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Solvents in organometallic chemistry

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NOTE TO USERS

SOLVENTS IN ORGANOMETALLIC CHEMISTRY

by

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I. INTRODUCTION

The role of solvents in the preparation of organometallic compounds is of great importance and deserves more systematic study than it has received in the past. In view of this fact, it seems advisable to have available a review of all the solvents which have been used in the preparation of organometallic compounds. This has been included in the HISTORICAL section of this thesis.

Since the group of organometallic compounds as a whole contains compounds of such varied reactivity, it is not surprising that nearly all types of solvents have been used in their preparation. However, ether has been the solvent most frequently used in this connection. This is probably due to its ready availability, its chemical inertness, its low boiling point, and its catalytic effect in organometallic formation. Although diethyl ether, as well as other ethers, is quite inert chemically, it is cleaved by the more active type of organometallic compounds. It is the aim of this work to study some of these cleavage reactions more closely.

It has long been known that organolithium compounds cleave ethers, but very little work has been done on the rate of this cleavage reaction. A knowledge of such cleavage rates would be very useful in predicting the optimum time in

which to carry out a reaction of an organolithium compound in an ether medium. It was with this purpose in view that the following problems were investigated:

1. An improved method for the analysis of alkyllithium compounds in solution.

2. The study of the rate of cleavage of various ethers with different organolithium compounds.

3. The adaptation of ether cleavage to synthetic problems.

II. HISTORICAL

A. Solvents Used in the General Methods of Preparing Organometallic Compounds

There has been little study of adjuvance* (1) in organometallic chemistry and seldom by the same investigator under comparable conditions. Therefore, in order to make this literature review as comprehensive as possible, it was thought best to discuss the solvents used in each general method of preparation of organometallic compounds. Due to the voluminous number of articles that have been published on the preparation of organometallic compounds, no attempt has been made to include all references. Rather, a critical review of the literature has been made. Only one or two papers on the solvents used in each specific method of preparation have been cited. Probably some important references have been unintentionally omitted, but the more recent literature citations have been included from which information on previous related work can usually be obtained.

For convenience, the general methods of preparing

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* The word adjuvance, from the Latin adjuvans from adjuvare, to help or to assist, has been used in expressing the effects of solvents on reaction velocity.

1. Norris and Prentiss, J. Am. Chem. Soc., 50, 3042 (1928).

organometallic compounds outlined by Jones (2) have been followed rather closely. The order in which these methods will be considered is as follows:

1. Solvents used for methods involving free metals

$$2M + RX \longrightarrow RM + MX$$

$$2M + ROR \longrightarrow RM + MOR$$

$$M + RH \longrightarrow RM + H$$

$$MM' + RX \longrightarrow RM + M'X$$

$$M + RM' \longrightarrow RM + M'$$

$$M + RM' \xrightarrow{\text{Electrolysis}} RM + M'$$

$$M + \text{ketone} \xrightarrow{\text{Electrolysis}} RM$$

$$M + R\cdot \longrightarrow RM$$

$$M + \text{double bond} \longrightarrow RM$$

$$2M + R\text{-}R' \longrightarrow RM + R'M$$

2. Solvents used for the methods involving metal salts

$$MX + RM' \longrightarrow RM + M'X$$

$$MX + RX + Na \longrightarrow RM + NaX$$

$$MX + RX \longrightarrow RMX_2$$

$$MX + Al_4C_3 \longrightarrow CH_3M$$

$$MX + RH \longrightarrow RM + HX$$

$$MX + \text{olefinic double bond} \longrightarrow RM$$

$$MX + ArN_2Cl \longrightarrow ArM + N_2$$

$$RCOOM \xrightarrow{\text{heat}} RM + CO_2$$

Special methods for organomercury compounds

2. R. G. Jones, Doctoral Dissertation, Iowa State College (1941), p. 11.

3. Solvents used for the preparation from organometallic compounds

$$RM + R'M' \longrightarrow R'M + RM'$$

$$RM + R'H \longrightarrow R'M + RH$$

$$RM + R'X \longrightarrow R'M + RX$$

$$RMX + M' \longrightarrow RMM' + M'X$$

$$2RMX \longrightarrow R_2M + MX_2$$

$$RM + \text{olefinic double bond} \longrightarrow R'M$$

$$RM + RX \longrightarrow R_2MX$$

$$RMX \xrightarrow{\text{Reduction}} RM$$

$$RR'M + X_2 \longrightarrow RM + R'X$$

$$RR'M + HX \longrightarrow RMX + R'H$$

1. Solvents used for methods involving free metals.

a. Reactions of metals with organic halides.-- The reaction $2M + RX \longrightarrow RM + MX$, probably the most fundamental in organometallic chemistry, has been carried out in more different solvents than any of the other types of preparation. The solvent chosen depends upon the reactivity of the organometallic compound, the speed at which the reaction takes place, the temperature best suited for the reaction, and the ease of separation of the final products from the solvent.

As is to be expected, diethyl ether is not a suitable solvent in which to prepare an organosodium or potassium

compound, because it facilitates the Wurtz reaction (3) and is cleaved too readily (4). The Wurtz reaction can be interrupted at the intermediate organometallic stage by the proper choice of a solvent. Morton and Heckenbleikner (5) obtained caproic and butylmalonic acids by carbonating the reaction mixture from n-amyl chloride and sodium sand. Gilman and Pacevitz (6), by reacting n-amyl chloride with sodium sand in petroleum ether (b.p. 85-100°), obtained 48 per cent caproic acid upon carbonation. With low-boiling petroleum ether (b.p. 28-38°) a 51.5 per cent yield of the acid was obtained. Only very small amounts of n-butylmalonic acid were obtained in each case. Under the proper conditions, alkylsodium compounds may be prepared from the corresponding chlorides in benzene or toluene without metalating the solvent (7). Morton (8) has shown that when n-butyl and n-propyl chlorides were used instead of n-amyl chloride in the preparation of sodium compounds the change to lower molecular weight alkyl radicals was progressively accompanied by: (1) more difficulty in effecting reaction between the

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3. Wurtz, Ann. chim., (III) 44, 275 (1855).
4. Schlenk and Holtz, Ber., 50, 262 (1917).
5. Morton and Heckenbleikner, J. Am. Chem. Soc., 58, 1697 (1936).
6. Gilman and Pacevitz, ibid., 62, 1301 (1940).
7. Gilman, Pacevitz, and Baine, ibid., 62, 1514 (1940).
8. Morton, Richardson, and Hallowell, ibid., 63, 327 (1941).

chlorides and sodium, (2) poorer yields, (3) greater tendencies towards disproportionation as judged by the proportion of malonic acid formed when the RNa compounds are carbonated under favorable conditions, and (4) a greater stability towards benzene and toluene. So much does the reaction with these hydrocarbons decrease that they can be used to advantage as solvents for the reaction. In a mixture of benzene and petroleum ether, for example, the yield of RNa reagent from n-butyl chloride was nearly as high as any obtained from n-amyl chloride, and best conditions for n-propylsodium were in fact realized in toluene as a solvent. Arylsodium compounds may be prepared in this manner. If aromatic hydrocarbons were used as solvents, the reaction was carried out at 40° for 45 minutes (7, 9). Table 1 gives the yields of p-toluic acid obtained in the carbonation of the reaction of sodium with p-chlorotoluene.

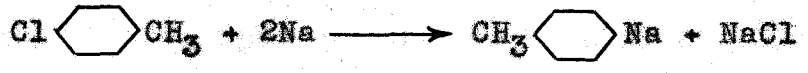

Table 1. Effect of Solvent on Yields of p-Tolylsodium

Solvent used	Per cent p-toluic acid
benzene	70
cyclohexane	57
petroleum ether (b.p. 70-80°)	74
toluene	80

9. H. A. Pacevitz, Doctoral Dissertation, Iowa State College (1941), p. 69.

Although the reactive organoalkali compounds cannot be prepared in ether, the unreactive types such as triphenylmethylpotassium may be prepared in this manner (10). Lithium, potassium, rubidium, and caesium react with triphenylmethyl chloride in ether, while only rubidium and caesium react with this compound in other organic solvents.

A small amount of organometallic compound was made by heating 3-iodofuran with sodium-potassium alloy at 115° without solvent (11).

Any attempts to prepare alkyl- and phenylalkali compounds in liquid ammonia were unsuccessful due to the ammonlysis of the organoalkali compounds as soon as they were formed. In a few instances organoalkali compounds have been formed. Benzylsodium and -potassium compounds have been prepared by the action of the corresponding alkali metal on benzyl halides in liquid ammonia. A deep red color developed in each case and then the color gradually faded until the solution became colorless. It has been concluded that the red color was due to the benzylalkali compound (12). Obviously this was not a suitable method for the preparation of these compounds. In the reduction of triphenylmethyl chloride with sodium, triphenylmethylsodium is formed (13),

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10. v. Grosse, Ber., 59, 2646 (1926).
11. Gilman and Wright, J. Am. Chem. Soc., 55, 2893 (1933).
12. Kraus and White, ibid., 45, 768 (1923).
13. Kraus and Greer, ibid., 44, 2629 (1922).

because it is more stable in liquid ammonia.

Unlike sodium and the more active alkali metals, lithium reacts readily with organic halides in diethyl ether to give excellent yields of organolithium compounds. Gilman, Zoellner, and Selby (14) have given the yields of a large number of organolithium compounds prepared in this manner. Preliminary reports by Mr. Stuckwisch (15) have shown that if the preparation of n-butyllithium in ether is carried out at low temperature, superior results are obtained. The reaction was started in the conventional manner. After the ether began to boil the reaction flask was surrounded by ice, and the n-butyl bromide was added at such a rate as to keep a gentle reflux of ether. When prepared in this manner, the reaction took less than half the time required in the usual procedure and an increase in the yield of compound was obtained. Although most organolithium compounds cleave ether, this reaction is of no perceptible importance unless the solutions are to be held for a considerable time. n-Butyllithium can be prepared in n-butyl ether if the temperature of the solution is kept low during the reaction (16).

Gilman, Langham, and Moore (17) have prepared

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14. (a) Gilman, Zoellner, and Selby, ibid., 55, 1252 (1933); (b) Gilman, Zoellner, Selby, and Boatner, Rec. trav. chim., 54, 584 (1935).

15. Unpublished studies by Mr. C. G. Stuckwisch.

16. Gilman and Moore, J. Am. Chem. Soc., 62, 1843 (1940).

17. Gilman, Langham, and Moore, ibid., 62, 2327 (1940).

organolithium compounds in low-boiling petroleum ether (b.p. 28-38°). A list of the yields of a number of these compounds is given in an article by Gilman, Moore, and Baine (18). This is a solvent of choice for the preparation of some RLi compounds, particularly when solutions are to be stored, or when special reagents are later used to replace most of the petroleum ether. The rate of formation of n-butyllithium in this solvent approaches that in diethyl ether, and butyl chloride is really more effective in petroleum ether than in diethyl ether. These authors mention four particular advantages of petroleum ether. First, the difficulty of secondary reactions, such as cleavage, present in diethyl ether, is obviated, and the coupling with RX compounds is minimized. Second, the simple acid-titration analysis is adequate. Third, the by-products, such as lithium halide, are insoluble in petroleum ether and can be removed on filtration. Fourth, compounds are formed in this solvent which do not form or give only small yields in diethyl ether. Isopropyllithium, prepared in only 20 per cent yield in diethyl ether, is obtainable in a 58 per cent yield in low-boiling petroleum ether. The hitherto inaccessible s- and t-butyllithium compounds can be prepared in yields of 85 and 50 per cent respectively (18). Since then t-butyllithium has been prepared in diethyl ether in about 20 per cent yields (19). Higher-boiling

18. Gilman, Moore, and Baine, ibid., 63, 2479 (1941).
19. Bartlett, Swain, and Woodward, ibid., 63, 3229 (1941).

petroleum ether is not so suitable as a solvent, for low yields are obtained. Lithium gave with n-butyl chloride in petroleum ether (b.p. 60-68°) a 25 per cent yield of valeric acid upon carbonation after 24 hours, and under the same conditions with petroleum ether (b.p. 85-100°) a 21 per cent yield was obtained (20). By modifying the usual procedure somewhat, Mr. Meals (21) obtained a 65 per cent yield of dodecyllithium and 72 per cent amyllithium in petroleum ether (b.p. 60-68°). The method consisted of heating the petroleum ether suspension of lithium metal, to reflux and then adding the organic chlorides all at once. The solution was then refluxed for one hour. Organic bromides gave poor results when treated in this manner.

It has been found by Ziegler and Colonius (22) that alkyllithium compounds may be prepared in aromatic hydrocarbons, although the reaction is slow. With n-butyl iodide no reaction took place; however, the corresponding bromide and chloride gave yields of 60 and 80-100 per cent, respectively. The slowness of the reaction in this solvent was confirmed by Gilman, Zoellner, and Selby (23). Cyclohexane, when used as a solvent, gave a slow reaction similar to benzene (22).

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20. Unpublished studies by F. W. Moore.

21. Unpublished studies by R. N. Meals.

22. Ziegler and Colonius, Ann., 479, 135 (1930).

23. Gilman, Zoellner, and Selby, J. Am. Chem. Soc., 54, 1957 (1932).

Aryllithium compounds were not investigated in these solvents due to their insolubility.

Spencer and Price (24) heated lithium with RX compounds either without solvent at reflux temperature or in a sealed tube and obtained the corresponding RH and RR compounds upon hydrolysis. No attempt was made to characterize the organometallic compound formed. They obtained 80 per cent aniline and small amounts of 3,3'-diaminobiphenyl by heating lithium and m-chloroaniline for one-half hour at 230°.

Gilman (25) was unable to prepare organoberyllium compounds from metallic beryllium and organic halides using ether, anisole, benzene, or β-ethoxynaphthalene as a solvent. These compounds were prepared later from alkyl iodides and powdered beryllium in ether heated to 80° or 90° in a sealed tube (26). In order to get the methyl compound to react, mercuric chloride or beryllium chloride had to be added.

Since Grignard (27) prepared the compound which bears his name, investigators have been trying to improve on diethyl ether as a solvent in this reaction. Other ethers have been used extensively in this connection.

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24. Spencer and Price, J. Chem. Soc., 97, 385 (1910).

25. Gilman, J. Am. Chem. Soc., 45, 2693 (1923).

26. Gilman and Schulze, ibid., 49, 2904 (1927).

27. Grignard, Compt. rend., 130, 1322 (1900).

Zerewitinoff (28) prepared methylmagnesium iodide in amyl and butyl ethers. Marvel (29) has listed the yields of a large number of organomagnesium compounds prepared in dibutyl ether. In the preparation of pentene, Kirrmann (30) used propyl ether as the solvent in the Grignard preparation in order to make the separation of the resulting olefin easier than in diethyl ether. An excellent yield was obtained by this means. It was noted that $MgBr_2$ is more insoluble in this ether than in diethyl ether and forms a white deposit on the bottom of the flask during the reaction.

Of the aromatic ethers which have been used in this reaction, anisole and phenetole are encountered most frequently. Majima and Kotake (31) prepared the Grignard in anisole using iodine as a catalyst. These authors attributed special properties to this solvent for the preparation of indole derivatives. Mihailesau and Caragea (32) reported p-diiodobenzene did not react completely with two atoms of Mg in ether because the surface of the metal became covered with a resinous layer--probably p-iodophenylmagnesium iodide--

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28. Zerewitinoff, Ber., 41 2244 (1908); Ber., 40, 2023 (1907).

29. Marvel, Blomquist, and Vaughn, J. Am. Chem. Soc., 50, 2810 (1928).

30. Kirrmann, Bull. soc. chim., (4) 39, 988 (1926).

31. Majima and Kotake, Ber., 55, 3859, 3865 (1922); Majima and Hoskino, Ber., 58, 2042 (1925).

32. Mihailesau and Caragea, Bull. sect. sci., acad. roumaine, 12, No. 4/5, 7 (1929) /C.A., 24, 2116 (1930)/.

which was insoluble in ether. This covering prevented further reaction, but the reaction went much better if the ether was replaced by anisole. Senier, Austin, and Clarke (33) claimed milder reactions giving products more easily crystallized when anisole or phenetole was used as solvent in the reaction between the Grignard reagent and acridines. These authors, as did most other investigators, found it more practical to prepare the Grignard in diethyl ether, and either to distill off the diethyl ether or to add the new solvent to the diethyl ether solution. Putochin (34) attributes the particular reactions obtained in anisole, not to the special solvent effects of anisole itself, but rather to the high temperature effect that may be realized.

In their chemiluminescence experiments, Evans and Diepenhorst (35) prepared the Grignard reagent in a large number of solvents in order to study the effect of the solvent on this reaction. These authors gave no detail on their method of preparation other than the fact that the solution was made up in molecular proportions. They admitted they did not know either the molecular proportions of the Grignard compound after reaction had taken place or whether they had an RMgX compound if no liminescence was obtained. The following

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33. Senier, Austin, and Clarke, J. Chem. Soc., 87, 1469 (1905).

34. Putochin, Ber., 59, 1987 (1926).

35. Evans and Diepenhorst, J. Am. Chem. Soc., 48, 715 (1926).

solvents gave positive results:

n-butyl ether	n-propyl ether
isoamyl ether	α-naphthyl ethyl ether
resorcinol dimethyl ether	benzyl ethyl ether
n-amyl ether	phenyl ether
isopropyl ether	anisole
α-naphthyl methyl ether	phenetole
α-naphthyl isoamyl ether	dimethylaniline
β-naphthyl isoamyl ether	benzene (negative)

Methylal was the unusual solvent employed by Bourgom (36) in the preparation of n-butylmagnesium bromide which was used for the reaction with trioxymethylene to give amyl alcohol. The Grignard reaction was carried out exactly as usual with about 500 cc. of methylal for every gram molecular weight of RMgX compound. If the same volume was used for two gram molecular weights, the mixture became partly solid. A 70 per cent yield of amyl alcohol was obtained with this solvent as compared to 60 per cent with the usual solvents.

In spite of the fact that hydrocarbons seem to have a retarding or inhibiting effect on the formation of Grignard reagents, a number of preparations have been made in these solvents. Schlenk (37) has prepared a large number of RMgX compounds using benzene as solvent. He found the RMgX

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36. Bourgom, Bull. soc. chim. Belg., 33, 101 (1924) /C.A., 18, 1814 (1924)/.

37. Schlenk, Ber., 64, 734 (1931).

compound to be less soluble in benzene than was the corresponding R_2Mg compound. Bafihl and Malmgren (38) have prepared the Grignard compound from bromocamphor and Mg in boiling xylene, but not, according to Malmgren, in boiling benzene. Upon protracted digestion, alkylmagnesium halides can be prepared from the alkyl halides and magnesium in boiling benzene and xylene (39). All the above reactions take place in the absence of catalysts.

Gilman and McCracken (40) have studied the effect of ether as a catalyst in bringing about the Grignard reaction in hydrocarbon solvents. The minimum quantity of ether that gave the maximum yield when the RX compound was added in benzene was about two moles for each mole of RX compound. Doubling the quantity of ether used under these conditions did not improve the yield. The maximum yield under these conditions was about 10 per cent below that obtained in ether; with toluene as solvent it was found that the yield increased to within 1-3 per cent. Xylene and petroleum ether gave yields approximating those obtained in benzene.

Tertiary amines are said to be better catalysts than ether (39), since the reaction proceeds more quickly and often quantitatively. Only a few drops of the tertiary amine was

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38. Brühl, Ber., 37, 746 (1904); Malmgren, Ber., 36, 2608 (1903).

39. Tschelinzeff, Ber., 37, 4534 (1904).

40. Gilman and McCracken, Rec. trav. chim., 46, 463 (1927).

sufficient to bring about reaction between RI and Mg in benzene, toluene, xylene, hexane, petroleum ether, terpene hydrocarbons, and other compounds which were not mentioned in the article.

The use of tertiary amines as solvents in the preparation of the Grignard reagent has been the source of a number of papers. There is a large variation in the success of this reaction as reported by the numerous authors. Stadnikov (41) carried out the Grignard reaction in dimethylaniline at room temperature and obtained only crystals of dimethylethylphenylammonium iodide. When a mixture of the tertiary amine and benzene was used as a solvent, a heavy oil, which came down after the reaction stood a year, analyzed for the compound $C_6H_5(CH_3)_2N \cdot C_2H_5MgI \cdot C_6H_6$. Tschelinzeff (42) was able to carry out this reaction with dimethylaniline as a solvent if a crystal of iodine was added to start the reaction. When benzaldehyde was added to the mixture, a 62 per cent yield of the expected carbinol was obtained. He found that the reaction proceeded better at an elevated temperature, and used mixtures of the amine with either benzene or toluene to achieve this effect. Attempts to prepare alkyllithium compounds and phenylsodium, from the metal and organic halide, in

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41. Stadnikov and Weizmann, J. prakt. chem., 112, 177 (1926).

42. Tschelinzeff, Ber., 37, 208 (1904); 38, 3664 (1905).

tributylamine were without success (43).

Tschelinzeff claimed that the tertiary amines and ether were true catalysts for these preparations since a small amount of catalyst brought about a large amount of conversion into the Grignard reagent. Other investigators (44) were unable to substantiate Tschelinzeff's conclusions. Even though ether may be a catalyst this does not exclude the formation of oxonium compounds that use up the ether. In order to further the study of the dependence of catalytic effect upon oxonium formation, Hepworth used a large number of substances as catalysts in the preparation of the Grignard compound in benzene solution. Alkyl sulfides accelerated the formation of methylmagnesium iodide in benzene but were less effective than ether. Diethyl selenide and dimethyl telluride in turn were less effective than the disulfides. Diphenylsulfoxide and diisoamylsulfoxide gave a catalysing action more pronounced than the sulfides, and it was suggested that this was due to the presence of an oxygen atom in the former compounds. Ethyl n-propyl sulfide, pentamethylene sulfide, 1,4-dithian, 1,4-thioxan, ethyl n-propyl ether, pentamethylene oxide, 1,4-dioxan, and 1,3-dioxan were also used. It was concluded from these studies that the oxygen compounds were more efficient than the sulfur compounds and that ring

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43. R. L. Bebb, Doctoral Dissertation, Iowa State College (1941), p. 59 and 99.

44. (a) Hepworth, J. Chem. Soc., 119, 1249 (1921); (b) Tingle and Gorsline, Am. Chem. J., 37, 483 (1907).

formation diminished the catalytic activity. Pickard and Kenyon (45) found no reaction to take place between methyl iodide and magnesium in boiling benzene after several hours, but a reaction started after the addition of tribenzylphosphine oxide. After the mixture cooled crystals of the addition compound formed. It must be remembered that, although all the above compounds are termed catalysts, enough of the reagent is added to form complexes (1 cc. of the catalyst to 50 cc. of benzene). Also, neither ethers, tertiary amines, nor high temperature was necessary to bring about this reaction provided that sufficient time was allowed, although the velocity of the reaction was increased by heating or by the addition of ether, pyridine, quinoline, or iodine to a mixture of RX and Mg in ligroin (44b).

When pyridine or quinoline is used as solvent, as in the active hydrogen determination, the Grignard compound is first prepared in ether, and the bases are then added (46). This addition produces a complex, $(C_5H_5N)_2 \cdot CH_3MgX \cdot O(C_2H_5)_2$, with pyridine (47) which gives the same reactions as the Grignard compound. There is much discussion of the solvents used in the Zerewitinoff determination. Since the organometallic compounds are seldom formed directly in these solvents, they

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45. Pickard and Kenyon, J. Chem. Soc., 89, 262 (1906).

46. Zerewitinoff, Ber., 40, 2023 (1907).

47. Sachs and Sachs, Ber., 37, 3088 (1904); Oddo, Atti accad. Lincei, (5) 13, II, 100 (1904); (5) 16, I, 413, 538 (1907) /Chem. Zentr., II, 836 (1904); I, 1543 (1907); II, 73 (1907)/.

will not be discussed here.

Grignard reagents have also been prepared from the organic halides and magnesium in the absence of solvent. Spencer (48) reacted magnesium with various alkyl halides in a sealed tube and upon hydrolysis obtained the corresponding hydrocarbon together with the coupling product. He used iodobenzene, p-bromoaniline, and p-bromophenol in this reaction. With the exception of o-chloroaniline, the chloro compounds did not show much reaction. Gilman and Brown (49) prepared phenylmagnesium chloride in 85 per cent yield by this method. The possibilities of preparing C_6H_5MgCl on a large scale in this manner were investigated by Shoruigin (50) who carried out the reaction in an autoclave. Catalysts offered no advantage although small amounts of $C_6H_5CH_2CH_2OH$ accelerated the reaction. Dimethylaniline, however, even slowed up the reaction. Alkyl halides gave only resinous material when heated with magnesium in a sealed tube (51). The Russian investigators, Andrianov and Gribanova (52), were able to make the reaction take place in toluene and benzene or even without solvent if a little tetraethoxysilicane was added as a catalyst.

48. Spencer and Crewdson, J. Chem. Soc., 93, 1821 (1908); Spencer and Stokes, ibid., 93, 68 (1908).
49. Gilman and Brown, J. Am. Chem. Soc., 52, 3330 (1930).
50. Shoruigin, Isagulyants, Guseva, Osipova, and Polyakova, Ber., 64, 2584 (1931).
51. Shoruigin, Isagulyants, and Guseva, Ber., 66, 1426 (1933).
52. Andrianov and Gribanova, J. Gen. Chem. (U.S.S.R.), 8, 557 (1938) [C.A., 32, 7892 (1938)].

The compounds of Group 2B form organometallic compounds that are not very active, so more drastic means should be required to prepare them by the reaction of the metal and organic halide. This is quite true, for organozinc compounds are prepared from the organic halides and zinc without a solvent (53). A zinc-copper couple has been used successfully for the preparation of diethylzinc from ethyl iodide (54). This reaction gives very high yields of pure product.

Although cadmium will react with alkyl iodides in ether solution the yields are small and the products are impure. Wanklyn (55) has prepared diethylcadmium from ethyl iodide, while Löhr (56) has used methyl iodide with cadmium to obtain dimethylcadmium.

Mercury will react with methyl or benzyl iodide in sunlight or strong illumination in the absence of solvent to give the corresponding RHgX compound (57). When α-bromotolunitrile is heated with mercury at 40-60° in the absence of solvent, $C_6H_5CH(CN)HgBr$ is produced (58).

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53. Frankland, Ann., 71, 171 (1849).

54. Lachman, Am. Chem. J., 24, 31 (1900); Dennis and Hance, J. Am. Chem. Soc., 47, 370 (1925); Noller, ibid., 51, 594 (1929).

55. Wanklyn, J. Chem. Soc., 9, 193 (1856).

56. Löhr, Ann., 261, 48 (1891)

57. Maynard, J. Am. Chem. Soc., 54, 2108 (1932).

58. Kretov and Abramov, J. Gen. Chem. (U.S.S.R.), 7, 1572 (1937) /C.A., 31, 8518 (1937)/.

All of the other metals which have been made to react with alkyl halides to give organometallic compounds have been used without solvent. This is a method of choice for making organoaluminum compounds. Hnizda and Kraus (59) used an aluminum alloy (8 per cent Cu) with methyl chloride, with $AlCl_3$ as a catalyst, to prepare an equimolar mixture of dimethylaluminum chloride and methylaluminum dichloride. This aluminum-copper alloy has been used with a large number of halides (60). Alkyl iodides when heated with tin gave dialkyltin diiodides (61). Cahours (62) prepared $(CH_3)_4AsI$ by heating arsenic and methyl iodide at 160-200°, while the same treatment with Sb gave R_3SbI_2 (63).

b. Cleavage of ethers.-- This group of reactions is confined to the alkali metals, but the organometallic compound formed is of low enough reactivity so that diethyl ether may be used without danger of cleavage. Triphenylmethylpotassium is obtained from the following reaction in diethyl ether (64).

$$(C_6H_5)_3COR + 2K \longrightarrow (C_6H_5)_3CK + KOR$$

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59. Hnizda and Kraus, J. Am. Chem. Soc., 60, 2276 (1938).

60. Grosse and Mavity, J. Org. Chem., 5, 106 (1940).

61. Frankland, Ann., 85, 329 (1853); Cahours, Ann., 114, 367 (1860).

62. Cahours, Ann., 122, 192 (1862).

63. Buckton, J. Chem. Soc., 13, 115 (1860).

64. Ziegler and Thielmann, Ber., 56, 1740 (1923).

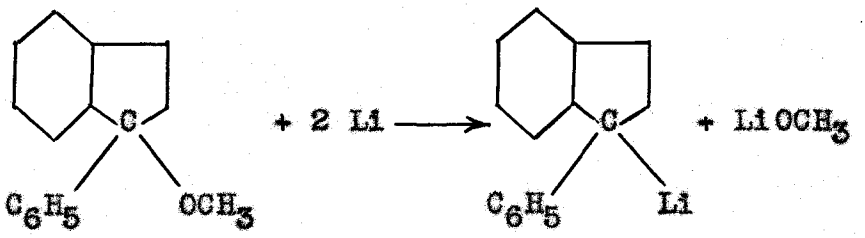
The R is an alkyl group, usually methyl. The ethoxy group is cleaved from 1,1,3,3-tetraphenylallyl ethyl ether

$$(C_6H_5)_2C\text{-}CH = C(C_6H_5)_2$$
$$\quad\quad OC_2H_5$$

in diethyl ether using sodium-potassium amalgam as the cleaving agent. Wittig and Obermann (65) used Na-K alloy in dioxan to cleave the ether in the following reaction

$$(C_6H_5)_2(OCH_3)\ C\text{-}CH_2C(OCH_3)(C_6H_5)_2 + Na\text{-}K \xrightarrow{\text{methanol}}$$
$$(C_6H_5)_2CHCH_2CH(C_6H_5)_2$$

This reaction takes place equally well with diethyl ether as solvent. Lithium metal also cleaves ethers (66), for one methoxy group is removed from benzophenone dimethyl acetal if allowed to react for three weeks in diethyl ether. The following reaction also takes place in ether.



Shoruigin (67) cleaved various ethers by sodium metal without solvent as well as with various solvents. Diphenyl ether began to decompose when heated with sodium at 180° to give 60-75 per cent C_6H_5ONa, 30 per cent C_6H_5Na (characterized

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65. Wittig and Obermann, Ber., 67, 2053 (1934).

66. Schlenk and Bergmann, Ann., 463, 1, 98 (1928); Ann., 464, 35 (1928).

67. Shoruigin, Ber., 56, 176 (1923).

as C_6H_6 by hydrolysis), and small amounts of biphenyl. If diphenyl ether was cleaved by sodium in boiling xylene (b.p. 160°) very little phenol was obtained; if it was cleaved in boiling biisoamyl (b.p. 180°) a better yield was obtained; with naphthalene (b.p. 220°) the yield of phenol was as good as that obtained when no solvent was used. Clearly, the important function of the solvent in this case is one of temperature control. If the ether to be cleaved boils above 200° cleavage may be obtained by boiling in an open flask. The lower-boiling ethers must be heated with the metal in a sealed tube.

c. Direct metalation.-- The title of this section suggests the use of very active metals and hydrocarbons with relatively acidic hydrogen atoms. Rubidium and caesium react with triphenylmethane in organic solvents (10). Although sodium will not react with $(C_6H_5)_3CH$ in organic solvents, sodium amalgam will (68). The necessity for active metals again manifests itself in the reaction with phenylacetylene. Potassium, rubidium, and caesium react in ether with $C_6H_5C \equiv CH$, but lithium and sodium are unreactive (69).

The replacement of a hydrogen in a hydrocarbon by a metal takes place with much greater ease in liquid ammonia than in organic solvents, for sodium reacts with

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68. Schlenk and Ochs, Ber., 49, 608 (1916).

69. Gilman and Young, J. Org. Chem., 1, 315 (1936).

phenylacetylene in this solvent (70).

When acetylene is bubbled through a U-tube containing sodium in liquid ammonia, C_2HNa is formed (71); the same reaction takes place with potassium. With lithium, acetylene forms crystals containing ammonia of hydration. Even calcium will react with acetylene in liquid ammonia to give the compound $C_2Ca \cdot C_2H_2 \cdot 4NH_3$. Both the lithium and calcium compounds mentioned above give acetylides upon heating. Vaughn and Danehy (72 claim the formation of HC ≡ CCaC ≡ CH from the liquid ammonia reactions of calcium with HC ≡ CH.

As has been seen before, more drastic conditions are created by carrying out a reaction without a solvent. This is shown by the fact that potassium in liquid ammonia displaces only one hydrogen in diphenylmethane to produce diphenylmethylpotassium (73), while in the absence of solvent two hydrogen atoms are displaced to give diphenylmethyldipotassium (74).

d. The reaction of an alkyl halide with an alloy.-- This type of reaction requires an alloy of an active metal with the more unreactive metals, usually the metals of the B Groups

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70. Hess and Munderlok, Ber., 51, 377 (1918).

71. Moissan, Compt. rend., 127, 911 (1898).

72. Vaughn and Danehy, Proc. Ind. Acad. Sci., 44, 144 (1935).

73. Wooster and Mitchell, J. Am. Chem. Soc., 52, 688 (1930).

74. Le Pierre, Bull. soc. chim., [3] 5, 299 (1891).

of the periodic table. Sodium amalgam reacts with alkyl halides, in ethyl acetate to produce dialkylmercury compounds (75). Likewise, sodium amalgam reacts with dialkyl sulfates in the presence of methyl acetate to give R_2Hg compounds (76). Dimethylmercury can be prepared in 55 per cent yields by this method.

No solvent is required for most reactions of this type. Tetraphenyltin is formed in 50 per cent yields from bromobenzene and 14 per cent sodium-lead alloy (77). Polis (78) used a small amount of ethyl acetate to catalyze this reaction. While aliphatic iodides will react with the lead alloy in ether (79), the aromatic halides will only react with sodium-lead alloy without a solvent (80). It is interesting to note that upon the reduction of acetone with sodium-lead alloy in dilute sulfuric acid a mixture of tetraisopropyllead and small amounts of diisopropyllead, triisopropyllead, and isopropyllead oxide are formed (81).

For the production of organic compounds of antimony and

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75. Frankland and Duppa, Ann., 130, 104 (1864).

76. Fuchs, J. prakt. Chem., 119, 209 (1928).

77. Chambers and Scherer, J. Am. Chem. Soc., 48, 1054 (1926).

78. Polis, Ber., 22, 2915 (1889).

79. Löwig, Ann., 84, 319 (1852); Cahours, Ann., 122, 48 (1862).

80. Polis, Ber., 20, 716 (1887).

81. Goldach, Helv. Chim. Acta., 14, 1436 (1931).

bismuth by the use of alloys, it is essential to carry the reaction out in the absence of solvent. Löwig prepared alkylantimony compounds in this manner by heating the alkyl halide and potassium-antimony alloy with a quartz sand catalyst (82). When p-bromoanisole was heated with sodium-antimony alloy in benzene solution, poor yields of $(CH_3OC_6H_5)_3Sb$ were obtained (83), but even less of the product was obtained in the absence of solvent. No arylbismuth compounds could be prepared in this manner if ether, benzene, or other indifferent organic solvent were used (84), although both aryl- and alkylbismuth compounds could be formed in the absence of solvent (85).

e. Metal-metal displacement reactions.-- Metal-metal displacement reactions cover the preparation of a broad variety of organometallic compounds with a wide range of reactivity, and, accordingly, a wide variety of solvents is to be encountered. The only preparation of organometallic compounds of rubidium and caesium by this method has been from the metal and diethylzinc, the latter acting as the

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82. Löwig and Schweizer, Ann., 75, 315 (1850); Landolt, Ann., 78, 91 (1851).

83. Löloff, Ber., 30, 2834 (1897).

84. Michaelis and Polis, Ber., 20, 54 (1887); Michaelis and Marquardt, Ann., 251, 323 (1889).

85. Gillmeister, Ber., 30, 2843 (1897); Dünhaupt, J. prakt. Chem., 61, 399 (1854).

solvent to give a complex with the organozinc compound (10,86).

$$3(C_2H_5)_2Zn + 2Rb \longrightarrow 2C_2H_5Rb\cdot(C_2H_5)_2Zn + Zn$$

$$3(C_2H_5)_2Zn + 2Cs \longrightarrow 2C_2H_5Cs\cdot(C_2H_5)_2Zn + Zn$$

Sodium gives a similar reaction. In Hein's (87) studies on the electrolysis of organometallic compounds, ethylsodium and ethyllithium were prepared in diethylzinc, while sodium compounds were also prepared in triethylaluminum and diethylcadmium. Even small amounts of diethylcalcium were prepared from calcium in diethylzinc. Ethylsodium was found to react with magnesium amalgam in diethylzinc (88).

Hydrocarbons seem to be a suitable solvent in which to carry out reactions of this type. Benzene has served adequately for the reaction of R_2Hg compounds with lithium (4, 89), sodium (4, 90), and magnesium (37). Xylene gives a little higher reflux temperature than benzene and is used for the reaction of zinc with diphenylmercury (91). Gilman and Marple (92) obtained quantitative yields of triarylaluminum compounds by boiling diarylmercury compounds with aluminum.

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86. Wanklyn, Ann., 107, 125 (1858); Ann., 108, 67 (1858).

87. Hein, Petzchner, Wagler, and Segitz, Z. anorg. allgem. Chem., 141, 161 (1924).

88. Wanklyn, Ann., 140, 353 (1866).

89. Shoruigin, Ber., 43, 1938 (1910).

90. Acree, Am. Chem. J., 29, 588 (1903).

91. Kocheshkov, Nesmeyanov, and Potrosow, Ber., 67, 1138 (1934).

92. Gilman and Marple, Rec. trav. chim., 55, 133 (1936).

Xylene is a solvent of choice for the preparation of these compounds. It is more rapid than if the reaction is carried out without a solvent (93), and loss by sublimation and decomposition is prevented. This does not apply to the trialkylaluminum compounds which are prepared without solvent in a sealed tube (94). Petroleum ether is used for the preparation of active organometallics such as organosodium (4, 69) and -lithium compounds (95) from the mercurials.

Talalaeva and Kocheshkov (96) used phenyllithium to prepare organometallics of Mg, Sn, Pb, As, Sb, and Hg. Both ether and xylene were used as solvents but no particulars were given as to differences between the two solvents. Triphenylthallium and diphenylthallium bromide were converted into the dimercurials by treating these compounds with mercury in ether (97).

Almost all of the organometallic compounds which are relatively unreactive have been prepared by the reaction of the corresponding metal with the dimercurial in the absence of a solvent. Often the reaction is reversible with poor yields.

Table 2 lists examples of various metals which react in this manner.

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93. Hilpert and Grüttner, Ber., 45, 2828 (1912); Krause and Dittmar, Ber., 63, 2401 (1930).
94. Buckton and Odling, Ann. chim. phys., (4) 4, 492 (1865).
95. Ziegler, Ber., 64, 445 (1931).
96. Talalaeva and Kocheshkov, J. Gen. Chem. (U.S.S.R.), 8, 1831 (1938) /C.A., 33, 5819 (1939)/.
97. Gilman and Jones, J. Am. Chem. Soc., 61, 1513 (1939).

Table 2. Metals Which React with R_2Hg Compounds in the Absence of Solvent.

R group of R_2Hg	Metal	Reference
methyl-	Be	98
aryl-	Be	99
alkyl-	Mg	100
aryl-	Mg	101
alkyl-	Zn	102
aryl-	Zn	103
alkyl-	Cd (large excess)	102
aryl-	Cd (large excess)	103
alkyl-	Al	93
aryl-	Al	104
alkyl-	Ga	105
aryl-	Ga	106
methyl-	In	107
aryl-	In	108
ethyl-	Bi	109

98. Lawroff, Bull. soc. chim., 41, 548 (1884).

99. Gilman and Schulze, J. Chem. Soc., 2663 (1927).

100. Löhr, Ann., 261, 72 (1891).

101. Gilman and Brown, Rec. trav. chim., 49, 724 (1930).

102. Frankland and Duppa, Ann., 130, 117 (1864).

103. Hilpert and Grüttner, Ber., 46, 1675 (1913).

104. Friedel and Crafts, Ann. chim. phys., (6) 14, 457 (1888).

105. Dennis and Patnode, J. Am. Chem. Soc., 54, 182 (1932).

106. Gilman and Jones, ibid., 62, 980 (1940).

107. Dennis, Work, Rochow, and Chamot, ibid., 56, 1047 (1934).

108. Schumb and Crane, ibid., 60, 306 (1938); Gilman and Jones, ibid., 62, 2353 (1940).

109. Frankland and Duppa, J. Chem. Soc., 17, 29 (1864).

Diphenylmercury has been made from diphenyllead dichloride and triphenyllead chloride with metallic mercury in acetone-alcohol solution (110).

f. Formation of organometallic compounds from the electrolysis of RM compounds.-- The reaction medium for the electrolysis of organometallic compounds must have a relatively high dielectric constant and, to be sure, must be chemically unreactive toward the organometallic compound. The fulfillment of these two criteria leaves little choice of solvent.

Although diethyl ether has a small dielectric constant, it has been used for electrolytic studies (111). When Konduirev used zinc, aluminum, or magnesium as the anode in the electrolysis of ethylmagnesium bromide in diethyl ether, some of the metal went into solution while a number of other metals did not dissolve. French found that aluminum, zinc, and cadmium were dissolved during electrolysis, but only the aluminum was found in solution. Evans and Field (112) claimed n-butyl ether to be less efficient in electrolysis than diethyl ether, since the free radicals formed during electrolysis attack the butyl ether more readily. Pyridine has a higher dielectric constant than diethyl ether and is

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110. N. Kaplan, Master's Thesis, Iowa State College (1939), p. 49.

111. Konduirev, Ber., 58, 459 (1925); French and Drane, J. Am. Chem. Soc., 52, 4904 (1930).

112. Evans and Field, ibid., 58, 2284 (1936).

more suitable for electrical conductance studies, but even this solvent cannot be used with such compounds as phenylisopropylpotassium (113). It can be used, however, with $(C_6H_5)_3CNa$. Hein and Segitz (114) have prepared organometallic compounds by the electrolysis of ethylsodium in diethylzinc solution using Sb, Al, Mg, Cd, Bi, and Tl as electrodes.

g. Preparation of organometallic compounds by the electrolysis of ketones.-- Such a specialized reaction as this could only be used with a few solvents. As a matter of fact, these reactions are all carried out in dilute acid solution. Diisopropylmercury (115) and diisopropyllead (116) were formed by the electrolysis of dilute H_2SO_4 solutions of acetone in the presence of Hg and Pb.

h. Reactions of metals with free radicals.-- Most investigators are familiar with the Paneth technique for the reaction of alkyl free radicals with metals (117). Of course no solvent is used in this reaction. All other free radical reactions have been carried out in diethyl ether. Triphenylmethyl reacts with sodium in ether providing the surface of

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113. Ziegler and Wollschitt, Ann., 479, 123 (1930).

114. Hein and Segitz, Z. anorg. allgem. Chem., 158, 153 (1926).

115. Haggerty, Trans. Am. Electrochem. Soc., 56, 421 (1929).

116. Tafel, Ber., 44, 323 (1911).

117. Paneth and Loleit, J. Chem. Soc., 366 (1935); Paneth and Hafedity, Ber., 62, 1335 (1929).

the sodium is kept clean by stirring with glass beads (118). Triphenylmethylmagnesium iodide is formed from the corresponding free radical and the system Mg - MgI_2 in diethyl ether (119).

i. The addition of metals to double bonds.-- There has been a large volume of work published on the addition of metals to double bonds. By far the largest number of articles has been written by Schlenk and Bergmann and their co-workers. Ether has been the solvent most used since the reaction takes place more rapidly in this solvent than in benzene (120). A splendid article was published by Schlenk and Bergmann (121) on the addition of lithium to double bonds in ether solution. When Bergmann (122) treated 1,1,8,8-tetraphenyl-1,7-octadiene with lithium in ether for four weeks, substantial quantities of 1,2-dibenzohydrylcyclohexane were obtained upon hydrolysis. Wittig (123) later showed that, upon the hydrolysis of the above reaction when carried out in dioxan, the products formed were 60 per cent of the cyclohexane derivative and 30 per cent of 1,1,8,8-tetraphenyloctane. This latter product indicates

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118. Bachmann and Wiselogle, J. Am. Chem. Soc., 58, 1943 (1936).

119. Gilman and Fothergill, ibid., 51, 3149 (1929).

120. Schlenk, Appenrodt, Michael, and Thal, Ber., 47, 473 (1914).

121. Schlenk and Bergmann, Ann., 463, 1 (1928).

122. Bergmann, Ber., 63, 2593 (1930).

123. Wittig and Waltnitzki, Ber., 67, 667 (1934).

that metal addition to the double bonds precedes cyclization. Dioxan seems to retard the cyclization but not the addition to the double bond.

Sodium adds to benzalfluorene in liquid ammonia (121). Wooster (124) has shown that the reduction of naphthalene with sodium in liquid ammonia proceeds via the intermediate 1,2,3,4-tetrasodium addition product.

Ethers of high oxygen content facilitate the addition of sodium to unsaturated links, especially those found in aromatic hydrocarbons (125). Scott (126) has used dimethyl ether as a solvent for the addition of sodium to naphthalene and biphenyl. This author claimed that if diethyl ether was added to the dimethyl ether the reaction slowed down. This was the only monoether in which this reaction occurred readily. The addition is slow but detectable in methyl propyl ether. The dimethyl ether of ethylene glycol is substantially equivalent to dimethyl ether. However, this ether is slowly attacked at room temperature by the sodium naphthalene with the formation of methyl vinyl ether.

$$C_{10}H_8Na_2 + 2CH_3OCH_2CH_2OCH_3 \longrightarrow C_{10}H_{10} + CH_3ONa + 2CH_3OCH{=}CH_2$$

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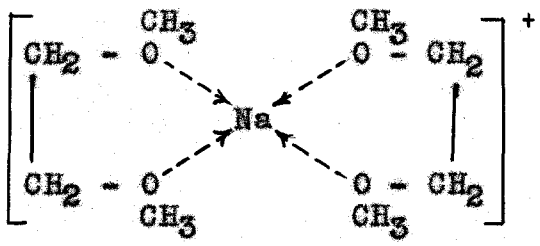
124. Wooster and Smith, J. Am. Chem. Soc., 53, 179 (1931).

125. U.S. Patent 2,054,303, Sept. 15, (1936) [C.A., 30, 7586 (1936)].

126. Scott, Walker, and Hansley, J. Am. Chem. Soc., 58, 2442 (1936).

Trimethylamine and a few other amino compounds were effective although they offered little advantage over the ethers. These solvents were necessary to initiate these reactions and also for the existence of the sodium addition products. When the sodium addition compound was evaporated to dryness and treated with water, the theoretical quantity of hydrogen was liberated, but if water was added to the ether solution, no hydrogen was evolved. If the solid was extracted with heptane a residue remained which consisted almost entirely of sodium.

The specific role of the ethylene glycol dimethyl ether in promoting the alkali addition to phenanthrene seems to be due to a number of factors (127). It may act merely as any other ionizing solvent to permit dissociation; it may stabilize the ionic products of the reaction through solvation; it may activate the sodium. The donor activity of the oxygens of the solvent might yield such a chelate ion as represented by



and thus stabilize the ions present in the solution. Evidence for the formation of the solvated ions like this is not lacking since the mixture becomes thick during the addition of the metal and upon carbonation the solution thins just as the

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127. Jeanes and Adams, ibid., 59, 2608 (1937).

last trace of dark-colored product is changed to the salt. This is assumed to mean that the solvent has been bound up in some manner and is later released.

There are numerous patents in the literature which are concerned with this addition reaction, only two of which will be discussed here. A number of low molecular weight mixed ethers, such as dimethyl, methyl ethyl, and methyl propyl ether, have been used (128). The other patent deals with polyethers (129), such as ethylene glycol dimethyl and diethyl ether, methylal, glycerol dimethyl ether, and methyl or ethyl orthoformate.

j. The cleavage of carbon-carbon bonds.-- Very little work has been done on this reaction in any solvent other than diethyl ether. However, 1,1,2,2-tetraphenylcyclopropane was cleaved by sodium-potassium alloy in dioxane to give 1,1,3,3-tetraphenylpropane (65). Conant and Garvey (130) cleaved substituted ethanes with sodium-potassium alloy in ether-benzene solution or in ether alone. No mention was made as to the difference in the effect of the solvent. Most of the other reactions took place using ether as solvent. Marvel (131)

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128. Fr. Patent.779,105, March 29, (1935) [C.A., 29, 4775 (1935)].

129. Brit. Patent 445,417, April 1 (1936) [C.A., 30, 6761 (1936)].

130. Conant and Garvey, J. Am. Chem. Soc., 49, 2599 (1927).

131. Salzberg and Marvel, ibid., 50, 1737, 2840 (1928); Rossander and Marvel, ibid., 51, 932 (1929); Gillespie and Marvel, ibid., 52, 2268 (1930); Stampfli and Marvel, ibid., 53, 4057 (1931).

has used sodium-potassium alloy or sodium amalgam as the cleaving agent in ether while Koelsch and Rosenwald have used lithium (132).

2. Solvents for the preparation of organometallic compounds from salts of the metals.

a. Reactions of organometallic compounds with salts.-- In general, a less reactive organometallic compound is formed from a more reactive compound in this manner. Due to its low toxicity and ease of preparation, the Grignard reagent has been used extensively in the preparation of most of the less reactive compounds. Consequently ether is an important solvent in this connection. Runge (133) gives an excellent review on the preparation of organometallic compounds from the Grignard reagent.

Many other reactions of this type are carried out in ether. Diphenylberyllium (134) and diphenylcadmium (135) were prepared from phenyllithium in ether solution. Even RMgX types, which are not readily prepared by the conventional

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132. Koelsch and Rosenwald, ibid., 59, 2170 (1937).

133. Runge, "Organometallverbindungen. I Teil: Organomagnesiumverbindungen," Wissenschaftliche Verlagsgesellschaft, m.b.h., Stuttgart (1932), pp. 279-303.

134. Gilman and Bailie, J. Org. Chem., 2, 84 (1937).

135. Nesmeyanov and Makasova, J. Gen. Chem. (U.S.S.R.), 7, 2649 (1937) /C.A., 32, 2095 (1938)/.

reaction, may be prepared from the magnesium halide etherate and organolithium compounds in ether. In this manner the inaccessible p-aminophenylmagnesium bromide has been prepared by the following sequence of reactions (136).

$$\underline{p}\text{-}BrC_6H_4NH_2 + \underline{n}\text{-}C_4H_9Li \longrightarrow \underline{p}\text{-}Li\cdot C_6H_4NH_2 + \underline{n}\text{-}C_4H_9Br$$

$$\underline{p}\text{-}LiC_6H_4NH_2 + MgBr_2 \longrightarrow \underline{p}\text{-}BrMgC_6H_4NH_2 + LiBr$$

An interesting adaptation of this reaction is represented by the equation

$$2R_3M + MX_3 \longrightarrow 3R_2MX$$

or by the formation of RMX_2, if an excess MX_3 is used. An example of this is the formation of diphenylbismuth bromide from an ether solution of triphenylbismuth and $BiBr_3$ (137), or the formation of mixed organoaluminum halides from R_3Al compounds (60).

One disadvantage of using ether as a solvent is that the organometallic compound results as an etherate. Sometimes these etherates give entirely different reactions from the ether-free compounds. This is notable in the smooth reaction of ether-free organoaluminum iodides with acid chlorides and anhydrides in contrast to the polymerization which occurs when the etherates are used (138).

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136. Gilman and Stuckwisch, J. Am. Chem. Soc., 64, 1007 (1942).

137. (a) Grüttner and Wiernik, Ber., 48, 1749, 1484, 1759 (1930).
(b) Dyke, Davies, and Jones, J. Chem. Soc., 463 (1930).

138. Haubein, Appersen, and Gilman, Proc. Iowa Acad. Sci., 46, 219 (1939).

A very useful application of the reaction of metal salts with ether solutions of organometallic compounds is the characterization of organic halides. First the halide is converted to the corresponding Grignard compound, after which the RMgX compound is treated with a mercuric halide in order to form the corresponding solid organomercury halide (139). Likewise, organomercury compounds react with a number of salts in ether to produce organometallic compounds (140).

Hydrocarbons have been used extensively in this type of reaction. No conclusion can be drawn as to the reason for their use since very little comparison of ethers and hydrocarbons has been made. Although most authors obtained low yields of tetraphenylgermanium from the chloride and Grignard compound in ether, an 86 per cent yeild of this compound was obtained by replacing the ether with toluene (141). It may be the difference in solubility phenomena, or, more likely, the higher temperature achieved with these solvents which accounts for the difference in reactivity. An ether-benzene solution was used to cause reaction between p-dimethylaminophenyllithium and stannic chloride (142).

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139. Marvel, Gauerke, and Hill, J. Am. Chem. Soc., 47, 3009 (1925).

140. (a) Goddard, J. Chem. Soc., 121, 36, 256, 482 (1922);
(b) Challenger and Allpress, ibid., 119, 913 (1921);
(c) Bauer and Burschkies, Ber., 65, 956 (1932).

141. Warrall, J. Am. Chem. Soc., 62, 3267 (1940).

142. Austin, ibid., 54, 3726 (1932).

Antimony trichloride dissolved in benzene was added to phenylmagnesium bromide in diethyl ether to produce triphenylantimony (143). Benzene alone was used as a solvent for the preparation of alkylboron compounds from dialkylmercury compounds, RBX_2 or R_2BX resulting, depending upon the quantity of the mercurial used (144). Chambers and Scherer (145) distilled the ether from C_6H_5MgBr and added toluene in order to carry out a reaction with stannic chloride. Goddard (146) reacted tetraphenyllead with stannic chloride, antimony chloride, and bismuth chloride in toluene. Tetraarylgermanium compounds were prepared from the mercurials in xylene (147). Birch (148) used ether in the reaction between aryllithium compounds and thallous chloride, but used benzene or pentane instead of ether when alkyllithium compounds were used. Ether was used with the aryl compound because of the insolubility of phenyllithium in hydrocarbons but no run of alkyllithium was made in ether to afford a comparison as to the efficiency of the two kinds of solvents.

n-Amylmercury has been prepared from n-amylsodium and

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143. Morgan and Micklethwait, J. Chem. Soc., 99, 2286 (1911).

144. Michaelis, Ber., 27, 244 (1894); Ann., 315, 19 (1901).

145. Chambers and Scherer, J. Am. Chem. Soc., 48, 1054 (1926).

146. Goddard, Ashley, and Evans, J. Chem. Soc., 121, 978 (1922).

147. Orndorff, Tabern, and Dennis, J. Am. Chem. Soc., 49, 2512 (1927); Bauer and Burschkies, Ber., 65, 956 (1932).

148. Birch, J. Chem. Soc., 1132 (1934).

mercuric chloride in petroleum ether (149). Likewise, Gilman and Apperson (150) used $AlCl_3$ in petroleum ether to cleave tetraphenyllead and tetraethyllead. Although mixed organothallium compounds could be prepared from organothallium chlorides and alkyllithium compounds in petroleum ether, ethylsodium would not react, due to the insolubility of the sodium compound in such indifferent media (151).

The reactions carried out without solvent usually involve the less reactive type of organometallic compounds which probably would give only a slow reaction in a solvent. A number of organomercury (152) and organozinc (153) compounds have been prepared in this manner. Tetraphenyllead has been cleaved by ammonium chloride at 180° to give a 75 per cent yield of triphenyllead chloride (154).

As is to be expected when less reactive organometallic

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149. Morton, Massengale, and Gibb, J. Am. Chem. Soc., 63, 324 (1941).

150. Gilman and Apperson, J. Org. Chem., 4, 162 (1939).

151. Groll, J. Am. Chem. Soc., 52, 2998 (1930).

152. (a) Buckton, J. Chem. Soc., 16, 22 (1863); (b) Michaelis and Reese, Ber., 15, 2876 (1882); (c) Michaelis and Becker, Ber., 15, 180 (1882).

153. (a) Stock and Zeidler, Ber., 54, 531 (1921); (b) Kraus and Toonder, Proc. Nat. Acad. Sci., 19, 292 (1933); (c) Frankland, Ann., 111, 44 (1859); Winkler, J. prakt. Chem., 36, 177 (1887); Frankland and Lawrence, J. Chem. Soc., 35, 130 (1879); Frankland and Duppa, Ann., 115, 319 (1860); Buckton, Ann., 109, 218 (1859).

154. Krause and Schlottig, Ber., 58, 427 (1925).

compounds are used, solvents with functional groups may be employed. This is especially true in the formation of mercurials. Ethylmercuric hydroxide reacts with $(C_6H_5)_2SnO$ in dilute alcohol containing sodium hydroxide to give ethylphenylmercury (155), and under the same conditions mercuric oxide reacts with C_6H_5SbO to give diphenylmercury (155b). Tetraphenyllead reacts with silver nitrate in alcohol solution to form triphenyllead nitrate and phenylsilver as evidenced by the formation of biphenyl upon warming the solution (156a). In the same manner, tetraphenyllead reacts with copper nitrate to give an organocopper compound. Tetraphenyltin reacts in alcohol with silver nitrate to produce phenylsilver. There is evidence that all the phenyl groups were cleaved from the organotin compound. The unsymmetrical triphenylethyllead and -tin compounds, when treated in alcohol with mercuric chloride or silver nitrate, give phenylmercuric chloride and $C_6H_5Ag \cdot AgNO_3$ respectively (156b). When R_2Hg compounds are cleaved by stannous chloride to give R_2SnCl_2 compound and mercury (157), some of the substances formed were found to be insoluble in alcohol. As a result, the reaction was quite slow, but desirable results were achieved with the

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155. (a) Freidlina, Nesmeyanov, and Kocheshkov, Ber., 68, 565 (1935); (b) Nesmeyanov and Kocheshkov, Ber., 67, 317 (1934).

156. (a) Unpublished studies by L. A. Woods; (b) Krause and Schmitz, Ber., 52, 2159 (1919).

157. Nesmeyanov and Kocheshkov, Ber., 63, 2496 (1930).

aryl compounds. However, this solvent gave negative results with alkylmercury compounds.

The above mentioned solvents are the ones most frequently encountered, but there are a few others that should be mentioned. Dibutyl ether was used by Burg (158) to prepare trimethylboron from the Grignard reagent and methyl borate. To prepare dimethylgold iodide, an ether solution of methylmagnesium iodide was added to auric chloride dissolved in pyridine (159). Triphenyllead chloride was prepared from diphenyllead dichloride and diphenyl mercury in pyridine solution (160). Phenylboric acid reacted in hot water with thallium trichloride to give R_2TlX or $RTlX_2$, depending on the ratio of reactants used (161). Iron carbide was said to be prepared from calcium carbide and a water solution of ferrous chloride (162).

b. The reaction of metal halides, organic halides, and metals.-- When the reaction

$$4C_6H_5Br + GeCl_4 + 8Na \longrightarrow (C_6H_5)_4Ge + 4NaCl + 4NaBr$$

was carried out in ether solution, poor yields of

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158. Unpublished studies by Dr. A. B. Burg [See J. Am. Chem. Soc., 64, 324 (1942)].

159. Brain and Gibson, J. Chem. Soc., 762 (1939).

160. Austin, J. Am. Chem. Soc., 54, 328 (1932).

161. Challenger and Parker, J. Chem. Soc., 1462 (1931).

162. Durand, Compt. rend., 177, 693 (1923).

tetraphenylgermanium were obtained (163). If toluene was substituted for the ether solution, excellent yields of the tetra compound were formed (141). Tetraphenyltin was prepared from chlorobenzene, stannic chloride, and sodium in ether (78). This same type of reaction was used to prepare triphenylantimony from the chloride and sodium (164).

c. The addition of organic halides to some metallic salts.-- The preparation of organometallic compounds in this manner seems quite limited in its scope and is usually carried out in the absence of solvent. A good example of this reaction is the heating of a mixture of stannous chloride with methyl iodide to produce methyltin triiodide (165). Potassium chlorostannite will produce methyltin triiodide when heated with methyl iodide in the absence of solvent (166). This may take place either by the reactions

$$KSnCl_3 + CH_3I \longrightarrow KI + CH_3SnCl_3$$

$$CH_3SnCl_3 + 3KI \longrightarrow CH_3SnI_3 + 3KCl$$

or more likely by the following reactions.

$$KSnCl_3 + CH_3I \longrightarrow KI + CH_3SnCl_3$$

$$KSnCl_3 + 2KI \longrightarrow SnI_2 + 3KCl$$

$$SnI_2 + CH_3I \longrightarrow CH_3SnI_3$$

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163. Tabern, Orndorff, and Dennis, J. Am. Chem. Soc., 47, 2039 (1925).

164. Morgan and Vining, J. Chem. Soc., 117, 777 (1920).

165. Pfeiffer and Heller, Ber., 37, 4618 (1904).

166. Tchakirian, Lesbre, and Lewinsohn, Compt. rend., 202, 138 (1936).

As a matter of fact, both reactions occur. In like manner, alkyllead triiodides are prepared from alkyl iodides and $CsPbCl_3$ (167). Here again the reaction probably takes place as a result of the action of caesium iodide on the initial alkyllead trichloride formed.

$$CsPbCl_3 + RI \longrightarrow RPbCl_3 + CsI$$

$$RPbCl_3 + 3CsI \longrightarrow RPbI_3 + 3CsCl$$

Ethyl iodide and GeI_2 react in a sealed tube to produce ethylgermanium triiodide (168). Unlike lead, $CsGeCl_3$ reacts with alkyl and aryl iodides to give good yields of $RGeCl_3$ compounds (169).

An analogous reaction has been carried out with potassium stannite and alkyliodides in dilute alcoholic base to give R_2SnO compounds (170). If carbon dioxide is bubbled through the reaction mixture at room temperature, $RSnO_2K$ is obtained instead of the R_2SnO formed at reflux temperature (170c).

d. Metalations of metallic salts with aluminum carbide.--All such reactions are carried out in aqueous acid solution to produce methylorganometallic compounds. In this manner,

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167. Lesbre, ibid., 204, 1822 (1937).

168. Flood, J. Am. Chem. Soc., 55, 4935 (1933).

169. Tshakirian and Lewinsohn, Compt. rend., 201, 835 (1935).

170. (a) Meyer, Ber., 16, 1439 (1883); (b) Pfeiffer, Z. anorg. Chem., 68, 102 (1910); (c) Pfeiffer, Ber., 35, 3303 (1902); Pfeiffer and Lehnardt, Ber., 36, 1054 (1903).

Hilpert and Ditmar (171) prepared CH_3HgCl, $(CH_3)_2Hg$, $(CH_3)_3Bi$, and CH_3SnCl_3.

e. Metalations with inorganic salts.-- Although other metal salts are used, this reaction particularly adapts itself to the metalation by mercuric acetate. The use of solvent plays a very important part in this reaction. Miller and Bachman (172) have been able to mercurate fluorene in the 4-position if acetic acid is used as the solvent, but if the reaction is carried out in the absence of solvent both the 3- and 4-positions are involved. If m-dimethylaminophenol is treated with mercuric acetate in acetic acid, only a complex dye is formed, but a 92 per cent yield of 2-hydroxy-4-dimethylaminophenylmercuric acetate is obtained from the reaction in aqueous alcohol (173). Benzene may be mercurated in 80 per cent yields if alcohol is used as a solvent; only 10 per cent yields result if the reaction is carried out without solvent at 110° under pressure, while no mercuration occurred with an excess of benzene as the solvent (174). Most of the reactions are carried out in alcohol or water depending on the solubility and ease of replacement of the hydrogen in the hydrocarbon (175).

171. Hilpert and Ditmar, Ber., 46, 3738 (1913).
172. Miller and Bachman, J. Am. Chem. Soc., 57, 2447 (1935).
173. Kharasch and Chalkley, ibid., 46, 1211 (1924).
174. Maynard, ibid., 46, 1510 (1924).
175. Gilman and Wright, ibid., 55, 3302 (1933).

Other solvents, however, have been used to carry out the reaction. Although m-dimethylaminophenol can be mercurated with mercuric acetate in dilute alcohol, much better yields are obtained in acetone solution containing a trace of water (173). The necessity of water in this reaction shows the possibility of the precipitation of the mercurial as a hydrate. If the reaction is carried out in acetic acid solution only metallic mercury and a complex mercury-free dye are obtained. Mention should be made of the preparation of a number of arylgold dichlorides from anhydrous auric chloride using aromatic hydrocarbons as solvents (176). In order to arrest this reaction at the $RAuCl_2$ stage, ether must be added to form a stable etherate of the $RAuCl_2$ compounds to prevent the following decomposition from taking place.

$$RAuCl_2 + RH \longrightarrow R_2AuCl + HCl \downarrow$$
$$RCl + AuCl + RH$$

Likewise, tetra-p-hydroxyphenylgermanium may be prepared from sodium phenolate and germanium tetrachloride in xylene solution (177).

Reactions of this class may be run in the absence of solvent. An example of this is the metalation of methylaniline and diethylaniline with germanium tetrachloride which, when heated in an autoclave, gives the corresponding para

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176. Kharasch and Isbell, ibid., 53, 3053 (1931).

177. Schwarz and Reinhardt, Ber., 65, 1743 (1932).

substituted organomermanium trichloride (147). Both mono- and dimetalation products are formed by the reaction of mercuric acetate with carbazole (178). This reaction may be run either in the absence of solvent or in alcohol.

f. Addition of inorganic salts to carbon-carbon double bonds.-- This reaction applies almost entirely to mercurials. If the reaction is carried out in water solution, the following takes place:

$$R_2C{=}CR_2 + HgX_2 \xrightarrow{H_2O} R_2C(OH)CR_2HgX$$

With alcohol as the solvent, the corresponding ether results. A number of reactions have been carried out with ethylene (179).

$$C_2H_4 + HgCl_2 \xrightarrow{H_2O} HOC_2H_4HgCl$$

$$C_2H_4 + HgCl_2 \xrightarrow{ROH} ROC_2H_4HgCl$$

Mercuric acetate reacts with cyclohexene in water to give 2-hydroxycyclohexylmercuric acetate (180); as before, alcohol gives the ether.

The commercial synthesis of acetaldehyde from acetylene in the presence of mercuric sulfate and sulfiric acid probably involves the above type of mercury compound as an intermediate (180).

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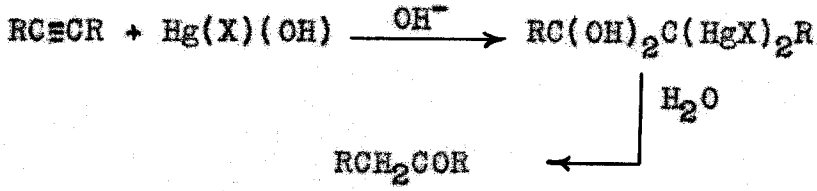
178. Gilman and Kirby, J. Org. Chem., 1, 146 (1936).

179. Hofmann and Sand, Ber., 33, 1340, 1353 (1900); Schoeller, Schrauth, and Essers, Ber., 46, 2864 (1913); Wright, J. Am. Chem. Soc., 57, 1993 (1935).

180. Nesmeyanov and Freidlina, Ber., 69, 1631 (1936).



Hall and Nash (181) obtained ethylaluminum dichloride and diethylaluminum chloride from aluminum chloride and ethylene by heating to 100-200° under pressure.

g. Preparation from aryldiazonium salts.-- This reaction, better known very broadly as the Bart reaction (182), is used for the preparation of mercury and antimony compounds. Bismuth and tin compounds can also be prepared in this manner although poor yields result. Nesmeyanov (183) has decomposed the double salt of diazonium halides and mercuric halides in the presence of copper to give the corresponding RHgX or R_2Hg, depending upon the proportion of reactants used. There seems to be little difference between alcohol and acetone as solvents, for the same yields were obtained. An aqueous solution of HCl was used to react o-nitrobenzenediazonium chloride and mercuric chloride (184). Dilute acetone can be used in the decomposition of a diazonium fluoride-boron fluoride complex with mercuric chloride (185).

181. Hall and Nash, J. Inst. Petroleum Tech., 23, 679 (1937) /C.A., 32, 1239 (1938)/.
182. Bart, Ann., 429, 55 (1922).
183. Nesmeyanov, Ber., 62, 1010 (1929).
184. Nesmeyanov, Glushnev, Epifanskii, and Flegontov, Ber., 67, 130 (1934).
185. Dunker, Starkey, and Jenkins, J. Am. Chem. Soc., 58, 2308 (1936).

Makin and Waters (186) found the best conditions for carrying out the reaction with metallic antimony or mercury to be in anhydrous acetone in the presence of calcium carbonate. Ethyl acetate was used as solvent, but a much slower rate of reaction prevailed. Water, ethyl alcohol, cyclohexane, benzene, carbon tetrachloride, carbon disulfide, ether, and dioxan all gave negative results. When an aryldiazonium chloride was decomposed either in a water suspension of finely divided mercury, or electrolyzed, using mercury electrodes, an RHgCl compound is formed. Acetone, ethyl alcohol, and benzene have been used but with different compounds so that their efficiency could not be judged (187). Antimony trichloride will react readily in an aqueous basic solution with a copper catalyst to give the corresponding stibonic acid (188). Table 3 shows the yields of R_2SnO which were obtained by the decomposition of the benzenediazonium chloride-stannic chloride complex in various solvents (189).

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186. (a) Makin and Waters, J. Chem. Soc., 843, (1938); (b) Waters, ibid., 864 (1939).

187. McClure and Lowry, J. Am. Chem. Soc., 53, 319 (1931).

188. Schmidt, Ann., 421, 174 (1920); Dyson, Rec. trav. chim., 57, 1016 (1938).

189. Nesmeyanov, Kocheshkov, and Klimova, Ber., 68, 1877 (1935).

Table 3. Effect of Solvent upon the Decomposition of Benzenediazonium Chloride-Stannic Chloride Complex

Solvent	Yield of R_2SnO
ethyl acetate	23
acetone	13
ether	4
alcohol	3.8
benzene	0.0
petroleum ether-ethyl acetate mixture	12

When the benzenediazonium chloride-bismuth trichloride complex was decomposed mono- and diarylbismuth chlorides were formed (190). With ethyl alcohol and copper bronze catalyst a 17 per cent yield of bismuth compound was obtained, with methyl alcohol 12 per cent, acetone 6 per cent, dioxan 5 per cent, and no detectible compound with ethyl acetate.

From the foregoing discussion it may be concluded that the solvent most suited depends entirely upon the type of metal salt used. Acetone, a solvent of choice with mercury and antimony chlorides, gives poor results with tin and bismuth halides.

There is a fundamental relationship between diazonium salts and iodonium salts in that the former are quaternary ammonium salts (i.e., fully substituted ammonium salts) and the latter are fully substituted derivatives of the

190. Gilman and Yablunky, J. Am. Chem. Soc., 63, 949 (1941).

hypothetical $(H_2I)^+X^-$. Waters (191) has shown that diazonium chlorides can decompose by a non-ionic mechanism.

$$(C_6H_5N_2)^+Cl^- \longrightarrow C_6H_5N{\equiv}NCl \longrightarrow C_6H_5\cdot + N_2 + \cdot Cl$$

It was only natural then for Sandin (192) to turn to this type of reaction in order to show that iodonium salts might possibly decompose via the non-ionic mechanism. Diphenyliodonium chloride and mercury react in boiling n-propyl alcohol to give phenylmercuric chloride. The same procedure carried out in the presence of finely divided calcium carbonate gives identical results. Changing the solvent from propyl alcohol to water does not seem to have any appreciable effect on the results. This seems peculiar, since one would expect a solvent such as water to favor an ionic decomposition. When a water solution of diphenyliodonium chloride is shaken at room temperature with sodium sulfide, finely divided antimony, and ether, the ether layer yields triphenylstibinic sulfide.

h. The conversion of an organic salt to an organometallic compound.-- Although di-benzoylmethylmercury can be prepared by boiling an alcoholic solution of the mercury salt of benzoylacetic acid (193), the reaction usually takes place by heating without solvent. Whitmore (194) came to this same

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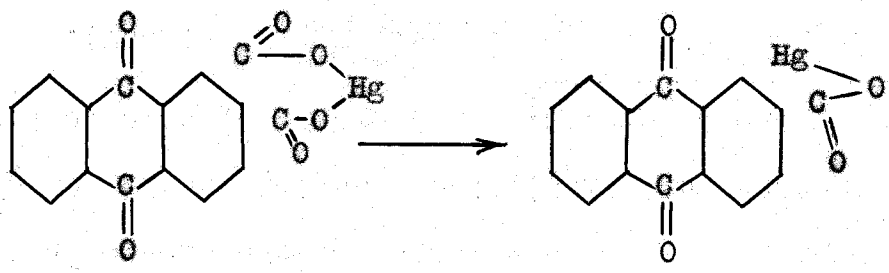
191. Hey and Waters, Chem. Rev., 21, 169 (1937).

192. Sandin, McClure, and Irwin, J. Am. Chem. Soc., 61, 2944 (1939).

193. Kharasch and Staneley, ibid., 45, 2961 (1923).

194. Whitmore and Carnahan, ibid., 51, 856 (1929).

conclusion after trying a wide variety of solvents in the following reaction.



It is a general rule that if the acid itself loses carbon dioxide easily, its mercury salt will lose carbon dioxide to give the corresponding mercury compound.

1. Special methods for organomercury compounds.-- This section pertains to a few miscellaneous reactions peculiar to mercury; therefore the use of various solvents is limited. Diazomethane reacts with mercuric chloride in ether to give chloromethylmercuric chloride (195). If p-tolylmercuric chloride is used instead of $HgCl_2$, chloromethyl-p-tolylmercury results. This compound is unstable and decomposes upon standing to yield di-p-tolylmercury and di-chloromethylmercury. Diazodiphenylmethane reacts with mercuric chloride, in like manner, to give diphenylchloromethylmercuric chloride (196).

The following reaction takes place in dilute alcohol to give arylmercuric halides (197).

195. Hellerman and Newman, ibid., 54, 2859 (1932).

196. Nesmeyanov and Powch, Ber., 67, 971 (1934).

197. Peters, Ber., 38, 2567 (1905); Kharasch, J. Am. Chem. Soc., 43, 607 (1921); Loudon, J. Chem. Soc., 823 (1933).

$$RSO_2H + HgCl_2 \longrightarrow RHgCl + SO_2 + HCl$$

This type of reaction, which is always carried out in dilute alcohol, has not been used extensively.

Aryliodoxy compounds react with mercuric oxide in 10 per cent aqueous potassium hydroxide to give an organomercury compound (198).

$$RIO_2 + HgO \xrightarrow{Ag_2O} RHgIO_3$$

These compounds, characterized by converting to the corresponding halides upon treatment with aqueous alkali halides, were formed in about 50 per cent yields.

$$RHgIO_3 + NaCl \longrightarrow RHgCl + NaIO_3$$

3. Solvents used in interconversion methods.

a. Metal-metal interconversions.-- The metal-metal interconversion reaction seems quite general. Cases are known involving organic compounds of at least one metal in Groups II, III, IV, and V of the Periodic System. Unlike many of the previous reactions, the most outstanding factor is the effect of the solvent. Many times the reaction is completely inhibited by the solvent. Gilman and Moore (199) found that, when tetraphenyllead and n-butyllithium were allowed to react in diethyl ether at room temperature for four hours, 54 per cent benzoic acid was obtained upon carbonation. When the

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198. Nesmeyanov and Makarowa, Ber., 66, 199 (1933).

199. Gilman and Moore, J. Am. Chem. Soc., 62, 3206 (1940).

same reaction was run in benzene for twenty-four hours at 60° a trace of benzoic acid was formed. No benzoic acid could be isolated when petroleum ether was used in the same reaction. Ziegler and Dersch (200) prepared benzyllithium from the interconversion of benzylmagnesium chloride and phenyllithium in diethyl ether. This reaction is slow and is applicable only when the resulting lithium compound is stable in ether. For example, ethyllithium could not be prepared in this manner for it cleaves ether too readily.

$$C_2H_5Li + C_2H_5OC_2H_5 \longrightarrow LiOC_2H_5 + C_2H_6 + C_2H_4$$

Even though isopropyllithium cleaves ether these authors prepared it from phenyllithium and isopropylmagnesium chloride. The alkyllithium compound was characterized by reacting with diphenylethylene and carbonating to give $(C_6H_5)_2C(COOH)CH_2CH\cdot(CH_3)_2$. Phenyllithium added so slowly to the double bond that it caused no trouble.

Organomagnesium compounds undergo reaction with organomercury compounds (201) in ether.

$$C_6H_5CH_2HgCl + \underline{t}\text{-}C_4H_9MgCl \longrightarrow \underline{t}\text{-}C_4H_9HgCl + C_6H_5CH_2MgX$$

This type of reaction was shown to be reversible by Gilman and Jones (202).

$$(C_6H_5)_2Hg + 2CH_3\text{C}_6\text{H}_4Li \underset{}{\overset{\text{ether}}{\rightleftharpoons}} (CH_3\text{C}_6\text{H}_4)_2Hg + 2C_6H_5Li$$

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200. Ziegler and Dersch, Ber., 64, 448 (1931).

201. Kharasch and Swartz, J. Org. Chem., 3, 405 (1938).

202. Gilman and Jones, J. Am. Chem. Soc., 63, 1439 (1941).

$$C_6H_5MgBr + (CH_3C_6H_4)_2Hg \rightleftharpoons 2CH_3C_6H_4MgBr + (C_6H_5)_2Hg$$

Triphenylthallium reacted with n-butyllithium in ether to yield phenyllithium and tributylthalium (203). When n-butyllithium reacted in ether with tri-α-naphthylbismuth for eighteen hours, 48.1 per cent α-naphthoic acid was isolated upon carbonation. No α-naphthoic acid was formed when the reaction was carried out in benzene for twenty hours (204). An ether-benzene mixture was used in the interconversion of phenylmercuric bromide and α-naphthylmagnesium bromide (205). The benzene was not used to increase the boiling point of the solvent, as the reaction took place at room temperature.

In these experiments the importance of ether again manifests itself, but ether is not indispensable in this reaction since other solvents have been used as well. Benzene may be used in the interconversion of ethyllithium and diethyl-, diphenyl-, and dibenzylmercury (206). Diphenylmercury and diethylzinc also react in benzene. When ethyllithium and dimethylmercury react in benzene, the methyllithium formed precipitates (4). No benzoic acid was isolated upon carbonation of a mixture of tetraphenyllead and benzylsodium, probably because of the solvent employed (199).

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203. Gilman and Jones, ibid., 62, 2357 (1940).

204. Gilman, Yablunky, and Svigoon, ibid., 61 1170 (1939).

205. Challenger and Ridgway, J. Chem. Soc., 121, 104 (1922).

206. Hein, Petzchner, Wagler, and Segitz, Z. anorg. allgem. chem., 141, 161 (1924).

As is to be expected, petroleum ether is a solvent of choice for metal-metal interconversions with organosodium compounds. This solvent was used in the interconversion of n-butylsodium with organomercury (207) and organobismuth compounds (204).

Although no interconversion took place between diphenylmercury and tri-α-naphthylbismuth in benzene or chloroform, these compounds were made to react in the absence of solvent (205). A number of products were isolated, however, which made this method undesirable.

Before leaving this section, mention should be made of the random distribution reaction of Calingaert (208). When two or more different organometallic compounds are mixed, the products of such a reaction give compounds resulting from a random distribution of the organic radicals. This type of reaction will proceed in the absence of solvent. To obtain the desired reaction temperature and at the same time to provide stirring, as well as to exclude air, it is best to use an inert solvent, such as hexane or decalin. Acetone has been used. There is no evidence that the solvent participates in any way in this reaction. There is no pronounced effect on the reaction velocity and certainly the relative proportions of compounds in the completed reaction are not altered. For

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207. Gilman and Bebb, J. Am. Chem. Soc., 61, 112 (1939).

208. Calingaert and Beatty, ibid., 61, 2748 (1939); Calingaert, Beatty, and Soroos, ibid., 62, 1099 (1940).

the $AlCl_3$ catalyst with R_4Pb compounds, the presence of hexane may have a retarding effect on the reaction velocity, but a ten-fold increase in the amount of hexane has no further perceptible effect upon the reaction.

b. Hydrogen-metal interconversions.-- Hydrogen-metal interconversions have, for the most part, been carried out in ether solution at reflux temperature. Gilman and Bebb (209) have given an excellent review of this subject. It is important to consider the relative instability of the ethers in the presence of reactive organometallic compounds lest the organometallic compound be destroyed by cleavage of the ether before metalation can take place. Gilman and Young (69) were able to use ether as a solvent for highly reactive metalating agents, since metalation occurs more rapidly than ether cleavage, and a less reactive organometallic compound is formed as the metalation product. Many times an ether-benzene mixture is used to effect metalation (210). The purpose of the benzene is to increase the reflux temperature of the solvent in order to permit shorter reaction time and increase the yields.

Aromatic hydrocarbons may be used as solvents for

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209. Gilman and Bebb, J. Am. Chem. Soc., 61, 109 (1939).

210. Gilman, Langham, and Willis, J. Am. Chem. Soc., 62, 346 (1940).

metalation, but here also, discretion must be used since the highly reactive organometallic compounds bring about metalation of the nucleus. Bibenzyl is metalated by n-butylsodium in benzene (211). However, the yields are usually very low in this solvent. If benzene is used as a solvent in the preparation of the n-butyl compounds of Ce, Rb, K (212), Na (213), or Li (214), the yields of benzoic acid upon carbonation vary with the reactivity of the organometallic compound. Shoruigin (215) has used a large number of aromatic solvents for the preparation of ethylsodium from diethylmercury, and in each case metalation took place. With toluene, phenylacetic acid is obtained; xylene gives m-tolylacetic acid; ethylbenzene produces hydratropic acid. A 41 per cent yield of phenylisopropylsodium is obtained by preparing ethylsodium in cumene in this manner (214).

Metalations in petroleum ether go with greater difficulty. Although diphenyl ether gives 51 per cent interconversion with n-butyllithium in diethyl ether after only six hours, the interconversion with petroleum ether is only 7 per cent at the end of twenty hours (207).

211. See reference 43, pp. 71 and 80.

212. Gilman, Jacoby, and Ludeman, J. Am. Chem. Soc., 60, 2336 (1938).

213. Gilman and Kirby, ibid., 58, 2074 (1936).

214. Gilman, Pacevitz, and Baine, J. Am. Chem. Soc., 62, 1519 (1940).

215. Shoruigin, Ber., 41, 2723 (1908).

Ethynylsodium metalated 1-heptyne and phenylacetylene in liquid ammonia, whereas the attempted metalation of diphenyl ether in this solvent gave only o-phenylphenol (43).

Phenylcalcium iodide can be made to metalate a number of compounds but the yields are poor, probably because of the low order of metalating activity of arylorganometallic compounds in general (216). Organomagnesium compounds are so inactive that metalation with them must be carried out at high temperature and with no solvent (217).

In order to determine the effect of solvents on the metalation of dibenzothiophene by n-butyllithium, Bebb (43) ran the reaction for twenty-four hours with various solvents, isolation the acid formed upon carbonation. Butyl ether gave a 61 per cent yield of acid when run at room temperature and 90 per cent when run at 80°. No acid was obtained with petroleum ether (b.p. 30-36° or 60-68°), benzene, or dioxan. With dioxan the color test became weaker during the period of twenty-four hours. Under the same conditions with butylsodium in petroleum ether (b.p. 60-68°) only a 37 per cent yield was obtained.

c. Halogen-metal interconversion.-- This reaction may be carried out in many solvents; however, the yield varies.

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216. Gilman, Kirby, Lichtenwalter, and Young, Rec. trav. chim., 55, 79 (1936); Gilman and Jacoby, J. Org. Chem., 3, 108 (1938); Gilman, Jacoby, and Pacevitz, ibid., 3, 120 (1938).

217. Challenger and Miller, J. Chem. Soc., 894 (1938).

For maximum yields of interconversion product, the use of petroleum ether is recommended. This solvent allows a satisfactory rate of halogen-metal interconversion in most cases but seemingly inhibits other reactions such as coupling, metalation, and metal-metal interconversions (17). This is brought to light in a striking manner in the interconversion of β-bromostyrene and n-butyllithium. If ether is employed as solvent in this reaction, phenylpropiolic is formed upon carbonation. Hydrogen bromide is probably first split out and then the phenylacetylene is metalated. When the reaction is carried out in petroleum ether, 23 per cent trans-cinnamic acid is formed.

When a rapid reaction is desired, it is advisable to use diethyl ether as the solvent. This is especially true if a halogen-metal interconversion reaction is to be run with a compound which also has another functional group. This type of reaction can be run at a low temperature for a short time and has been used successfully with compounds like o-bromonitrobenzene, bromo- and iodobenzoic acids (16), and bromopyridines and -quinolines (218). A mixture of ether and benzene has been used as a solvent to increase the temperature of the reaction mixture (219). Although the unreactive organometallics do not give interconversion, the presence of

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218. Gilman and Spatz, J. Am. Chem. Soc., 62, 446 (1940).

219. Gilman, Willis, and Swislowsky, ibid., 61, 1371 (1939); Gilman, Swislowsky, and Brown, ibid., 62, 348 (1940).

as little as two parts per thousand of organolithium compounds causes an interconversion with organomercury compounds (220).

The effect of solvent on halogen-metal interconversion can easily be seen from table 4.

Table 4. Yield of α-Naphthoic Acid from Interconversion of n-Butyllithium and α-Bromonaphthalene in Various Solvents.

Time in minutes	$(C_2H_5)_2O$	$(C_4H_9)_2O$	$C_6H_5N(CH_3)_2$	C_6H_6	C_6H_{12}	Petroleum ether
.5	84	88	23			
1.0	78	88	38			
5.0	73	91	69			
10.0	68	86	74	3	3	
30.0		83	70	8		10
60.0		60		17	15	16
120.0				29	24	30
240.0				45	41	
360.0				44	53	

Of all the solvents used n-butyl ether seems to give the highest yield of interconversion product.

d. The preparation of RMM' compounds.-- Most of these reactions are carried out in liquid ammonia, so the organometallic compound formed must be of such activity that it will not undergo ammonolysis. Triphenylgermanium-sodium compounds have been prepared from hexaphenyldigermanium (221). The same

220. Gilman and Jones, ibid., 63, 1443 (1941).

221. Kraus and Nutting, ibid., 54, 1622 (1932); Kraus and Foster, ibid., 49, 457 (1927).

type of reaction was used to prepare both triaryl- (222) and trialkyltin-sodium compounds (223). Gilman and Bailie (224) were the first to present definite evidence of triphenyllead-sodium prepared in this manner. Not only did sodium react with hexaphenyldilead in this manner, but lithium, potassium, rubidium, calcium, strontium, and barium reacted as well (225). The R_2BiM types with alkali and alkaline earth metals may also be prepared (226).

Triethylgermanium-sodium cannot be prepared from hexaethyldigermanium in liquid ammonia, but if ether is added, the reaction proceeds slowly (227). If triethylgermanium bromide is used with sodium in liquid ammonia the germanium-sodium compound undergoes ammonolysis to yield di-triethylgermaniumimine. Lithium reacts with the bromide in ethylamine solution but unfortunately solvolysis occurs to give triethylgermanium hydride and lithium amide as the final product. However, sodium and potassium in ethylamine give $(C_2H_5)_3GeM$ compounds which are more resistant to solvolysis (227). It might be mentioned here that since triethylgermanium-sodium

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222. Chambers and Scherer, ibid., 48, 1054 (1926).

223. Kraus and Sessions, ibid., 47, 2361 (1925).

224. Gilman and Bailie, ibid., 61, 731 (1939).

225. R. W. Leeper, unpublished studies.

226. Gilman and Yablunky, ibid., 63, 212 (1941).

227. Kraus and Flood, ibid., 54, 1635 (1932).

undergoes ammonolysis so readily the following reaction must be carried out in benzene (228).

$$(C_6H_5)_3GeNa + (C_2H_5)_3GeBr \longrightarrow (C_6H_5)_3GeGe(C_2H_5)_3 + NaBr$$

Triethylboron-sodium is unique in that boron has a valence of four instead of the usual three and that these compounds may be prepared in ether. This compound is formed by reacting triethylboron with sodium amalgam in ether (229).

e. Disproportionation of organometallic compounds.-- This important class of reactions includes the studies on the equilibrium of the Grignard reagent.

$$2RMgX \rightleftharpoons R_2Mg + MgX_2$$

No attempt will be made to discuss the work done on the proof of this equilibrium; however, the effect of solvents will be mentioned briefly. If dioxan is added to an ether solution of a Grignard reagent, the halogen-containing compounds are precipitated, leaving the R_2Mg compound in solution (230). Phenyl- and methylmagnesium bromide are less disproportionated in n-butyl ether than in diethyl ether (231) and even less so in benzene (231, 232).

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228. Kraus and Sherman, ibid., 55, 4691 (1932).

229. Bent and Dorfman, ibid., 54, 2132 (1932); ibid., 57, 1259 (1935).

230. Noller and White, ibid., 59, 1354 (1937); Schlenk and Schlenk, Ber., 62, 920 (1929).

231. Cope, J. Am. Chem. Soc., 57, 2238 (1935).

232. Miller and Rockman, ibid., 57, 767 (1935).

Austin has shown the following equilibrium to exist (160).

$$(C_6H_5)_3PbCl \rightleftharpoons (C_6H_5)_2PbCl_2 + (C_6H_5)_4Pb$$

By the use of n-butyl alcohol as the solvent, 10 per cent of the expected compounds were isolated from triphenyllead chloride. Benzene and toluene as solution media seemed to make no difference in the equilibrium. An 86 per cent recovery of triphenyllead chloride was made from the reverse reaction.

A number of these disproportionation reactions can be carried out by distilling in the absence of solvent. If RBeX compounds are heated, the beryllium halide sublimes, leaving the R_2Be compound (26). Diethylzinc was obtained by distilling ethylzinc iodide (53). Even dimethylmagnesium can be obtained by distilling the methyl Grignard in a high vacuum (233). v. Grosse and Mavity (60) obtained dimethylaluminum iodide by the distillation of methylaluminum diiodide.

f. The addition of organometallic compounds to double bonds.-- Diethyl ether seems to be used exclusively for the addition of organometallic compounds to double bonds. This fact again brings out the significance of the role of diethyl ether in organometallic chemistry. From what has been found in general in this discussion of solvents, it can be predicted

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233. Gilman and Brown, ibid., 52, 5045 (1930).

that other inert solvents may be substituted for ether but that the reaction would be quite slow. Ziegler (234) has given an excellent review on the significance in synthesis of the addition of organoalkali compounds to ethylenic double bonds.

g. Addition of organic halides to organometallic compounds.-- A reaction such as this seems to go better with only the organic halide as a solvent. This type of reaction seems to adapt itself to the use of alkyl iodides with alkylgermanium compounds (235), both alkyl- (236) and aryltin compounds (237), and organoantimony compounds (152b, 137). Löwig (238) modified this reaction by covering the reactants with water and allowing them to stand at room temperature. If no reaction occurred at this temperature the mixture was heated until the water boiled.

h. The reduction of organometallic compounds.-- Reduction of organometallic compounds represented by the formula RMX may be divided into the reactions which give symmetrical R_2M compounds, a dimerized product RM-MR, or an organometallic

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234. Ziegler, Angew. Chem., 49, 499 (1936).

235. Howity and Flood, J. Am. Chem. Soc., 55, 5055 (1933).

236. Grüttner, Ber., 50, 1808 (1917); Krause and Pohland, Ber., 57, 532 (1924).

237. Ladenburg, Ber., 4, 19 (1871).

238. Löwig, Ann., 97, 322 (1856).

compound, RM, with the metal in a lower state of valence. There are a number of reagents that achieve these reductions; accordingly, it is not surprising to find a number of different solvents employed. There has been little systematic study of the effect of solvents on these reactions.

A very good method of making the symmetrical mercurial is the reduction of the RHgX compound with hydrazine in the presence of sodium carbonate with alcohol as a solvent (239). This reaction is fine for arylmercury compounds but is not so satisfactory for the alkyl type. This is of little consequence since it is possible to prepare the dialkylmercury compounds in about 90 per cent yields from the Grignard reagent. This has been adapted to the conversion of phenylbismuth dichloride into triphenylbismuth. Here again alcohol was used as the solvent (240).

An interesting reaction takes place between phenylmercuric chloride and diazomethane (241).

$$C_6H_5HgCl + CH_2N_2 \xrightarrow{\text{ether}} (C_6H_5)_2Hg + (ClCH_2)_2Hg + N_2$$

Mercuric chloride even reacts with an ether solution of CH_2N_2.

$$HgCl_2 + CH_2N_2 \xrightarrow{\text{ether}} N_2 + ClCH_2HgCl$$

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239. Gilman and Barnett, Rec. trav. chim., 55, 563 (1936).

240. Gilman and Yablunky, J. Am. Chem. Soc., 62, 665 (1940).

241. Hellermann, ibid., 54, 2859 (1932).

In the reaction

$$2RHgI + 2NaI \rightleftharpoons R_2Hg + Na_2HgI_4$$

alcohol was used as solvent by Whitmore (242), while Steinkopf (243) used acetone because the mercurials he used were more soluble in this solvent.

Water has been the solvent for a number of these reactions. Sodium stannite will reduce phenylmercuric acetate to diphenylmercury in 95 per cent yield (174). A basic solution of zinc chloride reacts in the same manner (244).

Copper powder will reduce both alkyl- and arylmercuric halides if pyridine is used as the solvent (245). This is a very useful reaction, giving from 70 to 90 per cent yields. Hydrogen sulfide may be substituted for copper powder in these reactions. The compound, $(RHg)_2S$, is first formed, which then decomposes upon heating to give the R_2Hg compound. With copper powder in alcohol solution the reduction proceeds very slowly and this method is not used to any great extent. The increased reaction in pyridine over that in alcohol is said to be due to the solvation with pyridine.

When diphenylthallium bromide is treated with sodium in liquid ammonia, triphenylthallium is formed (108).

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242. Whitmore and Sobatzki, ibid., 55, 1128 (1933).

243. Steinkopf, Ann., 413, 315 (1916).

244. Dimroth, Ber., 35, 2853 (1902).

245. Hein and Wagler, Ber., 58, 1499 (1925).

$$3(C_6H_5)_2TlBr + 3Na \longrightarrow 2(C_6H_5)_3Tl + Tl + 2NaBr$$

The same type of reaction occurs with phenyltin trichloride and sodium in xylene solution (177).

Usually the compounds that form RMM' compounds in liquid ammonia give RM-MR compounds when the reaction is carried out in other solvents. Diethyl ether is used with triethyltin bromide (236), while Nesmeyanov (246) uses isoamyl ether as solvent. There is no way to tell the relative merits of these two solvents as both authors claim good yields. Of the hydrocarbons, benzene has been used to prepare hexamethyldiplatinum (247), while xylene was used for the preparation of hexacyclohexylditin (236) and hexaphenyldigermanium (221).

A number of electrolytic reductions have been carried out on organometallic compounds. When an alkylmercuric chloride is electrolyzed in liquid ammonia, an RHg compound is formed which decomposes to the R_2Hg compound (248). The chromium compounds are reduced by electrolysis in liquid ammonia. Tetraphenylchromium iodide forms triphenylchromium (249). Not only liquid ammonia but also alcohol

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246. Nesmeyanov, Kocheshkov, and Puzyreva, J. Gen. Chem. (U.S.S.R.), 7, 118 (1937) /C.A., 31, 4290 (1937)/.

247. Gilman and Lichtenwalter, J. Am. Chem. Soc., 60, 3085 (1938).

248. Kraus, ibid., 35, 1732 (1913).

249. Hein and Eissner, Ber., 59, 362 (1926); Hein and Markert, Ber., 61, 2255 (1928).

has been used in electrolytic reductions. Upon the electrolysis of triethyllead hydroxide in the latter medium, triethyllead is produced (250).

An unusual reaction is the reduction of dimethylgallium chloride to dimethylgallium by sodium in liquid ammonia (251).

When trinitrophenylantimonic hydroxide is reduced by zinc and ammonium chloride in alcohol, both the nitro group and the antimony atom are reduced to give triaminophenylantimony (143). Another interesting reaction is the reduction of triphenylbismuth dibromide with hydrogen sulfide in ammonium hydroxide (84).

$$(C_6H_5)_3BiBr_2 + H_2S \longrightarrow (C_6H_5)_3Bi + 2HBr + S$$

One of the phenyl groups is cleaved from pentaphenylchromium hydroxide by hydrogen iodide in chloroform. During this process the chromium undergoes reduction to give tetraphenylchromium iodide as one of the final products (252).

1. Cleavage of organometallic compounds with halogens.-- The treatment of organometallic compounds with halogens results in two types of reactions. One of these is an oxidation of the metal to a higher valence state; the other is a cleavage of the R groups from the metal. All the solvents

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250. Midgley, Hochwalt, and Calingaert, J. Am. Chem. Soc., 45, 1821 (1923).

251. Kraus and Toonder, ibid., 55, 3547 (1933).

252. Hein, Ber., 54, 2708 (1921).

used here are typical of halogenation reactions. Although ether usually ranks first as a solvent in organometallic preparations, it has been used only for the chlorination and bromination of R_3Sb compounds to give oxidation to R_3SbX_2 types (253, 152b).

Iodine in benzene has been used with success to cleave one phenyl group from tin (223, 236) and to oxidize triphenylindium to triphenylindium iodide. Excess iodine removes one phenyl group to give diphenylindium diiodide (108).

Just as in other halogenations, chloroform and carbon tetrachloride are popular solvents. When gold compounds of the type R_2AuBr are treated with bromine in either of these two solvents, one of the R groups is cleaved to give $RAuBr_2$ compounds (254, 159). Bromination of tetraphenylgermanium in carbon tetrachloride gives triphenylgermanium bromide (221). Krause (255) found that when tetraphenyltin is brominated in ordinary solvents two phenyl groups are replaced by bromine and very little $(C_6H_5)_3SnBr$ is formed. When, however, the reaction is carried out in pyridine, a 90-95 per cent yield of this compound is obtained with only a small quantity of $(C_6H_5)_2SnBr_2$. The reaction works equally well with iodine or chlorine. Krause and Pohland (236) claimed to be able to

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253. Basenbäumer, Ber., 31, 2911 (1898); Krause and Renwanz, Ber., 65, 777 (1932).

254. Kharasch and Isbell, J. Am. Chem. Soc., 53, 2701 (1931).

255. Krause, Ber., 51, 912 (1918).

cleave only one R group from tetracyclohexyltin with bromine in cold $CHCl_3$ or CCl_4, but Chambers and Sherer (77) found two groups cleaved by this method. However, they found that iodine when refluxed in chloroform cleaves only one group from tetraphenyltin. This can be converted to triphenyltin hydroxide by sodium hydroxide. This compound, in turn, gives triphenyltin bromide in 50 per cent yields when treated with HBr. The essential reaction in the halogenation of bismuth (84) and antimony compounds (83) in chloroform is the oxidation of the metal atom in these compounds to the pentavalent state. Cleavage can be attained, however, for diphenyl-α-naphthylbismuth, when treated in ether-chloroform solution with iodine monochloride, gives diphenylbismuth chloride (256).

When carbon tetrachloride is used as a bromination solvent, it takes several hours' boiling to cleave one phenyl group from tetraphenylgermanium, but when ethylene dibromide is used, very pure triphenylgermanium bromide is formed after a few minutes warming (147). Ethyl bromide was found to be superior to either carbon tetrachloride or ethylene bromide as a solvent for the cleavage of tetraethylgermanium. With ethyl bromide, an 82 per cent yield of $(C_2H_5)_3GeBr$ was obtained, while the two last named solvents gave mixtures of products (227).

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256. Challenger and Allpress, J. Chem. Soc., 119, 913 (1921).

A number of other solvents have been used to carry out reactions with halogens. Two phenyl groups were cleaved from tetraphenyltin by treatment with bromine in carbon disulfide (78). Depending upon the amount of chlorine used either dimethyllead dichloride or methyllead trichloride may be obtained from hexamethyldilead in ethyl acetate (257). It is interesting that tetraphenyllead may be formed by the reaction of hexaphenyldilead with bromine in pyridine (258). As in the example with chloroform as a solvent, petroleum ether causes R_3Bi compounds to be oxidized by halogens to R_3BiX_2 compounds (259). When triphenylantimony is treated with chlorine in the absence of solvent the reaction goes one step farther to produce diphenylantimony trichloride (260). Likewise tri-n-butylboron is cleaved with bromine in the absence of solvent to produce a mixture of n-butylboron dibromide and di-n-butylboron bromide (261).

j. Cleavage of organometallic compounds by acids.-- In general about the same solvents are used in these reactions as have been used in the reactions with halogens. No special

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257. Grüttner and Krause, Ber., 49, 1415 (1916).

258. Krause and Reissans, Ber., 55, 888 (1922).

259. Michaelis, Ber., 20, 52 (1887).

260. Michaelis and Günther, Ber., 44, 2316 (1911).

261. Johnson, Snyder, and Van Campen, J. Am. Chem. Soc., 60, 115 (1938).

effect has been attributed to these solvents other than solubility and temperature gradient. Ether and chloroform are most frequently used in the cleavage of organolead compounds (262). Dimethyllead sulfide is formed by the action of hydrogen sulfide on dimethyllead chloride in acetic acid (257).

No discussion of the cleavage of organometallic compounds would be complete without a short discourse on the cleavage of unsymmetrical mercurials by hydrogen chloride.

$$RR'Hg + HCl \longrightarrow RHgCl + R'H$$

This splendid work, which enabled Kharasch to formulate an electro-negativity series of organic radicals, was carried out, for the most part, in alcohol solution (263). A thorough study of the effect of the solvents alcohol, ether, benzene, and glacial acetic acid shows that the most electro-negative radical is cleaved from the mercurial irrespective of the solvent used, even if one of the two possible products formed is insoluble in the solvent used (264).

B. The Cleavage of Ethers by Organometallic Compounds

The previous discussion has emphasized the importance of diethyl ether as a solvent for the preparation of

262. Gilman and Baillie, ibid., 61, 731 (1939).

263. Kharasch, Legault, and Sprawls, J. Org. Chem., 3, 409 (1938); Kharasch and Flenner, J. Am. Chem. Soc., 54, 674 (1932).

264. Kharasch, Pines, and Levine, J. Org. Chem., 3, 347 (1938).

organometallic compounds. It is unfortunate that such a large number of these organometallic compounds are unstable in this solvent. The amount of ether cleavage produced depends upon six factors: (1) the metal atom of the organometallic compound, (2) the R group attached to the metal atom, (3) the temperature, (4) the halogen component of the organometallic compound, (5) the reaction carried out with these compounds, and (6) the ether employed.

Obviously, the organometallic compounds of the more active metals will cleave ether more rapidly. Benzylsodium, prepared from dibenzylmercury and sodium in petroleum ether, may be dissolved in ether, but the solution must be kept cold or the ether will be cleaved immediately (4). Even in the cold the ether solution becomes reddish yellow and decomposes rapidly. Benzyllithium, however, is known with certainty to be stable in ether for at least four weeks (265). Lüttringhaus and Sääf (266) bring out the significance of this in Table 5.

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265. Ziegler and Schäfer, Ann., 479, 150 (1930).

266. Lüttringhaus and Sääf, Angew. Chem., 51, 915 (1938).

Table 5. The Cleavage of the Ether C_6H_5OR with Organometallic Compounds at 50°.

R	C_6H_5MgBr	C_6H_5Li	C_6H_5Na
phenyl	-	-	+
n-butyl	-	-	+
benzyl	-	+	+
allyl	+(a)	+	+

(a) Cleavage is represented by +.

The nature of the R groups on an organometallic compound is of major importance in determining the rate of cleavage of ether. Although benzyl- (4) and ethylsodium (267) cleave ether rapidly, phenylisopropylsodium and even phenylisopropylpotassium are fairly stable in ether since this solvent is used to prepare these compounds by cleavage of the ether, $C_6H_5C(CH_3)_2OCH_3$, with alkali metals (268). As mentioned before, benzylsodium decomposes ether in a short time (4, 268). This does not hold true for diphenylmethylsodium (269) and diphenylmethylpotassium (270) which are fairly stable in ether. Triphenylmethylsodium seems to be quite stable (118). Methyllithium is reported to be stable for weeks in diethyl ether (271) although ethyllithium (200) is known to cleave

267. Shoruigin, Ber., 43, 1931 (1910).
268. Ziegler, Corssmann, Kleiner, and Schäfer, Ann., 473, 1 (1928).
269. Schlenk and Bergman, Ann., 464, 18 (1928).
270. Ziegler and Schnell, Ann., 437, 227 (1924).
271. Ziegler and Zeiser, Ann., 485, 174 (1931).

ether to an appreciable extent, while t-butyllithium cleaves this solvent immediately. Most simple alkyllithium compounds cleave ether, but the aryl types are relatively stable in this solvent (14a, 22). However, Müller and Töpel (272) claim that the preparation of α-naphthyl-, p-biphenyl-, and 9-phenanthryllithium would be of no use for synthetic purposes because of their rapid decomposition by ether. Later work in this thesis shows this statement to be in error.

The effect of temperature is of vital importance to the rate of ether cleavage. Grignard (273) has observed that phenyl ether, which is quite indifferent to cleavage, is decomposed by RMgX compounds at a temperature of 180-200°. When phenyl allyl ether was treated with n-butylmagnesium bromide for 40 hours at 17° only 12 per cent cleavage resulted, but at 34° under identical conditions 61 per cent cleavage occurred (266). Even the stable methyllithium (271) was cleaved at the boiling point of butyl ether as shown by a negative color test (43). This is further substantiated by the work of Mr. Christian (274). During the course of his investigations on a modification of the Zerewitinoff determination, methyllithium in n-butyl ether was stored in a Grignard machine (275). The normality decreased only from

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

273. Grignard and Ritz, Bull. Soc. Chim., [5] 3, 1181 (1936).

274. Unpublished work by Mr. R. V. Christian.

275. Kohler, Stone, and Fuson, J. Am. Chem. Soc., 49, 3181 (1927).

0.777 to 0.764 during four months. The normalities were based upon gas analyses of the methyllithium. When a solution which was 0.598N was heated at 80° for one-half hour, gas was evolved and the normality was reduced to 0.513. After an hour it had dropped to 0.451.

The halogen component of the Grignard reagent has a moderate influence on the amount of ether cleavage (273). Under the same conditions, phenetole was cleaved to the extent of 16 per cent with methylmagnesium bromide and 80 per cent with the iodide.

It is quite obvious that the type of reaction carried out with the ether solution of the organometallic compounds is of great importance in ether cleavage. This is especially true if there is a time factor involved, for if the reaction requires but a short time for completion, ether cleavage is of no serious consequence. However, there is another type of reaction in which the time factor is not involved. It is undesirable to use diethyl ether as a solvent for the oxidation of arylmagnesium halides since there is auto-oxidation of the ether to produce secondary alcohols (276). It is highly significant that good yields of phenol are obtainable by the oxidation of phenylmagnesium bromide prepared in phenetole, an ether which shows no evidence of auto-oxidation. The main product from the reaction of the ethylaluminum iodides with propiophenone in ether is a condensation

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

product of ethyl benzoate (277). The ethyl benzoate comes from the cleavage of ether. This is not surprising since $AlCl_3$ also cleaves ether (278). Organozinc compounds cannot be used in ether solution with acid chlorides because esters are formed by cleavage as with organoaluminum halides (279). The only case of this type of cleavage with cadmium is the reaction of diphenylcadmium and benzoyl chloride.

Hirao (280) has studied a series of ether cleavages between the Grignard reagent and guaiacol alkyl ethers. In general the smaller alkyl group is attacked in the reaction and the larger alkyl group remains unchanged. However, $1,2\text{-}C_2H_5O(C_6H_5CH_2O)C_6H_4$ loses the benzyl group rather than the smaller radical to give $1,2\text{-}C_2H_5O(OH)C_6H_4$.

Grignard found that in order to obtain cleavage, the organomagnesium compound must be in the form of the ether complex. No cleavage of anisole occurred when it was heated to 160° with $C_2H_5MgBr\cdot(C_2H_5)_2O$ (281). If, however, the ethylmagnesium bromide was first prepared in anisole in order

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277. L. D. Apperson, Doctoral Dissertation, Iowa State College, 1940, p. 54.

278. Meerwein and Maier-Heiser, J. prakt. Chem., 134, 51 (1932).

279. Gilman and Nelson, Rec. trav. chim., 55, 518 (1936).

280. Hirao, J. Chem. Soc. Japan, 53, 488 (1932) [C.A., 27, 276 (1933)].

281. Grignard, Compt. rend., 151, 322 (1910).

to form the etherate, $C_2H_5MgX \cdot C_6H_5OCH_3$, and then heated, phenol was obtained. This result has been substantiated by Späth and Simonis (282).

Benzylsodium cleaves di-chloromethyl ether to give β-phenyllethyl alcohol in about 15 per cent yield together with about 19 per cent di-β-phenylethyl ether, the normal coupling product (283).

When benzyl phenyl ether was cleaved with phenyllithium only a small amount (14 per cent) of the expected cleavage product, diphenylmethane, was obtained (266). The chief product in the neutral fraction was 1,1,2-triphenylethane. The following series of reactions was proposed to explain the presence of this product.

$$C_6H_5OCH_2C_6H_5 + C_6H_5Li \longrightarrow C_6H_5 + C_6H_5O\underset{\displaystyle Li}{\underset{|}{C}}HC_6H_5$$

$$C_6H_5O\underset{\displaystyle Li}{\underset{|}{C}}HC_6H_5 + C_6H_5OCH_2C_6H_5 \longrightarrow C_6H_5OLi + C_6H_5O\underset{\displaystyle CH_2C_6H_5}{\underset{|}{C}}HC_6H_5$$

$$C_6H_5O\underset{\displaystyle CH_2C_6H_5}{\underset{|}{C}}HC_6H_5 + C_6H_5Li \longrightarrow C_6H_5OLi + (C_6H_5)_2CHCH_2C_6H_5$$

Ether cleavage by organometallic compounds finds frequent use as a synthetic tool. Alkyl phenyl ethers with a double bond in the β-position of the alkyl component are

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282. Späth, Monatsh., 35, 319 (1914); Simonis and Remmert, Ber., 47, 269 (1914).

283. Morton, Massengale, and Gibb, J. Am. Chem. Soc., 63, 324 (1941).

readily cleaved to form unsaturated hydrocarbons (284); allyl phenyl ether is the simplest case.

$$C_6H_5OCH_2CH{:}CH_2 + RMgX \longrightarrow C_6H_5OMgX + RCH_2CH{:}CH_2$$

Runge (285) has written an excellent review on synthesis by the cleavage of acetal type compounds by the Grignard reagent.

$$CH_3CH(OC_2H_5)_2 + C_6H_5CH_2MgCl \longrightarrow C_2H_5OMgCl + C_2H_5OCH(CH_3)CH_2C_6H_5$$

A very satisfactory method of preparing tertiary amines is by the cleavage of dialkylaminomethyl butyl ether with the Grignard reagent (286). These amine ethers are quite easily prepared by distilling a mixture of the dialkylamine, commercial formalin, and butyl alcohol in the presence of potassium carbonate. The yields of the tertiary amine by cleaving these ethers are in the neighborhood of 50 per cent. An example of this reaction is the cleavage of diethylaminomethyl butyl ether by α-naphthylmagnesium bromide.

$$(C_2H_5)_2NH + HC(=O)-H + C_4H_9OH \xrightarrow{K_2CO_3} (C_2H_5)_2NCH_2OC_4H_9 + H_2O$$

$$C_2H_5NCH_2OC_4H_9 + \text{C}_{10}\text{H}_7\text{-MgBr} \longrightarrow C_4H_9OMgBr + \text{C}_{10}\text{H}_7\text{-CH}_2\text{N}(C_2H_5)_2$$

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284. Lüttringhaus, Sääf, and Hauschild, Ber., 71, 1673 (1938).

285. See reference 133, p. 170.

286. Robinson and Robinson, J. Chem. Soc., 123, 532 (1923).

Although much has been written about the cleavage of ethers by organometallic compounds, there appears to be only one article on the rate of cleavage of ether by these compounds. Ziegler (268) studied the rate of cleavage of n-butyllithium in diethyl ether. His results are shown in Table 6.

Table 6. Cleavage of Ether by n-Butyllithium

Time (hours)	Free alkali	Organometallic alkali	Total alkali
0.33	0.025	0.156	0.181
2.33	0.025	0.156	0.181
4.33	0.034	0.153	0.187
24.00	0.071	0.111	0.182
32.00	0.086	0.093	0.179
48.00	0.125	0.053	0.178

This study was carried out in connection with the addition of n-butyllithium to 1,1-diphenylethylene in order to be sure ether did not enter into the reaction. Since there was little cleavage within three or four hours, it had no significance. The rate of cleavage was determined by removing aliquots from the solution and analyzing for the organolithium contents by the Ziegler method. This consists in hydrolyzing a portion to obtain the total alkali by titration with standard acid. Another aliquot is reacted with dibenzylmercury in the presence of n-butyl bromide to give the following reactions.

$$2\underline{n}\text{-}C_4H_9Li + (C_6H_4CH_2)_2Hg \rightleftharpoons 2C_6H_5CH_2Li + (C_4H_9)_2Hg$$

$$C_6H_5CH_2Li + \underline{n}\text{-}C_4H_9Br \longrightarrow C_6H_5CH_2C_4H_9 + LiBr$$

Hydrolysis of this reaction mixture and titration gives only inorganic alkali. The difference between the two titrations gives the amount of organometallic compound.

III. EXPERIMENTAL

A. An Improved Method for the Analysis of Alkyllithium Compounds

1. Procedure of the analysis.

This analysis is based on the fact that most alkyllithium compounds will couple instantaneously with benzyl chloride to split out lithium chloride. The reaction gives a negative color test within a half minute after the two reagents are mixed. If such a reaction mixture is hydrolyzed, the base formed can come only from inorganic sources, such as LiOH, Li_2O, and ROLi. When the original solution of organolithium compound is hydrolyzed the base formed consists of the inorganic alkali plus the lithium hydroxide formed by the hydrolysis of the RLi compound.

$$RLi + H_2O \longrightarrow RH + LiOH$$

The difference between the amount of alkali formed in each case is the amount of organolithium compound in the solution.

To run the analysis, the solution of alkyllithium compound was filtered under nitrogen through a sintered glass funnel (17) to remove all insoluble material. An aliquot of 5 or 10 cc. was withdrawn, by means of a rubber suction bulb connected to a pipette, and hydrolyzed in 10 cc. of distilled

water. Titration with standard acid, using phenolphthalein as indicator, gave the amount of total alkali. Another 5 or 10 cc. aliquot was added to 10 cc. of sodium-dried ether containing 1 cc. of pure benzyl chloride, purified by drying Eastman benzyl chloride over P_2O_5 and distilling it at reduced pressure. As the alkyllithium solution dropped into the benzyl chloride a yellow color flashed through the liquid. If the organolithium solution is concentrated, a white precipitate of lithium chloride forms with the disappearance of the yellow color. The ether solution may become hot enough to boil but is not cooled. The alkyllithium solution was added as fast as it would drain from the pipette. The mixture was allowed to stand one minute after the addition and then hydrolyzed. The base, which was inorganic alkali, was titrated with standard acid as before. Care must be taken not to overstep the end point in this titration since the aqueous layer decolorizes before the ether layer. This may be overcome by shaking the solution vigorously on the addition of each drop of acid when near the end point. The latter titration gives the inorganic base dissolved in the solution. The difference between the two titrations gives the concentration of alkyllithium compound.

The benzyl chloride must be dissolved in ether because coupling with the organolithium compound takes place much less readily in other solvents.

When the organolithium compound was prepared in petroleum

ether the second titration of a 5 cc. aliquot usually required 2.5 cc. of 0.1 N acid for neutralization. This was due either to dissolved or colloidal inorganic lithium compounds. If C_4H_9OLi was refluxed in petroleum ether and filtered in the same manner as the organolithium compounds, 2.7 cc. of acid was required to neutralize 5 cc. of the solution.

Lithium butoxide did not cleave benzyl chloride under the conditions of the analysis. When these two reagents were refluxed for one minute and hydrolyzed no chloride ion was found in the aqueous layer.

This analysis worked well for all alkyllithium compounds tried except methyllithium. When methyllithium was mixed with benzyl chloride, a positive color test remained after the mixture stood for 8 hours. This analysis was found to be unsuitable for use with aromatic lithium compounds and phenylethynyllithium.

2. Reaction of benzyl chloride with n-butyllithium.

n-Butyllithium was prepared in the usual manner and found to be 0.634 N by the benzyl chloride titration method. A 250 cc. portion (0.158 mole) was added drop-wise to a large excess (0.6 mole) of benzyl chloride in ether at such a rate that very vigorous refluxing took place. After the addition, the yellow color of the solution soon faded and the mixture was hydrolyzed in ice water. The ether layer was dried over calcium chloride and distilled. The residual oil was

fractionally distilled; 40 g. of benzyl chloride, a small amount of impure octane, 5 g. (21%) amylbenzene, and 8.2 g. (31%) bibenzyl, as well as a higher-boiling residue, were obtained. The slightly impure amylbenzene was identified by a refractive index of 1.499 as compared with the 1.494 value given in the literature. The bibenzyl, which gave no depression with a mixed melting point with a known sample, was converted to the 1,3,5-trinitrobenzene-bibenzyl complex, m.p. 103-104° (287).

3. Reaction of benzyl chloride with α-naphthyllithium.

The reaction was carried out as above only the solution was stirred for 5 hours after addition of all the α-naphthyllithium. The mixture was hydrolyzed and distilled as before; no bibenzyl was obtained. A large amount of high-boiling fraction, probably phenyl-α-naphthylmethane, was not further purified.

4. Reaction of benzyl chloride with p-dimethylaminophenyllithium.

This reaction, when carried out as above, likewise gave no bibenzyl, but a high-boiling fraction, probably phenyl-p-dimethylaminophenylmethane, remained as a residue in the distillation flask.

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287. Sudborough, J. Chem. Soc., 109, 1339 (1916).

5. Capture of benzyllithium from the reaction of benzyl chloride and ethyllithium.

Ethyllithium was prepared in the usual manner from 43.2 g. (0.4 mole) of ethyl bromide and 5.6 g. (0.8 g. atom) of lithium in 400 cc. of ether. The solution, free from lithium metal, was cooled to -50° in a dry ice-acetone bath, and 15 g. of benzyl chloride in 50 cc. of cold ether was quickly added. The usual characteristic yellow color was formed. The yellow-colored solution was carbonated with dry ice within one minute after the benzyl chloride had been added. The carbonated mixture was dissolved in a small amount of water. After separating the basic layer from the organic layer, the aqueous solution was boiled to remove the last traces of ether. This solution was placed in a continuous extractor and extracted over night with low-boiling petroleum ether. The basic aqueous solution was then acidified with HCl and again extracted for 12 hours with low-boiling petroleum ether. The petroleum ether solution containing the phenylacetic acid and large amounts of propionic acid was allowed to evaporate by placing it, 2 cc. at a time, into a 10 cc. vial. The petroleum ether and propionic acid evaporated leaving a small amount of oil possessing a strong odor of phenylacetic acid. The oil, 20 mg., solidified after standing a week. This solid was neutralized with sodium hydroxide and converted into the p-bromophenacyl ester, by treating with p-bromophenacyl

bromide. Unfortunately, this also came out as an oil but solidified after standing two weeks. The crude product was recrystallized from alcohol in a capillary tube and gave a melting point of 86-88°. The mixed melting point with a known sample was 88°.

B. Rate of Cleavage of Ethers by Organolithium Compounds

1. Cleavage of diethyl ether by n-butyllithium.

a. In petroleum ether-diethyl ether solution.-- The method of determining the rate of cleavage of ether described here will be referred to later in this work as the usual procedure. A filtered petroleum ether solution of n-butyllithium was placed in a three-necked flask with an equal volume of sodium-dried diethyl ether and kept under nitrogen at room temperature. A 10 cc. aliquot was removed from time to time and analyzed by the benzyl chloride method of analysis. The results are shown in table 7 and in the graph, fig. 1.

Table 7. Cleavage of $(C_2H_5)_2O$ by n-Butyllithium at Room Temperature Using 10 cc. Aliquots. (50% Petroleum Ether)

Time (in days)	Total alkali (cc. 0.1 N H_2SO_4)	Inorganic alkali (cc. 0.1 N H_2SO_4)	Molarity of n-C_4H_9Li
0	26.4	1.9	0.245
1	25.4	6.4	0.190
2	25.0	8.3	0.167
3	25.2	13.5	0.117
4	26.2	16.0	0.102
5	26.7	20.2	0.065
6	27.8	25.5	0.032

b. In diethyl ether solution.-- The analysis was carried out in the usual manner. However, the organolithium compound was prepared in ethyl ether. The rate of cleavage is given in table 8 and is the same as in the petroleum ether-diethyl ether solution. (See fig. 1.)

Table 8. Cleavage of $(C_2H_5)_2O$ by n-Butyllithium at Room Temperature. (10 cc. Aliquots)

Time (in days)	Total alkali (cc. 0.1 N H_2SO_4)	Inorganic alkali (cc. 0.1 N H_2SO_4)	Molarity of n-C_4H_9Li
0	41.5	15.4	0.261
1	41.9	23.3	0.186
2	42.8	28.1	0.147
3	43.6	32.6	0.110
5 1/4	45.9	40.6	0.053
6 1/4	43.6 (a)	39.8	0.038
7 1/3	40.4	38.0	0.024
8 1/6	37.0	35.5	0.015
9 1/6	34.6	34.6	0.005
10	(negative color test)		

(a) A precipitate began to form.

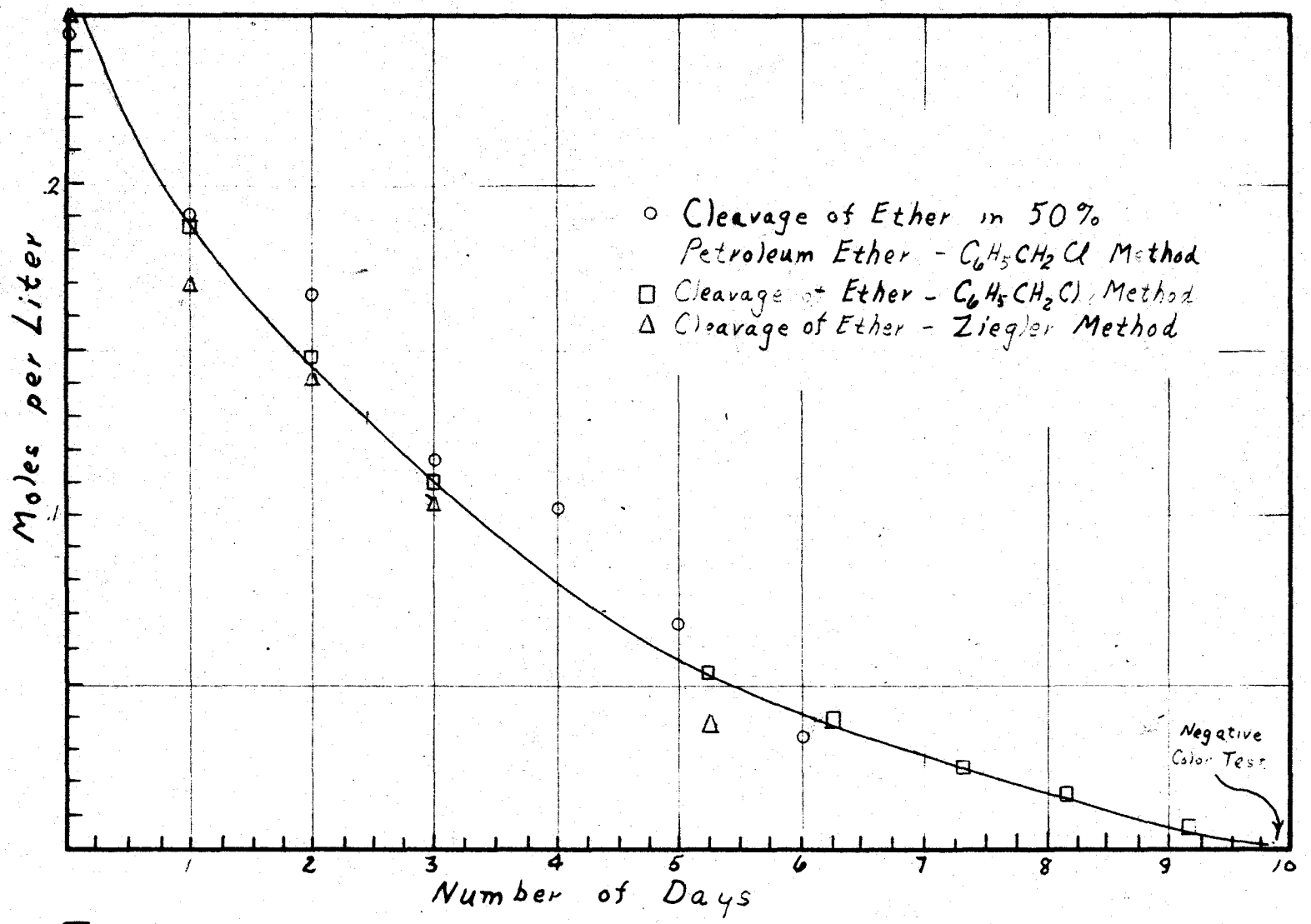

Fig. 1. Cleavage of Ether by n-Butyllithium Compound at 25°

c. In diethyl ether solution using the Ziegler analysis.--To use the Ziegler analysis (268), a 5 cc. aliquot of the same solution as that used in the above experiment was hydrolyzed and titrated to obtain the total alkali. A second aliquot was added to 10 cc. of ether containing 2 cc. of n-butyl bromide. Dibenzylmercury was added bit by bit to this solution. Upon each addition a yellow color of benzyllithium was noted. The failure of this yellow color to form upon the addition of a crystal of the mercury compound was taken as a sign that all the n-butyllithium had been decomposed. This process usually required about 20 minutes. The solution was hydrolyzed and titrated to give the inorganic alkali. The difference between these two titrations gave the concentration of the n-butyllithium. Table 9 gives the data for this cleavage. (See fig. 1.)

Table 9. Cleavage of $(C_2H_5)_2O$ by n-Butyllithium Using Ziegler's Analysis.

Time (in days)	Total alkali (cc. 0.1 N H_2SO_4)	Inorganic alkali (cc. 0.1 N H_2SO_4)	Molarity of n-Butyllithium
0	41.5	16.8	0.249
1	41.9	25.0	0.169
2	42.8	28.8	0.140
3	43.6	33.2	0.104
5 1/4	45.9	42.5	0.035

As can be seen from Fig. 1, as long as there is an excess of diethyl ether in the solution, the presence of an inert solvent does not change the rate of cleavage. Ziegler's method

of analysis was found to give values slightly lower than the benzyl chloride method. It must be remembered that these cleavages were run at room temperature without a constant temperature bath. As will be shown later, this reaction is very sensitive to temperature change; so it can be readily understood why the points did not all fall on the curve.

2. Order of the ether cleavage reaction.

The reaction

$$RLi + (C_2H_5)_2O \longrightarrow C_2H_5OLi + C_2H_5R$$

in the presence of excess ether was found to be of the first order and the equation

$$K = \frac{2.303}{t} \log \frac{a_o}{a}$$

applies, where a_o is the initial concentration and a is the concentration at time t. The rate constant for the cleavage of ether by n-butyllithium at reflux temperature (35°) was calculated and the results are shown in table 10. The data were taken from fig. 3.

Table 10. Calculation of K for the Cleavage of Diethyl Ether by n-Butyllithium at Reflux Temperature.

t (in hours)	$\frac{a_o}{a}$	$\log \frac{a_o}{a}$	K
12.8	1.25	0.0969	0.0175
25.5	1.72	0.2355	0.0221
44.3	2.51	0.4005	0.0209
61.0	4.00	0.6020	0.0228
107.0	12.90	1.1105	0.0235

The constant for the cleavage of ether by n-amyllithium at reflux temperature (35°) was calculated from the data in fig. 3. The results are shown in table 11.

Table 11. Calculation of K for the Cleavage of Ethyl Ether by n-Amyllithium at Reflux Temperature

t (in hours)	$\frac{a_o}{a}$	$\log \frac{a_o}{a}$	K
18.8	1.768	0.2474	0.0316
29.5	2.48	0.3944	0.0308
50.8	4.33	0.6365	0.0294
74.6	9.54	0.9795	0.0302

3. Cleavage of diethyl ether by organolithium compounds.

a. Normal alkyllithium compounds.-- The rate at which a number of n-RLi compounds cleave diethyl ether was studied, using the benzyl chloride analysis in the usual manner. The cleavage of ether at room temperature by ethyl-, n-propyl-, n-butyl-, n-amyl-, and dodecyllithium is shown in the graph in fig. 2. The results for the cleavage of ether by these compounds at the boiling point of the solution (35°) are shown in fig. 3.

b. Methyllithium.-- Methyllithium would not couple with benzyl chloride as did the other alkyllithium compounds; so the rate of cleavage was studied using the Ziegler method of titration. A 0.606 N solution of methyllithium in diethyl ether was found to be 0.608 N at the end of one week. This

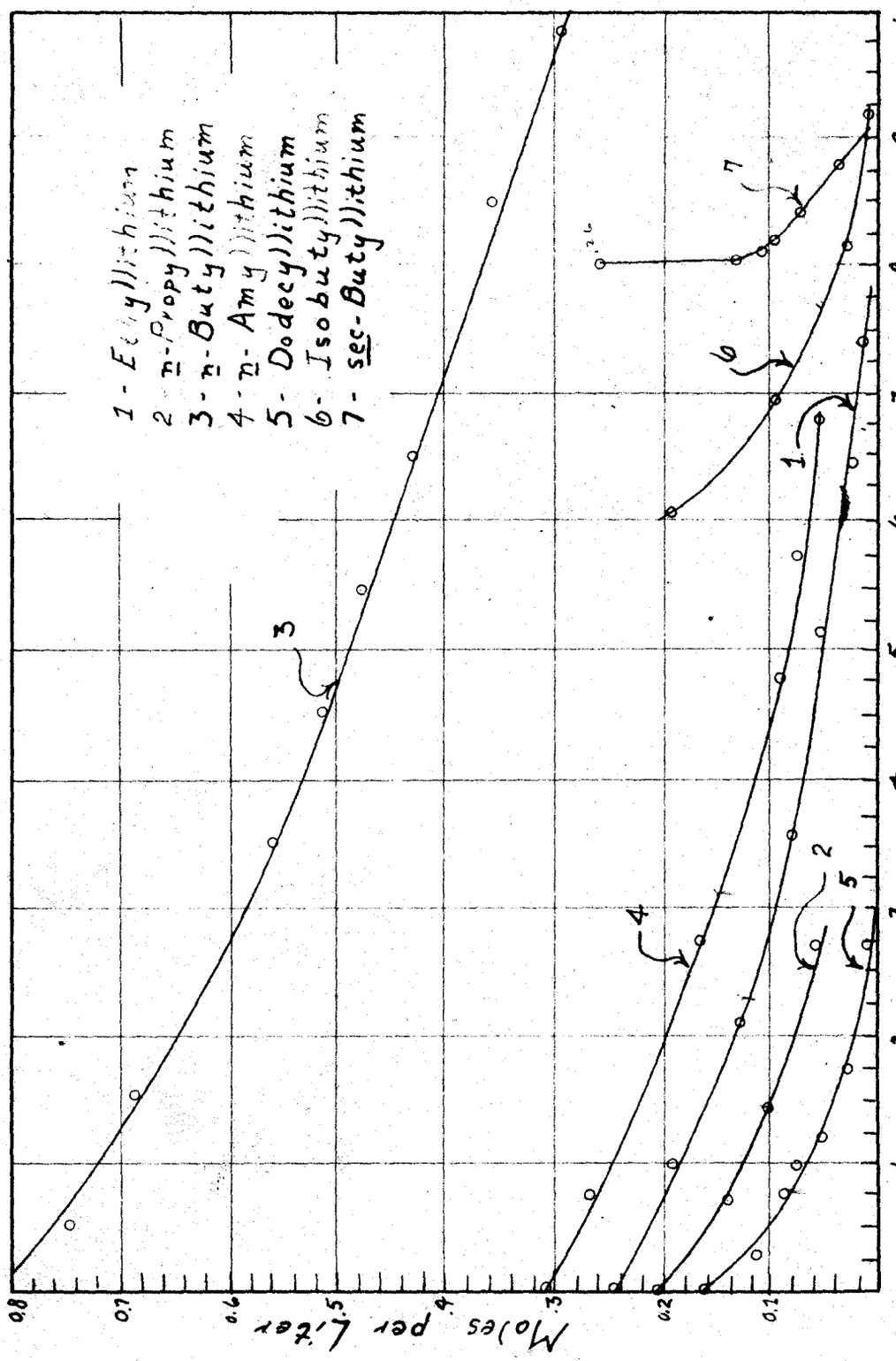

Fig. 2. Cleavage of Ether by Alkyllithium Compounds at 25°

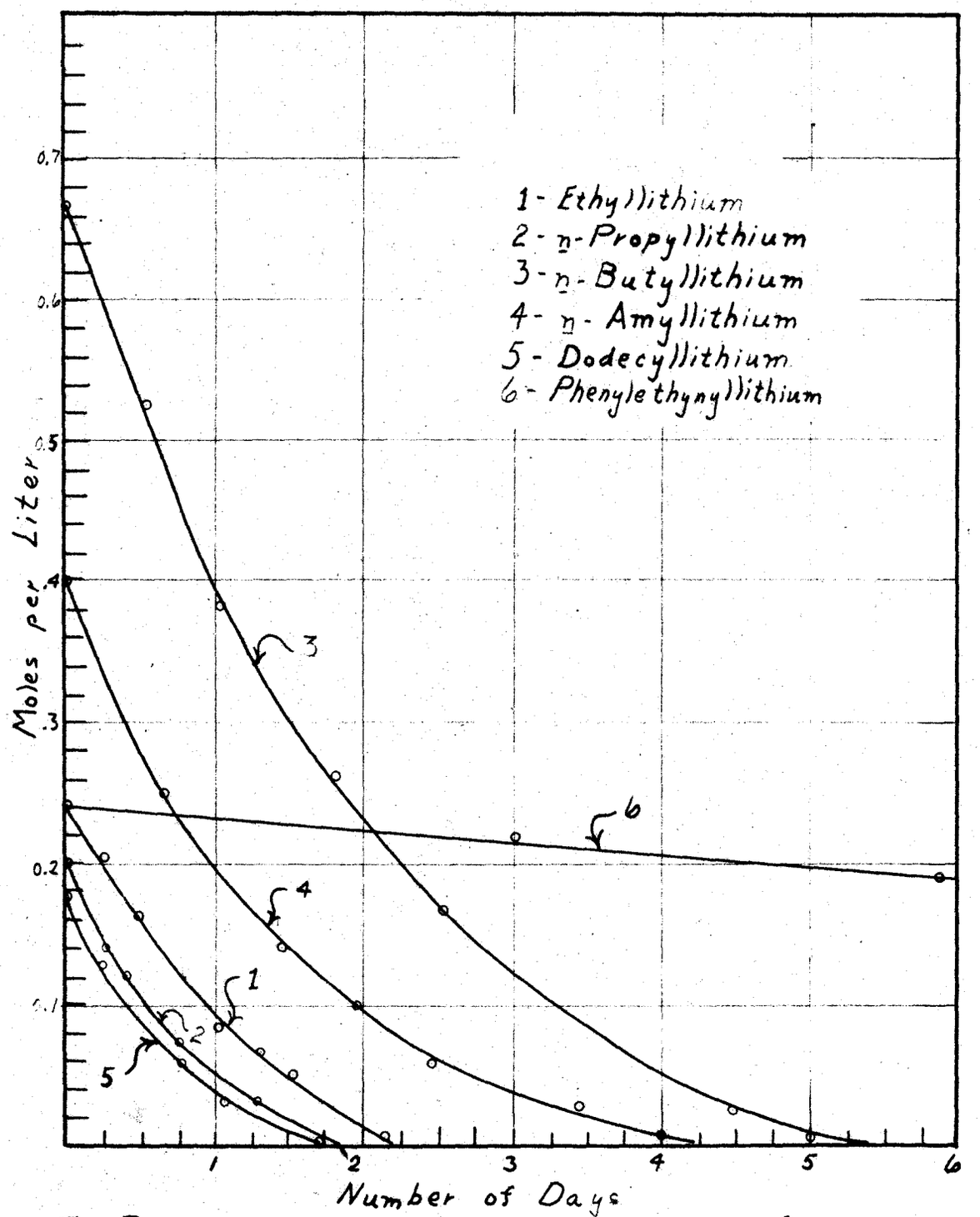

Fig. 3. Cleavage of Ether by Alkyllithium Compounds at 35°

was well within the error of the analysis. The same solution after being refluxed for twelve days was found to be 0.602 N which showed slight cleavage. A 0.54 N solution of CH_3Li was sealed in a Schlenk tube under nitrogen for one year after which it was found to be 0.14 N.

c. Branched chain alkyllithium compounds.-- The benzyl chloride method of analysis was applied with success to isobutyllithium. The cleavage was carried out in the usual manner at room temperature. As can be seen from fig. 2, isobutyllithium cleaves ether at a more rapid rate than n-butyllithium. When ether was added to a petroleum ether solution of s-butyllithium, the solution became yellow and began to reflux. At the end of 30 minutes, 50 per cent of the lithium compound had decomposed as determined by the benzyl chloride analysis. During this time the solution had ceased to reflux. After the initial decomposition this compound decomposed ether little faster than n-butyllithium (fig. 2). When the ether was added to the s-butyllithium, cooled in ice, the same initial decomposition occurred but less rapidly.

The rapid initial cleavage phase was noted with all the branched chain compounds. The cleavage was run with s-butyl-, t-butyl-, isopropyl-, and cyclohexyllithium. All of these compounds gave about the same cleavage with ether, except t-butyllithium, which gave initial cleavage to a greater extent, followed by more rapid final cleavage. A 0.14 N

solution of t-butyllithium in petroleum ether was cleaved by ether in 30 minutes.

d. Phenylethynyllithium.-- The phenylethynyllithium was prepared by adding an excess, 7.6 g. (0.0744 mole), of phenylacetylene to 200 cc. of 0.248 N n-butyllithium in ether and refluxing for 4 hours. When some of this solution was added to benzyl chloride in ether a positive color test remained after 4 hours. Likewise, when excess dibenzylmercury was added to a portion of the phenylethynyllithium solution containing 1 cc of n-butyl bromide, a color test remained after 6 hours. Since neither the benzyl chloride analysis nor the Ziegler analysis was satisfactory for the analysis of this compound, the rate of cleavage was studied by carbonating aliquots and isolating the phenylpropiolic acid formed. The rate of cleavage of $C_6H_5C{\equiv}CLi$ may be found in fig. 3.

e. Aryllithium compounds.-- When α-naphthyllithium was added to benzyl chloride in ether solution a positive color test remained for 10 minutes. A solution of α-naphthyllithium was analyzed by the benzyl chloride method, Ziegler's method, and by the isolation of α-naphthoic acid upon carbonation. The first method of analysis gave the concentration of the solution as 0.16 N, the second 0.198 N, while the third gave 0.21 N. The same discrepancy was observed when other aryllithium compounds were analyzed by the three

methods. Since carbonation seemed to be the most reliable of the methods of analysis, it was used to study the cleavage rates of the aryllithium compounds. The results for p-dimethylaminophenyl-, p-biphenyl-, phenyl-, α-naphthyl-, and β-naphthyllithium are shown in fig. 4.

4. Cleavage of various ethers by organolithium compounds.

a. Straight chain ethers.-- In each case the ether to be cleaved was added to a petroleum ether solution of the organometallic compound and the solution was used to cleave n-butyl, n-hexyl, and dodecyl ether (fig. 5). Since n-butyl ether was cleaved less rapidly by n-butyllithium than ethyl ether, s- and t-butyllithium were used in this solvent. A 0.25 N solution of s-butyllithium in diethyl ether which was cleaved completely in one day, required about 15 days when in n-butyl ether solution. The greater stability of n-butyl ether toward cleavage manifests itself in the fact that a 0.14 N solution of t-butyllithium, which would be cleaved in a diethyl ether solution in 30 minutes, required a day and a half for complete decomposition in n-butyl ether. Although s-butyllithium cleaved n-butyl ether less rapidly than ethyl ether, it cleaved n-hexyl ether more rapidly. These results are shown in fig. 5.

b. Isopropyl ether.-- This cleavage was run in the usual manner by the use of n-butyllithium. Although this

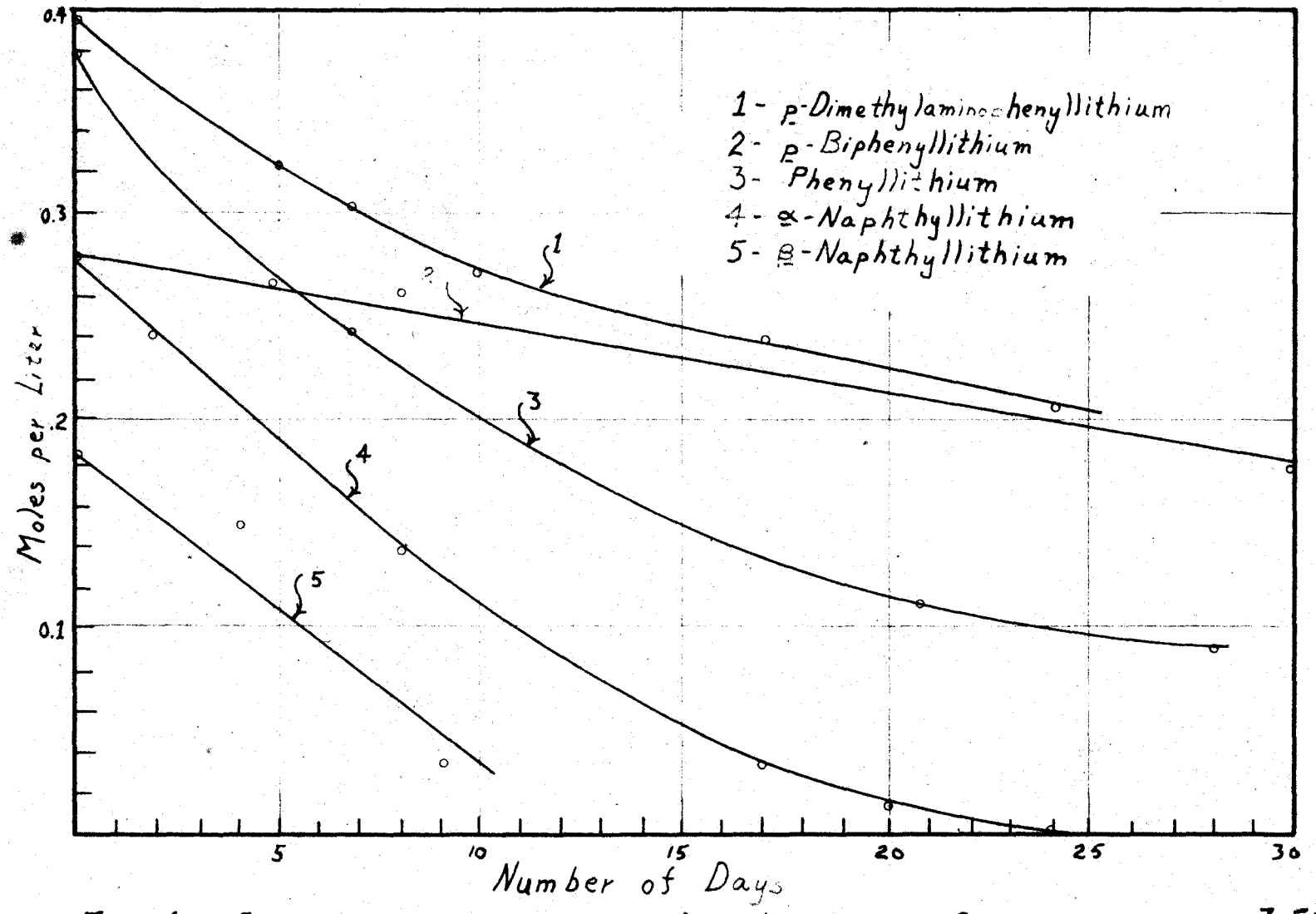

Fig. 4. Cleavage of Ether by Aryllithium Compounds at 35°

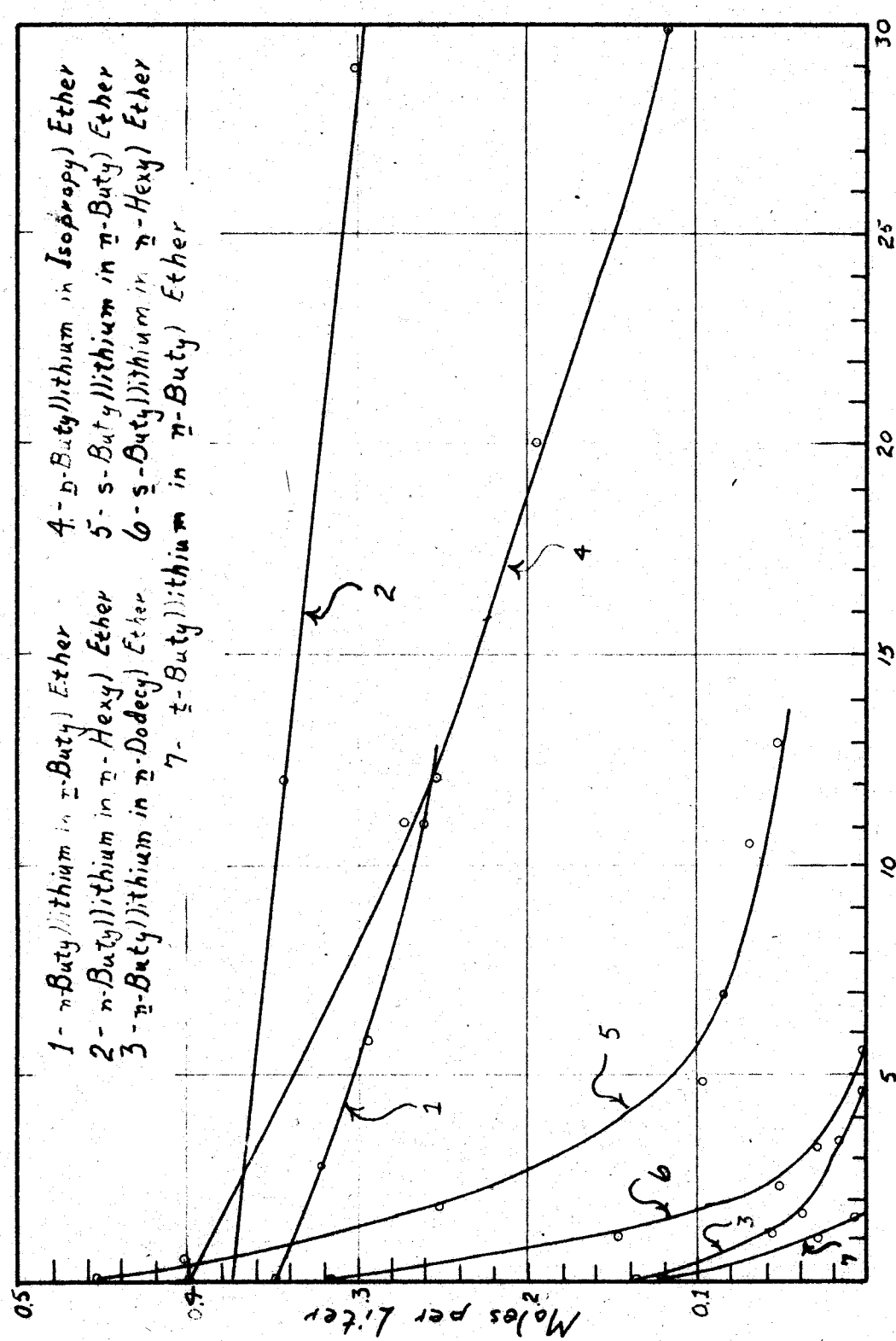

Fig. 5. Cleavage of Ethers by Lithium Compounds at 25°C

ether is cleaved more rapidly than n-butyl ether, it is much more stable than diethyl ether. The one disadvantage of using this ether as a solvent is the rapid peroxide formation in this ether when it is allowed to stand in contact with air.

c. Dioxan.-- Dioxan, freshly distilled from sodium, was added to a 0.6 N solution of n-butyllithium in petroleum ether. The solution became warm and a negative color test resulted after the mixture had stood for 55 minutes. When the dioxan was added to the n-butyllithium solution, cooled in ice, a negative color test resulted after one hour.

d. Ethylene glycol dimethyl ether.-- The ethylene glycol dimethyl ether was dried over sodium and distilled in dry apparatus protected from moisture by a $CaCl_2$ tube. About 100 cc. of this ether was added to 150 cc. of 0.542 N n-butyllithium in petroleum ether. A precipitate formed immediately, the solution became warm, and a negative color test was obtained in 20 minutes.

e. N-Methylmorpholine.-- The N-methylmorpholine was dried over solid KOH and distilled. Since none of the conventional methods of analysis for organolithium compounds would work in this basic solvent, only the end-point of the cleavage was obtained by the color test. When 50 cc. of N-methylmorpholine was added to 50 cc. of 0.33 N n-butyllithium in petroleum ether, a negative color test was obtained after 24 hours. When

0.6 mole of N-methylmorpholine was added to 0.25 mole of phenyllithium in 200 cc of ethyl ether it required five days refluxing to obtain a negative color test. With 0.3 N butylmagnesium bromide, 20 days at room temperature were required to produce a negative color test.

f. Anisole.-- To 0.3 mole of ethylaluminum iodides, prepared in the absence of solvent in the conventional manner, was added 5.4 g. (0.05 mole) of anisole. A violent evolution of gas accompanied this addition. After heating at 155° for 6 hours, benzene was added and the reaction carbonated by bubbling CO_2 through the refluxing benzene solution until a negative color test was obtained. The mixture was hydrolyzed by pouring on HCl-ice. The ether solution was extracted with potassium hydroxide, carbon dioxide was bubbled through the basic solution to precipitate the phenol formed from cleavage. Upon purification 2.35 g., or a 51 per cent yield, of phenol was obtained. No acid was obtained on acidification of the $KHCO_3$ solution.

g. Phenyl ether.-- The reaction described above for anisole and ethylaluminum iodides was run with phenyl ether, but under these conditions neither phenol nor acid material was obtained.

To a 0.21 N solution of t-butyllithium, prepared from 4.6 g. (0.05 mole) of t-butyl chloride and 0.7 g. (0.1 mole) of lithium in 100 cc. of low-boiling petroleum ether, was

added 4.6 g. (0.027 mole) of phenyl ether. The solution was refluxed for 24 hours and carbonated with dry ice. No phenol was obtained but acidification gave 0.8 g. (14%) of almost pure o-phenylbenzoic acid (m.p. 111-113°).

C. Synthesis by Ether Cleavage

1. α-Homonaphthyldiethylamine.

Diethylaminomethyl n-butyl ether was prepared according to the directions of Robinson and Robinson (286) from diethylamine, formalin, and n-butyl alcohol. An ether solution containing 15.3 g. (0.096 mole) of this ether was added slowly to an ether solution of α-naphthyllithium prepared by adding 44 g. (0.22 mole) of α-bromonaphthalene to 3 g. (0.44 g. atom) of lithium in 300 cc. of ether. The solution became warm and refluxed furing the addition of the amine ether. Upon heating the solution for an additional half hour after the amine had been added, a negative color test was obtained and the mixture was immediately hydrolyzed by the cautious addition of water. The ether solution was extracted with dilute HCl; the acid solution was evaporated to dryness; the free amine was liberated from the hydrochloride by treatment with a small amount of concentrated sodium hydroxide followed by extraction with ether. The ether solution was dried over solid KOH and distilled. The remaining oil was fractionally distilled

to give 14.4 g. (67% yield) of α-homonaphthyldiethylamine, b.p. 148-150° at 6 mm.

2. p-Dimethylaminophenylmethyl-diethylamine.

To a solution of p-dimethylaminophenyllithium, prepared from 40 g. (0.2 mole) of p-bromodimethylaniline and 2.8 g. (0.4 g. atom) of lithium in 300 cc. of ether, was added 16.5 g. (0.103 mole) of diethylaminomethyl n-butyl ether, dissolved in 25 cc. of ether. The mixture stood for 12 hours and was then refluxed for 5 additional hours. During this period of refluxing a precipitate formed. The mixture was hydrolyzed by the cautious addition of water and worked up as in the above reaction. Fractionation at reduced pressure gave a fraction, 80-120° at 6 mm., of 6.4 g., which was dimethylaniline, and a second fraction of 19.3 g., which distilled at 134-135° at 6 mm., was p-dimethylaminophenylmethyl-diethylamine and represented a 90% yield.

The compound was converted into the monopicrate which was a bright red compound. This compound changed its crystal structure from 130-150° and melted at 153-154°.

Anal. Calcd. for $C_{29}H_{25}N_5O_7$: N, 16.09.

Found: N, 16.10.

A portion of the amine was converted into the dimethiodide by treatment with methyl iodide. The reaction took place with violence accompanied by the formation of a white precipitate. Crystallization from methyl alcohol gave white crystals

which melted at 141°.

Anal. Calcd. for $C_{25}H_{28}N_2I_2$: N, 5.71.

Found: N, 5.78.

3. 1-p-Dimethylaminophenylmethylpiperidine.

Butoxymethylpiperidine was prepared from piperidine, formaline, and n-butyl alcohol by the method of Robinson and Robinson (286). An ether solution containing 17.1 g. (0.1 mole) was added to a p-dimethylaminophenyllithium solution, prepared from 40 g. (0.2 mole) of p-bromodimethylaniline and 2.8 g. (0.4 g. atom) of lithium. On working up the reaction as before, 10.5 g. of a fraction, boiling from 154-155° at 5 mm. was obtained. This was p-dimethylaminophenylmethylpiperidine and represented a 45.6% yield.

The compound was converted into an orange-red colored dipicrate which melted at 149°.

Anal. Calcd. for $C_{26}H_{28}N_8O_{24}$: N, 16.56.

Found: N, 16.52.

A portion of the amine was converted into the dimethiodide which when crystallized from methyl alcohol melted at 180-181°.

Anal. Calcd. for $C_{26}H_{28}N_2I_2$: N, 5.58.

Found: N, 5.68.

4. 1-n-Amylpiperidine.

To an excess of n-butyllithium in ether was added 8.5 g. (0.05 mole) of butoxymethylpiperidine in 20 cc. of ether. The solution was boiled for 15 minutes and, after hydrolysis, was worked up as in the experiment before. Distillation under reduced pressure gave 4 g. (52% yield) of 1-n-amylpiperidine. The picrate prepared from this compound gave a melting point of 106-107°, the same as recorded in the literature (286).

5. 5-Ethyl-2-diethylaminomethylcarbazole.

5-Ethyl-2-bromocarbazole was prepared by the acetylation of carbazole (288); bromination to 5-acetyl-2-bromocarbazole (289); removal of the acetyl group by alcoholic potash hydrolysis (289); followed by ethylation with ethyl sulfate (290).

A 40 cc. benzene solution containing 5 g. (0.018 mole) of 5-ethyl-2-bromocarbazole was mixed with an 80 cc. ether solution containing 0.04 mole of n-butyllithium as determined by the benzyl chloride analysis. The mixture was refluxed for 40 minutes after which 6.4 g. (0.04 mole) of diethylaminomethyl n-butyl ether dissolved in 20 cc. of ether was added.

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288. Boeseken, Rec. trav. chim., 31, 364 (1912).
289. Ciamician and Silber, Gazz. chim. ital., 12, 276 (1882).
290. Stevens and Tucker, J. Chem. Soc., 123, 2140 (1923).

The solution was refluxed for an hour, when a negative color test was obtained. The solution was hydrolyzed and worked up as in the preceding experiments. When the solution was distilled at 15 mm., 1 cc. of material came over at 50-55°. This was impure diethyl-n-amylamine. A brown viscous oil remained which could not be crystallized. This was distilled at less than 0.5 mm. to give a fraction boiling at 185-187°. This fraction which was 5-ethyl-2-diethylaminomethylcarbazole weighed 3 g. (61% yield).

This amine gave a hydrochloride which formed as an oil that could not be crystallized. The methiodide was not suitable as a derivative for it was a low-melting solid which only crystallized after standing a number of weeks.

The dipicrate formed quite easily and, when pure, melted at 123-124°.

Anal. Calcd. for $C_{31}H_{30}N_8O_{24}$: N, 15.18.

Found: N, 15.30.

6. 4-Diethylaminomethyldibenzofuran.

To 100 cc. of 0.5 molar solution of n-butyllithium in ether was added 8.4 g. (0.05 mole) of dibenzofuran in 40 cc. of ether. Metalation of the dibenzofuran was effected by refluxing the solution for 4 hours. To this solution was then added 8 g. (0.05 mole) of diethylaminomethyl n-butyl ether. A negative color test was obtained after refluxing for one hour. The mixture was hydrolyzed and the products

isolated in the usual manner. No diethyl-n-amylamine was isolated, but 5 g. of material boiling at 205-209° at less than 0.5 mm. was obtained. This represented a 40% yield of 4-diethylaminomethyldibenzofuran.

As with the carbazole compound, both the hydrochloride and methiodide were oils. The monopicrate, however, formed readily and after purification melted at 172-173°.

Anal. Calcd. for $C_{23}H_{22}N_4O_8$: N, 11.62.

Found: N, 11.80.

7. Attempted preparation of 3-diethylaminomethylquinoline.

To a filtered ether solution of 0.098 mole of n-butyllithium cooled externally to -35° with a dry ice-acetone bath, was added, over a two-minute period with stirring, 15 g. (0.072 mole) of 3-bromoquinoline (291) in 50 cc. of ether also cooled to -35°. The solution, which became dark red, was stirred for 15 minutes at this temperature. An ether solution of 15.9 g. (0.1 mole) of diethylaminomethyl n-butyl ether cooled to -35° was added to the mixture and the solution was stirred for an additional 15 minutes at this temperature. The cooling bath was removed and the mixture was allowed to warm to room temperature. During this time a sample was removed for a color test every 10 minutes. A negative color test resulted after 50 minutes. The reaction mixture was then

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291. Claus and Collischonn, Ber., 19, 2763 (1886).

hydrolyzed and worked up in the usual manner. Besides a small amount of unreacted diethylaminomethyl n-butyl ether and some diethyl-n-amylamine there remained a residue which was non-distillable and quite insoluble in most solvents. This was probably a high molecular weight compound resulting from the addition of organolithium compounds to the anil linkage of quinoline.

D. Miscellaneous Reactions

1. Metalation.

a. Metalation of dibenzofuran by ethylmagnesium bromide.--This reaction was carried out according to the method of Challenger (217). Ethylmagnesium bromide was made in the usual manner from 43.5 g. (0.4 mole) of ethyl bromide and 14.5 g. (0.6 g. atom) of magnesium in 400 cc. of ether. To this solution which had been filtered through glass wool was added 16.8 g. (0.1 mole) of dibenzofuran dissolved in 50 cc. of ether. The ether was distilled from the mixture and the residue heated by means of a metal bath for 6 hours at 165°. After the mixture had been cooled to room temperature it was dissolved in 300 cc. of ether and carbonated by pouring jet-wise on dry ice. The carbonated product was dissolved in dilute HCl, and the ether layer was extracted with KOH. No phenolic compounds were precipitated by bubbling carbon dioxide through the KOH solution. Upon acidification of the

solution 1.05 g. (5% yield) of 4-dibenzofurancarboxylic acid, m.p. 202-204°, was obtained. Recrystallization from dilute alcohol gave a product which melted at 209-210°. The methyl ester, prepared from the acid and diazomethane, melted at 93-94°.

b. Attempted metalation of dibenzofuran by triethylaluminum.-- Ether-free triethylaluminum was prepared by heating a mixture containing 10 g. (0.039 mole) of diethylmercury and 3.78 g. (0.14 g. atom) of aluminum chips at 150° for 6 hours. A 35% yield of triethylaluminum was obtained. A benzene solution containing 25 g. (0.15 mole) of dibenzofuran was added to the organoaluminum compound. The benzene was then distilled from the mixture and the residue heated for 24 hours at 145-150°. Benzene was again added to the cooled residue and the mixture was carbonated by bubbling carbon dioxide through the solution until a negative color test was obtained. (Usually about 2 hours were required to complete this operation.) Neither phenolic compounds nor acid was obtained on working up the reaction products. The recovery of dibenzofuran was 15 g., or 89.5%.

c. Attempted metalation of dibenzofuran by ethylaluminum iodides.-- To 0.3 mole of ethylaluminum iodides in a Carius tube filled with dry nitrogen was added 16.8 g. (0.1 mole) of dibenzofuran. The tube was sealed and heated in an electric oven at 210° for 72 hours. The tube was

opened; 50 cc. of benzene was added to the mixture; the solution was siphoned under nitrogen into a three-necked flask connected with a stirrer and reflux condenser. The reaction was carbonated in the usual manner at reflux temperature with gaseous carbon dioxide. The acid isolated weighed 0.25 g. and had a melting point of 235-237°. A mixed melting point with a sample of 2-dibenzofurancarboxylic acid gave 238-240°. The yield of this acid was 1.1%. It was converted into the methyl ester, which melted at 82-83°, by the use of diazomethane.

The 2-acid rather than the predicted 4-acid probably came as a result of a Friedel-Crafts reaction between the AlI_3 formed from the equilibrium reaction of mixed organometallic compounds.

$$3(C_2H_5)_2AlI \longrightarrow 2(C_2H_5)_3Al + AlI_3$$

This was substantiated by the isolation of a 1.4% yield of 2-dibenzofurancarboxylic acid from the carbonation of dibenzofuran and anhydrous AlI_3 under the equivalent conditions used in the above reaction.

2. Halogen-metal interconversion reactions.

a. Interconversion of phenylethynyl bromide with n-butyllithium.-- The phenylethynyl bromide was prepared according to the directions of Grignard and Courtot (292) from

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292. Grignard and Courtot, Bull. soc. chim., [4] 17, 228 (1915).

phenylethynylmagnesium bromide and cyanogen bromide. To 0.05 mole of n-butyllithium in 200 cc. of ether cooled to 0° was added 7.6 g. (0.042 mole) of phenylethynyl bromide. The solution immediately turned yellow. After 5 minutes, 100 cc. of the solution was carbonated, the remainder being carbonated 40 minutes later. The acid was isolated in the usual manner. The first aliquot gave 2.8 g. of phenylpropiolic acid (89%); the second aliquot gave 2.6 g. (84.8%). The combined neutral fractions gave 1.2 g. (42%) of n-butyl bromide.

b. Interconversion of phenylethynyl chloride with n-butyllithium.-- Phenylethynyl chloride was prepared from phenylethynylsodium and benzenesulfonyl chloride according to directions of Bourguel and Truchet (293). After the third fractionation, the product gave an index of refraction n_d^{18} =1.5768 as compared with n_d^{18} =1.5760 reported in the literature. To 200 cc. of ether containing 0.02 mole of n-butyllithium was added 1.05 g. (0.0103 mole) of phenylethynyl chloride. The solution became yellow as in the preceding reaction. The solution was refluxed for 2-1/2 hours and carbonated. From this mixture was isolated 0.24 g. (16%) of phenylpropiolic acid (m.p. 136-137°).

In order to be sure this product did not form as the result of the metalation of phenylacetylene which might have been an impurity in the phenylethynyl chloride, another

293. Bourguel and Truchet, Compt. rend., 190, 753 (1930).

sample was prepared by the following sequence of reactions. ω-Chlorostyrene was prepared by the addition of chlorine to cinnamic acid followed by boiling with sodium carbonate to split out CO_2 and HCl (294). This compound was reacted with chlorine to give 1-phenyl-1,2,2-trichloroethane (294) which was then boiled with alcoholic potassium hydroxide to produce phenylethynyl chloride (295) in an over-all yield of 18%. This product when treated in the same manner as the phenylethynyl chloride, prepared by Bourguel's method, gave a 15.3% yield of phenylpropiolic acid.

c. Attempted interconversion of vinyl bromide and n-butyllithium.-- The vinyl bromide was prepared by treating ethylene dibromide with alcoholic potassium hydroxide according to the directions given by Kharasch (296). A solution of 5.4 grams. (0.05 mole) of vinyl bromide dissolved in 50 cc. of ether cooled to 0° was added to 0.05 mole of n-butyllithium in 100 cc. of ether at 0°. The reaction was stirred for 15 minutes after which it was carbonated with dry ice. During the 15 minutes before carbonation, the solution became milky white. On working up the acid material in the usual manner 2 g. (32%) of crude acetylenedicarboxylic acid was isolated. When pure, the acid melted at 170° with evolution of gas and

294. Biltz, Ann., 296, 266 (1897).

295. Nef, Ann., 308, 316 (1899).

296. Kharasch, McNab, and Mayo, J. Am. Chem. Soc., 55, 2521 (1933).

was identified by a mixed melting point with a known sample.

The same process was repeated using petroleum ether as the solvent instead of diethyl ether and running the reaction at 14° for 10 hours before carbonation. The solution turned white as before but only after 2 hours. A small amount of impure propionic acid was isolated together with 1.5 g. (26%) acetylenedicarboxlic acid.

d. Interconversion of o-bromophenol with ethylmagnesium bromide.-- The Grignard was prepared in the usual manner from 21.8 g. (0.2 mole) of ethyl bromide and 9.7 g. (0.4 g. atom) of magnesium in 200 cc. of ether. To this solution was added 7.5 g. (0.043 mole) of o-bromophenol dissolved in 50 cc. of ether. The o-bromophenol had to be added to the mixture with care as there was violent gas evolution. The ether was distilled from the mixture and the reaction heated to 120° for 2 hours. Ether was then added to the cooled mixture and the solution carbonated with dry ice. Upon isolating the acid material in the usual manner, 3.8 g. (51.2%) of o-bromophenol was recovered and 2.7 g. (15.1%) of salicylic acid was obtained (m.p. 156-157°).

e. Attempted interconversion of o-bromophenol with ethylaluminum iodides.-- To a 100 cc. benzene solution of 0.2 moles of ether-free ethylaluminum iodides was added drop-wise 8.3 g. (0.05 mole) of o-bromophenol. The benzene was

distilled from the mixture and the residue heated at 120° for 5 hours. Benzene was added to the cooled solution; the mixture was heated to reflux, and carbon dioxide gas was run through the solution until a negative color test was obtained. On working up the products in the usual manner, 88 per cent of o-bromophenol was recovered and no acid material was obtained.

f. Interconversion of 4-iododibenzofuran with ethylaluminum iodides.-- To 0.3 mole of ethylaluminum iodides dissolved in 50 cc. of benzene was added 29.2 g. (0.1 mole) of 4-iododibenzofuran dissolved in 20 g. of benzene. The benzene solution was distilled from the reaction mixture and the residue heated at 145° for 24 hours. Benzene was added to the cooled residue and the solution carbonated by passing carbon dioxide gas into the hot solution. On isolating the acid substance in the usual manner 3.19 g. (15%) crude 4-dibenzofurancarboxylic acid was obtained. By repeated crystallization from dilute alcohol a product melting at 208-210° was obtained which gave no melting point depression when mixed with a sample of known 4-dibenzofurancarboxylic acid.

IV. DISCUSSION

Those who have worked with organolithium compounds appreciate the need for an exact yet rapid method of analysis for solutions of these compounds. Unlike the Grignard reagent, which can be analyzed by hydrolysis of a sample followed by titration of the base formed, the acid titration method with organolithium compounds gives only a rough approximation. This method has been found to be in error to the extent of from 12 to 20 per cent, depending upon the concentration of the solution, the length of time required for the preparation, the amount of time the solution was maintained at reflux temperature, and the time which has elapsed between preparation and analysis. This method of analysis gives the total alkali present in the solution. Unfortunately, lithium oxide and hydroxide are more or less soluble in diethyl ether, while lithium alkoxide is quite soluble in this solvent. When organolithium compounds cleave diethyl ether, one of the products formed is lithium ethoxide, and, as has been shown in the experimental part of this thesis, the rate of cleavage is a function of the concentration, time, and temperature. Therefore, the amount of lithium ethoxide varies with each preparation, causing a deviation in the error of the acid titration. This method of analysis is not suitable even for

petroleum ether preparations of organolithium compounds, since inorganic basic lithium compounds are either soluble or form a colloidal suspension to the extent of about 0.02 to 0.05 moles per liter.

The analysis of organolithium compounds using Ziegler's n-butyl bromide-dibenzylmercury method, although it gives better results than the acid titration method, has a number of disadvantages. In the first place it is time-consuming. It requires from twenty to thirty minutes to add the dibenzylmercury. The dibenzylmercury used is quite costly, and of course there are the undesirable poisonous properties of this organomercury compound as well as of the dialkylmercury compounds which are formed as a result of the metal-metal interconversion between the organo-mercury compound and alkyllithium compound. A marked odor of these dialkylmercury compounds may be noted furing the analysis. This analysis was found to be unsuitable for phenylethynyllithium and aryllithium compounds. Dibenzylmercury gave no complete reaction with phenylethynyllithium during the course of six hours. There are two objections to the use of this method with aryllithium compounds. The first is the fact that, since all these types of organolithium compounds tend to be colored, the flash of yellow formed when the mercurial is added is masked, and it is impossible to know when enough of the dibenzylmercury has been added. This necessitates the addition of an excess of this expensive material in each analysis.

The second objection is that the analysis with α-naphthyllithium always gives a lower result than is obtained by carbonation and isolation of the acid formed.

The benzyl chloride analysis offers a number of advantages over these two methods. It couples the speed of the acid titration with the accuracy of the Ziegler method. With practice this analysis may be run in less than 5 minutes, since it consists essentially of two acid titrations. This method of analysis gives values for alkyllithium which are consistently about 2 per cent higher than the Ziegler analysis. The accuracy of the benzyl chloride analysis has been shown by the fact that the total alkali content of a petroleum ether solution of n-butyllithium may be accounted for by adding a small blank to the amount of n-butyllithium obtained by this analysis. The blank was procured by carrying a fine suspension of inorganic lithium alkali in petroleum ether through the same processes of refluxing and filtration that were used with the n-butyllithium solution. The basic components of this solution corresponded to the inorganic alkali as found by the benzyl chloride analysis.

The fact that this analysis is always a little higher than the Ziegler analysis might be explained by the assumption that benzyl chloride is hydrolyzed by the inorganic lithium compounds present resulting in a decrease of base in the second titration value. However, when benzyl chloride was treated under the same conditions with inorganic basic

lithium compounds, no cleavage took place. At the present time no explanation can be offered for this discrepancy.

The benzyl chloride used in this analysis is relatively inexpensive, and after it is purified by distillation it may be kept for months, if stored in a brown glass bottle. Although this compound is a lachrymator no trouble was encountered from this source if the flasks were emptied into a sink in a hood after completion of the analysis.

This analysis may be applied to RLi compounds in which R is an alkyl group, either normal or branched chain, or a benzyl or triphenylmethyl group. Unfortunately this method fails with methyllithium. The Ziegler analysis has the advantage in this case in that it can be used successfully. As with the Ziegler method, the benzyl chloride analysis cannot be used with phenylethynyllithium or aryllithium compounds. Since these compounds do not cleave ether rapidly at room temperature, the acid titration method gives less error than with alkyllithium compounds. The aryllithium compounds adapt themselves to reactions such as carbonation or reactions with benzophenone which give products that are easy to isolate. Therefore, aryllithium compounds can be analyzed by these reactions.

This analysis may be carried out with the lithium dissolved in any non-basic solvent so long as it is added to benzyl chloride in ether solution. If there is no ether present, no rapid coupling with the benzyl chloride occurs.

A simple analysis such as this adapts itself to many uses. The foremost of these is, of course, the calculation of the yield in the preparation of alkyllithium compounds. A knowledge of the exact concentration of these compounds makes it possible to calculate with more assurance the yields of reactions based upon these compounds. This analysis is particularly suitable to rate studies, not only of the cleavage of ethers, which has been studied in this thesis, but also rate studies with functional groups where previously only the end point of such reactions could be obtained by means of a negative color test.

When the products are isolated from the coupling of benzyl chloride with n-butyllithium, bibenzyl, amylbenzene, and octane are found to be present. The reaction may be represented in this manner:

$$C_6H_5CH_2Cl + \underline{n}\text{-}C_4H_9Li \longrightarrow (C_6H_5CH_2)_2 + C_6H_5C_5H_{11} + C_8H_{18} + \underset{LiCl}{}$$

The isolation of these products immediately suggests a free radical mechanism. However, if free radicals were formed as an intermediate in the coupling of benzyl chloride and n-butyllithium, there should be other products typical of a free radical reaction. The free radicals should disproportionate and also react with the solvent. None of these products could be found in the reaction mixture. Therefore, attention was focused upon other mechanisms to explain this reaction. As has been mentioned before, a yellow color

flashed through the solution upon the addition of n-butyllithium to benzyl chloride. Since benzyllithium is yellow in color and since it couples with organic halides so readily (268) it was thought that perhaps benzyllithium was formed momentarily in the reaction.

An attempt was made to capture the benzyllithium by carbonating the mixture at room temperature immediately after addition of the two reagents, but the reaction between the benzyl chloride and ethyllithium was too rapid. However, if benzyl chloride was added to an ethyllithium solution at -50° the coupling reaction was diminished while the halogen-metal interconversion, which seems to go readily even at low temperature, predominated, so that the yellow color remained long enough for the carbonation operation to be carried out. Some phenylacetic acid was isolated and characterized as the p-bromophenacyl ester by a mixed melting point with a known sample.

With this fact in mind the formation of the products of the coupling reaction between benzyl chloride and n-butyllithium may be postulated by the following series of reactions:

$$C_6H_5CH_2Cl + n\text{-}C_4H_9Li \longrightarrow C_6H_5CH_2C_4H_9 + LiCl \qquad (1)$$

$$C_6H_5CH_2Cl + n\text{-}C_4H_9Li \longrightarrow C_6H_5CH_2Li + n\text{-}C_4H_9Cl \qquad (2)$$

$$C_6H_5CH_2Li + C_6H_5CH_2Cl \longrightarrow C_6H_5CH_2CH_2C_6H_5 + LiCl \qquad (3)$$

$$C_6H_5CH_2Li + n\text{-}C_4H_9Cl \longrightarrow C_6H_5CH_2C_4H_9 + LiCl \qquad (4)$$

$$\underline{n}\text{-}C_4H_9Li + \underline{n}\text{-}C_4H_9Cl \longrightarrow \underline{n}\text{-}C_8H_{18} + LiCl \qquad (5)$$

$$\underline{n}\text{-}C_4H_9Br + Li \longrightarrow \underline{n}\text{-}C_4H_9Li + LiBr + \underline{n}\text{-}C_8H_{18} \qquad (6)$$

Equation (1) is self-evident because this is a normal coupling reaction and no doubt accounts for a large amount of the n-amylbenzene that is obtained from the coupling reaction.

There is evidence for the occurrence of the reaction shown in equation (2). Gilman and Jones (297) have shown that halogen-metal interconversions are possible between alkyllithium compounds and alkyl halides. Although halogen-metal interconversion with an organic chloride is rare this reaction is known to take place. Mr. Melstrom (298) has shown interconversion to take place between 2,4,5-triphenyl-3-chlorofuran and butyllithium while the interconversion of phenylethynyl chloride and n-butyllithium has been described in this thesis.

Once benzyllithium is formed, it will couple with any organic halide that is available and give the products represented in equations(3) and (4). Probably most of the benzyllithium reacts according to equation (3) because of the excess benzyl chloride that is present in the reaction mixture.

A large part of the octane is probably formed during the preparation of the butyllithium (equation 6). The coupling reaction between alkyllithium compounds and alkyl chlorides

297. Gilman and Jones, J. Am. Chem. Soc., 63, 1441 (1941).

298. Unpublished studies by Mr. D. S. Melstrom.

is known to be a slow process (22); so little reaction would take place according to equation (5).

Gilman and Jones (297) have shown that halogen-metal interconversion takes place between an alkyl halide and an alkyllithium compound, an aryl halide and an alkyllithium compound, and an aryl halide and an aryllithium compound; there is no known case, however, of interconversion between an alkyl halide and an aryllithium compound.

This might account for the fact that the benzyl chloride analysis gives poor results with aryllithium compounds. The coupling reaction of these compounds is much slower than with alkyllithium compounds. Since aryllithium compounds always have some color, it was impossible to note any benzyllithium color that might form in the solution during the reaction. No bibenzyl could be isolated from any of the coupling reactions with aryllithium compounds showing that there must be some other coupling mechanism involved. Likewise, methyllithium, which is so unreactive that it will not undergo halogen-metal interconversion reactions, will not couple successfully with benzyl chloride.

A number of coupling reactions, of the type given with n-butyllithium and benzyl chloride, have been reported in the literature. For example, Marvel (299) has isolated 1-phenylhexene-1 and trans-trans-1,4-diphenylbutadiene-1,3 from the

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299. Marvel, Hager, and Coffman, J. Am. Chem. Soc., 49, 2323 (1927).

reaction of β-bromostyrene and n-butyllithium. Because of the isolation of these two products, together with the fact that the solution became colored during the reaction and later became colorless, it was assumed that free radicals were formed during this reaction. It was admitted that if free radicals were formed during this reaction six other products resulting from disproportionation of the free radicals should be formed, none of which could be isolated.

This reaction can be explained by means of a halogen-metal interconversion reaction followed by coupling as in the reaction of benzyl chloride and n-butyllithium. It is known that halogen-metal interconversion does take place between β-bromostyrene and n-butyllithium (17). Such interconversion reactions produce colored solutions.

Another example of this type of coupling is the reaction of triphenylmethyl chloride with n-butyllithium to give the characteristic color of triphenylmethyl which deepened on heating and faded on cooling. When the reaction vessel was opened the color was discharged. The products isolated were triphenylcarbinol (presumably from triphenylmethylperoxide), butyl alcohol, and 1,1,1-triphenylpentane. As before, free radicals were predicted; however, triphenylmethyl could easily be formed as a result of halogen-metal interconversion followed by coupling to give hexaphenylethane which dissociated into the free radical.

From the foregoing discussion it is not unreasonable to

assume that this same mechanism might account for certain abnormal coupling reactions of Grignard reagents. Fuson (300), on reacting methylmagnesium bromide with benzyl chloride, isolated bibenzyl, ethylbenzene, and octane. Although the reaction is not as rapid as with organolithium compounds, Grignard reagents have been shown to undergo halogen-metal interconversion reactions.

The rapid development of organolithium chemistry during the last few years has created the urgent need for more definite knowledge concerning the stability of these compounds in ether. Except for one article by Ziegler which gives the rate of cleavage of ether by n-butyllithium, only general statements, such as, the compound cleaves ether rapidly, or the compound is stable in ether for a number of weeks, may be found in the literature. A knowledge of exact cleavage rates is essential in order to predict with any degree of accuracy the optimum reaction time for reactions with organolithium compounds in ethers, and certainly for a more precise interpretation of yields based upon organolithium compounds.

A study of the cleavage of ethers by organolithium compounds has revealed a number of enlightening facts. All of these cleavage reactions, with the exception of those of the s- and t-alkyllithium compounds, are first order reactions. Since, in these reactions, ether is present in excess, its

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300. Fuson, ibid., 48, 2681 (1926).

concentration is essentially constant and the second order equation reduces to a first order equation.

When ether is added to a petroleum ether solution of s- or t-alkyllithium compounds, there is a rapid initial cleavage phase in which about half of the organometallic compound is decomposed. After this initial phase, cleavage takes place at a slower rate (fig. 2). This same type of reaction occurs with cyclohexyllithium. It was thought that perhaps the ether-free organolithium compounds cleaved ether more rapidly than the etherate so that when a little of the etherate was formed, cleavage was less rapid. This would explain the two phases of the reaction. In order to prove this, advantage was taken of the fact that s-butyllithium does not cleave n-butyl ether readily. Therefore, if n-butyl ether was added to a petroleum ether solution of s-butyllithium, the s-butyllithium-n-butyl etherate should be formed. If diethyl ether was added to this solution, no initial rapid cleavage should be noted. This was not the case, however, for the same two phases of cleavage were observed.

Temperature is a vital factor in the rate of the cleavage reactions. At room temperature (25°) 18 days are required to cleave a 0.65 N solution of n-butyllithium. However, at the reflux temperature of ether, only 10° higher, a solution of the same concentration requires only 5-1/2 days for complete decomposition. A comparison of fig. 2 and fig. 3 shows this influence of temperature on a number of organolithium compounds.

The ability of various organolithium compounds to cleave ether varies over a wide range. The most stable of these compounds is methyllithium, a solution of which decreased as a result of cleavage from 0.54 N to 0.14 N in one year. The least stable is t-butyl, a 0.14 N solution decomposing in 30 minutes. Although an inspection of fig. 2 shows no great difference in the rates of cleavage of most alkyllithium compounds at room temperature there is a marked difference at reflux temperature (fig. 3). For example, a 0.2 N solution of dodecyl- and n-propyllithium is decomposed in 1-3/4 days, while the same strength solution of ethyllithium requires 2 days, n-butyllithium requires 3-1/4 days, and n-amyllithium requires 3-1/2 days for decomposition. Evidently in the homologous series between n-amyllithium and dodecyllithium there is a compound of maximum stability in diethyl ether after which the lengthening of the carbon chain in the R group of RLi compounds decreases the stability of this solvent. The order of increasing stability in diethyl ether has been found to be: dodecyl=n-propyl<ethyl<n-butyl<n-amyl<methyl. This has been found to follow the order of reactivity of normal alkyllithium compounds toward halogen-metal interconversion with α-bromonaphthalene (301) which gives the order of decreasing activity as n-propyl>ethyl>n-butyl>n-amyl>methyl.

The order of increasing stability for branched chain

301. Moore, Doctoral Dissertation, Iowa State College (1941), p. 113.

alkyllithium compounds in ether has been found to be t-butyl< s-butyl= isopropyl= cyclohexyl<isobutyl<n-butyl. This in turn follows the reactivity of these compounds towards the metalation of dibenzofuran which in the order of decreasing reactivity is t-butyl>s-butyl>isobutyl= n-butyl. It might be mentioned that the difference in cleavage of ether between s-butyl- and isobutyllithium compounds is much greater than between isobutyl- and n-butyllithium compounds. The reactivity of petroleum ether solutions of these compounds towards intercomversion with α-bromonaphthalene is not in such close agreement for the order of decreasing reactivity is s-butyl> isopropyl>t-butyl>n-butyl= isobutyl> n-propyl.

The aromatic organolithium compounds are much more stable in ether than the aliphatic types. While a 0.4 N solution of n-amyllithium is decomposed by refluxing in ether for only 4 days, a 0.4 N solution of phenyllithium, after refluxing for 30 days, was found to still be 0.09 N. Phenylethynyllithium seems to have cleavage properties comparable to those of the aromatic organolithium compounds. The order of increasing stability of aryllithium compounds has been found to be β-naphthyl<α-naphthyl<phenyl<p-dimethylaminophenyl<phenylethynyl<p-biphenyl. Mention has already been made of the fact that Müller and Töpel (272) claim α-naphthyl-, p-biphenyl- and 9-phenanthryllithium to be of no synthetic value since they are too unstable in diethyl ether. This can hardly be true since p-biphenyllithium was more stable in ether than all

other organolithium compounds studied except methyllithium. Although α-naphthyllithium cleaves ether to a greater extent than p-biphenyllithium, the fact that a 0.28 N solution of α-naphthyllithium at 35° required 25 days to be decomposed makes it impossible to say the cleavage was rapid. 9-Phenanthryllithium cannot be prepared directly from the organic halide and lithium metal so its stability in ether could not be studied. However, from the above studies it would be expected to be stable in diethyl ether for a number of days.

In general the stability of organolithium compounds is found to be in the following increasing order: tertiary alkyl<secondary alkyl<iso alkyl<normal alkyl<aromatic types<methyl. This follows exactly the reactivity of organolithium compounds in regard to metalation or halogen-metal interconversion reactions. A rule may be stated then, that in general the more rapid an organolithium compound cleaves ether, the better metalating and halogen-metal interconverting agent it is.

The stability of ethers in the presence of n-butyllithium has been found to increase in the order: dodecyl<ethyl<isopropyl<n-butyl<n-hexyl. There is evidently an ether of maximum stability between n-hexyl ether and dodecyl ether. In view of the fact that Gilman and Moore (16) found n-butyl ether to be a much better solvent than diethyl ether in which to carry out halogen-metal interconversions, it might be

interesting to see if n-hexyl ether, in view of its stability, would be a better solvent for this reaction than n-butyl ether.

Although t-butyllithium cleaved aliphatic ethers more readily than other organolithium compounds, it did not cleave diphenyl ether even though the two reagents were refluxed together for 24 hours. Ethylaluminum iodides which cleave anisole were also unable to bring about the cleavage of diphenyl ether.

A number of ethers are cleaved quite readily by organometallic compounds. This pertains especially to the dialkylaminomethyl alkyl ethers which are cleaved readily with Grignard reagents (286). A number of advantages are offered by cleaving these ethers with organolithium compounds instead of the Grignard reagent. The reaction is more rapid and the yields are increased. α-Homonaphthyldiethylamine, which is prepared in 39 per cent yields with the Grignard reagent, is obtained in 69 per cent yields using α-naphthyllithium. This synthesis produces tertiary amines of the type R_2NCH_2R' where R is an alkyl group and R' is the group derived from the organometallic compound. When organolithium compounds are used in place of the Grignard reagent a much wider variety of R' groups may be introduced into the amine. The p-dimethylaminophenyl group may be introduced in excellent yields in this manner. This is not possible when the Grignard reagent is used. The vast number of organolithium compounds prepared by metalation reactions may be used to cleave these ethers. 4-Diethylaminomethyldibenzofuran was prepared in this manner. It has

been found that cleavages of this type go with greater speed with organolithium compounds than do the coupling reactions between organic halides and organolithium compounds. This makes it possible to prepare the organolithium compound by halogen-metal interconversion and then to react it with the amine ether. In this manner excellent yields of 5-ethyl-2-diethylaminomethylcarbazole were prepared. This gives a superior method for introducing the $R_2NCH_2^-$ group into a large variety of compounds, many of which have possibilities of physiological activity. Unfortunately in preferential reactions between ether cleavage and addition to the anil linkage the latter predominates so this reaction cannot be used with such compounds as 3-quinolyllithium.

Since phenylethynyl bromide underwent halogen-metal interconversion so readily it was thought this reaction might take place with phenylethynyl chloride. This has been found to be true and brings to three the number of cases of halogen-metal interconversion with a chlorine atom which have been reported. One, reported by Mr. Melstrom (297) was with 2,4,5-triphenyl-3-chlorofuran and, the other, reported in this thesis, was between benzyl chloride and alkyllithium compounds.

A halogen-metal interconversion was attempted with vinyl bromide to determine if this might be a means of introducing the vinyl radical into compounds. Unfortunately, only acetylenedicarboxylic acid was isolated. This probably

results from the splitting out of HBr leaving acetylene which is immediately metalated to give the above acid upon carbonation. An example of this type has been noted in the reaction of β-bromostyrene and n-butyllithium to give phenylpropiolic acid upon carbonation (17). This elimination of HBr was diminished in the case of β-bromostyrene by running the reaction in petroleum ether; however, this had no effect upon the reaction with vinyl bromide.

The halogen-metal interconversion reaction is quite common to organolithium compounds. In order to determine whether it is a matter of degree of reactivity or whether the less reactive organometallic compounds react in a different manner, a number of halogen-metal interconversions were run with some less reactive organometallic compounds. It has been found that the reaction is quite general but more drastic means are necessary to bring about this interconversion. While n-butyllithium will undergo interconversion with o-bromophenol in ether, the reaction with ethylmagnesium bromide must be carried out in the absence of solvent and at high temperature. Even under these drastic conditions no reaction takes place between o-bromophenol and ethylaluminum iodides. When 4-iododibenzofuran, a compound which undergoes interconversion much more readily than o-bromophenol, is reacted under these conditions with ethylaluminum iodides, a halogen-metal interconversion does take place.

By running the reaction in the absence of solvent at high temperature the Grignard reagent was found to metalate dibenzofuran. Triethylaluminum would not metalate dibenzofuran under these conditions. Organoaluminum iodides have been found to be unsatisfactory for the metalation of dibenzofuran since a Friedel-Crafts reaction takes place during carbonation to give 2-dibenzofurancarboxylic acid. Xylene has been found to be an unsatisfactory solvent in which to carry out a carbonation with organoaluminum halides, for a Friedel-Crafts reaction takes place with the carbon dioxide and the solvent to give 2,4-dimethylbenzoic acid.

V. SUMMARY

A survey of the literature concerning the solvents used in the preparation of organometallic compounds has been made. Also, a review was made of the cleavage of ethers by organometallic compounds.

An improved method of analysis of solutions of organolithium compounds has been given. Studies have been made on the applications and limitations of this analysis.

The mechanism of the reaction between benzyl chloride and organolithium compounds has been discussed.

The rate of cleavage of ethers by organolithium compounds has been made. The cleavage of ethers has been utilized in synthesis.

Some metalations and halogen-metal interconversions have been carried out with organometallic compounds which are less reactive than organolithium compounds.