color test indicated the presence of an organometallic compound. The mixture was hydrolyzed with a hydrobromic acid solution having the same concentration as that used in the preparation of tetraphenylphosphonium bromide. No tetraphenylphosphonium bromide was obtained. A 72% recovery of triphenylphosphine oxide, m.p. 152°, was realized.

Attempted Reaction of Phenylmagnesium Bromide with  
Triphenylphosphine Oxide

An ether solution of 5.56 g. (0.02 mole) of triphenylphosphine oxide was added to 41 cc. of 0.487/N phenylmagnesium bromide. The solution was warmed for a few minutes until a precipitate began to form. Stirring was continued for two hours. The mixture was carbonated with solid carbon dioxide and was hydrolyzed with hydrobromic acid. No

tetraphenylphosphonium bromide was obtained. The amount of triphenylphosphine oxide recovered was not recorded.

#### Attempted Reaction of Triphenylphosphine with

##### Lithium Phenoxide

A solution containing 0.025 mole of lithium phenoxide was prepared by dropping an ether solution of phenol into a clear solution of *n*-butyllithium until the mixture no longer gave a color test. Triphenylphosphine, 6.55 g. (0.025 mole) dissolved in ether, was added and the solution was refluxed with stirring for 3 hours. After hydrolysis with hydrobromic acid, no tetraphenylphosphonium bromide was found and 95% of the triphenylphosphine was recovered.

##### Oxidation of Phenyllithium<sup>89</sup>

Dry oxygen gas was passed into 145 cc. of 1.16 N phenyllithium solution in ether for 2 hours. The mixture was cooled with an ice bath. Water, slightly alkaline with potassium hydroxide, was added. The alkaline layer was separated and was treated with bromine water, according to the method of Autenrieth and Beattell<sup>130</sup>, for the quantitative determination of phenol. The yield of phenol was 21.6 per cent of the theoretical.

<sup>130</sup>. Autenrieth and Beattell, Arch.d.pharm., 248, 112 (1910).

Attempted Oxidation of Triphenylphosphine with  
Oxygen Gas

Dry oxygen gas was passed into a stirred ether solution of 4 g. of triphenylphosphine for 90 minutes. The flask was cooled with an ice bath. The ether solution was washed with dilute hydrobromic acid and was dried over anhydrous calcium chloride. The ether was removed and 4 g. of a white crystalline residue, melting at 79°, was obtained. Since triphenylphosphine oxide does not depress the melting point of triphenylphosphine, the residue was distilled. The compound came over at the boiling point of triphenylphosphine, 170 - 175°/4 mm., leaving no liquid residue in the flask. The temperature of the heating bath was kept below the boiling point of triphenylphosphine oxide, which was found to be above 225°/4 mm.

Oxidation of Triphenylphosphine with  
Potassium Permanganate

Triphenylphosphine can be converted to triphenylphosphine oxide in nearly quantitative yields by several oxidizing agents<sup>67,68,69,70</sup>; however, it was desirable to determine the fate of triphenylphosphine when it was subjected to the conditions used for the oxidation of a side chain. For this purpose 1.5 g. of powdered potassium permanganate

was added to a finely divided suspension of 2.22 g. (0.01 mole) of triphenylphosphine in water. The suspension was stirred for 8 hours and was filtered. The precipitate was dried and extracted with ether. The ether was evaporated and 2.73 g., a 98.3% yield, of triphenylphosphine oxide melting at 153 - 4° was obtained.

#### Reaction of Aniline with n-Butyllithium<sup>25</sup>

The n-butyllithium, prepared from 41.1 g. (0.3 mole) of n-butyl bromide and 4.16 g. (0.6 g. atom) of lithium metal, was strained through a glass wool plug into a nitrogen-filled flask containing 4.6 g. (0.05 mole) of aniline dissolved in ether. During the addition of the first one-third of the n-butyllithium solution, the reaction was quite vigorous. The reaction mixture was refluxed for 50 hours. During the course of the reaction a yellow precipitate formed and the solution became purple in color. The mixture was carbonated with crushed dry ice. Considerable effervescence was observed when water was added to the carbonated mixture. The insoluble carbonates were decomposed with hydrochloric acid and the solution was extracted with potassium hydroxide.

The ether solution was dried over anhydrous sodium sulfate and was distilled to give 2.9 g., a 63% recovery, of aniline and 4.5 g. of octane.

The alkaline extract was warmed to expel the ether, acidified with hydrochloric acid, made slightly basic with ammonium hydroxide and acid again with acetic acid. When, after standing over night, only a small black gummy precipitate formed, the filtrate was extracted with ether. The ether extract exhibited a fluorescence that is characteristic of ether solutions of anthranilic acid. The ether was evaporated and the residual oil resisted early attempts to cause it to crystallize. A small portion of the oil was dissolved in hydrochloric acid, diazotized, and added to an alkaline solution of  $\beta$ -naphthol. The red coupling product, when crystallized once from methanol, melted at  $270^{\circ}$ . A mixed melting point with  $\beta$ -naphtholazo-o-benzoic acid, prepared from anthranilic acid, was not depressed. Later 0.3 g., 4.2% of the theoretical yield, of anthranilic acid was isolated. The yield based on the unrecovered aniline was 7.1% of the theoretical amount.

#### Reaction of o-Bromoaniline with n-Butyllithium

The n-butyllithium solution, prepared from 41.1 g. (0.3 mole) of n-butyl bromide and 4.16 g. (0.6 g. atom) of lithium, was added to an ether solution of 8.6 g. (0.05 mole) of o-bromoaniline. Ether was added to make the volume of the solution up to 250 cc. The solution was refluxed for 40 minutes before it was carbonated with dry ice. The reaction



mixture was hydrolyzed with hydrochloric acid and then made alkaline with potassium hydroxide. Three grams, or 34.9%, of the o-bromoaniline were recovered from the ether layer.

The alkaline extract was acidified with HCl, made alkaline with ammonium hydroxide and acid once more with acetic acid. The acid solution was extracted with ether and the ether was distilled off to give 2.4 g., or a 35% yield, of anthranilic acid which melted at 142 - 3°. The yield based on the unrecovered o-bromoaniline was 54% of the theoretical amount.

#### Attempted Reaction of p-Bromoaniline with n-Butyllithium

The same molar quantities of butyllithium and p-bromoaniline were used in this experiment as were used above in the reaction with o-bromoaniline. The method of carrying out the experiment and working up the product was also identical to the above described procedure. The product was an oil that resisted all efforts to change it to the crystalline form. A recovery of 1.2 g., or 14%, of the p-bromoaniline was obtained.

#### Reaction of Triphenylamine with n-Butyllithium<sup>26</sup>

A reaction mixture consisting of 12.25 g. (0.05 mole) of triphenylamine, 0.1 mole of n-butyllithium, and ether

was stirred and refluxed for forty-eight hours prior to carbonation with crushed dry ice. The yield of acidic material was 2.16 g. from which was isolated 1.00 g., or 7% of the theoretical amount, of yellow crystals melting at 186°. The compound was found to be identical (mixed melting point) with the authentic sample of N,N-diphenyl-m-aminobenzoic acid prepared below. Another run, identical with the one described above with the exception that 0.5 g. of copper bronze was added to the reaction mixture, gave 1.02 g. or approximately the same yield of pure acid.

Anal. Calcd. for  $C_{19}H_{15}O_2N$ : N, 4.84. Found: N, 4.93 and 5.10.

#### Preparation of Methyl N, N-diphenyl-m-aminobenzoate<sup>26</sup>

A mixture of 12 g. (0.05 mole) of methyl m-iodobenzoate, 9 g. (0.051 mole) of diphenylamine, 8.5 g. of powdered anhydrous potassium carbonate, 2 cc. of xylene, and 2 g. of copper bronze powder was stirred and heated to 190 - 200° for eleven hours. The cold mixture was extracted with dry ether and the ether was removed by distillation. Since the residue could not be induced to crystallize it was distilled. A yield of 10.1 g., or 70.5% of the theoretical quantity of the ester boiling at 205°/3 mm., was obtained. The ester is a light yellow viscous liquid.

Anal. Calcd. for  $C_{20}H_{17}O_2N$ :  $OCH_3$ , 10.23. Found:

OCH<sub>3</sub>, 10.08.

Preparation of N,N-Diphenyl-m-aminobenzoic Acid<sup>26</sup>

A mixture of 2 g. of methyl N,N-diphenyl-m-aminobenzoate and 20 cc. of 10% potassium hydroxide solution was refluxed vigorously for thirty minutes. Acidification of the resulting solution gave a quantitative yield of acid material which, when crystallized once from acetic acid, melted at 186° and proved to be identical with the acid obtained by metalation of triphenylamine with n-butyllithium.

Decarboxylation of N,N-Diphenyl-m-aminobenzoic acid<sup>26</sup>

A mixture of 0.25 g. of N,N-diphenyl-m-aminobenzoic acid and 2 g. of soda-lime was ground in a mortar and placed in a small pyrex test tube. A bubble counter was attached to the test tube, and the mixture was gently heated with a free flame until gas was no longer evolved. The soda-lime mixture was extracted with ether which was in turn extracted with dilute potassium hydroxide. The ether was removed and the residue was crystallized from alcohol to give 0.2 g. (94% of theoretical quantity) of triphenylamine, melting at 125°. A mixed melting point determination with an authentic specimen showed no depression.

Attempted Preparation of N,N-Diphenyl-p-aminobenzoic  
Acid

A mixture of 4.96 g. (0.02 mole) of p-iodobenzoic acid, 5.07 g. (0.03 mole) of diphenylamine, 4 g. of potassium carbonate, 30 cc. of nitrobenzene and a small quantity of potassium iodide and copper bronze was heated in a metal bath at 205 - 215° for 22 hours. The nitrobenzene was removed by steam distillation and dilute potassium hydroxide was added to the residue. The cold solution was filtered and the filtrate was treated with Norit. Upon acidification 0.075 g. of acid material was obtained. This was shown, by a mixed melting point determination, to be p-iodobenzoic acid.

Preparation of Methyl N,N-Diphenyl-p-aminobenzoate<sup>26</sup>

The suspension resulting from the mixing of 13 g. (0.05 mole) of methyl p-iodobenzoate, 9 g. (0.051 mole) of diphenylamine, 8.5 g. of powdered anhydrous potassium carbonate, 2 cc. of xylene, and 2 g. of copper bronze was stirred and heated at 200° for fifteen hours. The oil, obtained by extraction of the reaction mass with ether and subsequent removal of the ether, crystallized from cyclohexane to give 10 g., a 66.5% yield, of the ester melting at 89°.

Anal. Calcd. for  $C_{20}H_{17}O_2N$ : N, 4.62. Found: N, 4.78.

Preparation of N,N-Diphenyl-p-aminobenzoic Acid<sup>26</sup>

A 3 g. sample of methyl N,N-diphenyl-p-aminobenzoate was added to 30 cc. of a 10% potassium hydroxide solution and the mixture was refluxed for 30 minutes. The solution was poured into a hydrochloric acid-ice mixture to give a quantitative yield of acid which melted at 202° after crystallization from acetic acid.

Anal. Calcd. for C<sub>19</sub>H<sub>15</sub>O<sub>2</sub>N: N, 4.84. Found: N, 4.85 and 4.82.

Preparation of Methyl N-Phenyl-p-aminobenzoate<sup>26</sup>

Seventy-five grams (0.2 mole) of iodobenzene, 7.5 g. (0.05 mole) of methyl p-aminobenzoate, 13.8 g. of anhydrous potassium carbonate, one-half gram of potassium iodide, 1 g. of copper bronze, and 40 cc. of nitrobenzene were mixed in a round-bottomed flask, and the mixture was heated to 200° for six hours. The excess iodobenzene and the nitrobenzene were removed by steam distillation. The oil obtained from the ether extract of the residue was crystallized from methanol to give 3 g., or a 27% yield, of the ester melting at 115°.

Anal. Calcd. for C<sub>14</sub>H<sub>13</sub>O<sub>2</sub>N: N, 6.17. Found: N, 6.20.

### Preparation of N-Phenyl-p-aminobenzoic Acid<sup>26</sup>

One gram of methyl N-phenyl-p-aminobenzoate was refluxed with 10 cc. of 10% potassium hydroxide solution until a homogeneous mixture was obtained. The acidified solution gave a quantitative yield of acid which, when crystallized from acetic acid or alcohol, melted at 156°.

Anal. Calcd. for  $C_{12}H_{11}O_2N$ : N, 6.57. Found: N, 6.64.

### Preparation of Methyl N,N-Diphenylanthranilate

An ether solution of diazomethane was added to 0.15 g. of N,N-diphenylanthranilic acid. The solution was filtered onto a watch glass. Pale yellow crystals formed as the ether evaporated. These were crystallized once from methanol and melted at 131 - 2°. The yield of the ester was 0.14 g. or 90% of the theoretical quantity.

### Preparation of 4-Iododibenzofuran

A n-butyllithium solution, prepared from 2.36 g. (0.34 g. atom) of lithium metal and 23.3 g. (0.17 mole) of n-butylbromide, was added to an ether solution of 16.8 g. (0.1 mole) of dibenzofuran. This solution was refluxed in a nitrogen atmosphere for four hours. It was transferred under nitrogen to a large dropping funnel and was subsequently added dropwise to a solution of 25 g. (0.2 mole) of iodine in

ether. The oil obtained by removal of the ether was dissolved in hot methanol but separated as an oil upon cooling of the solution. Crystals slowly formed upon the surface of the oil. These were collected and recrystallized from methanol to give 3.8 g. of 4-iododibenzofuran melting at 70 - 71°. Since the unreacted dibenzofuran could not be removed in a satisfactory manner by crystallization methods, the residues from several runs were combined and distilled under reduced pressure. The 4-iododibenzofuran distilled smoothly at 180° and 3 mm. Mr. A. H. Haubein checked the procedure as outlined above, distilling the reaction mixture to obtain a 37.5% yield of 4-iododibenzofuran.

The acid obtained by carbonating the Grignard reagent prepared from this compound was found to be identical with an authentic sample of 4-dibenzofurancarboxylic acid<sup>24</sup>.

SUMMARY

The study of the metalation reaction of organolithium compounds has been extended in the foregoing work with aromatic phosphines and amines. A review of the methods of preparation and the substitution reactions of the arylphosphorus compounds has been made. The preparation and substitution reactions of the arylamines have been briefly reviewed.

A number of reactions, designed to test a mechanism for the formation of tetraphenylphosphonium bromide by the oxidation and subsequent hydrolysis of a mixture of triphenylphosphine and phenylmagnesium bromide, have been described and the mechanism has been discussed.

Metalation of primary and secondary arylamines by n-butyllithium has been observed to take place in the position ortho to the nitrogen atom. In analogous reactions with triphenylamine and triphenylphosphine the substitution has been shown to involve the position meta to the hetero element.

Some carboxydiphenyl- and -triphenylamines have been synthesized. The methyl esters of amino- and iodobenzoic acids have been found to be satisfactory reagents for these condensations.

4-Iododibenzofuran has been prepared.