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Synthesis and Properties of Diorganomagnesium Compounds

Conrad William Kamienski
University of Tennessee - Knoxville

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To the Graduate Council:

I am submitting herewith a dissertation written by Conrad William Kamienski entitled "Synthesis and Properties of Diorganomagnesium Compounds." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

Jerome F. Eastham, Major Professor

We have read this dissertation and recommend its acceptance:

Bruce M. Anderson, George K. Schwitzer, David A. Shirley

Accepted for the Council:

Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

November 27, 1967

To the Graduate Council:

I am submitting herewith a dissertation written by Conrad William Kamienski entitled "Synthesis and Properties of Diorgano-magnesium Compounds." I recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

Jerome F. Eastham
Major Professor

We have read this dissertation
and recommend its acceptance:

Bruce M. Anderson
Geo. K. Schweitzer
David A. Shirley

Accepted for the Council:

Hilton A. Smith
Vice President for
Graduate Studies and Research

SYNTHESIS AND PROPERTIES OF DIORGANOMAGNESIUM COMPOUNDS

A Dissertation
Presented to
the Graduate Council of
The University of Tennessee

In Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy

by
Conrad William Kamienski
December 1967

To my dear wife, Diane

769836

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CHAPTER I

INTRODUCTION

Although dialkylmagnesium compounds have been known for over a hundred years, relatively little effort has been directly expended on these reagents per se; much of what we know about magnesium alkyls has been an outgrowth of previous studies concerned with the nature of the Grignard reagent. Only recently has any effort been made to elaborate on methods for preparing these reagents, to determine carefully their physical and chemical properties, and to develop practical uses for these reagents. It has been the purpose of the present study to review the presently known methods of preparation of dialkylmagnesium compounds, to investigate some new preparative techniques for these reagents, to examine their physical and chemical properties, and to carry out some basic chemical reactions involving their use. A summary of previous studies of magnesium alkyls follows.

A. METHODS OF PREPARATION OF DIALKYL MAGNESIUM COMPOUNDS

In 1929 Gilman and Brown¹ obtained a small amount of dimethylmagnesium as colorless crystals by a process which involved a distillation of methylmagnesium chloride at 190° under a vacuum of 0.2 mm over a period of nine hours. Gilman's work confirmed von Löhrs² and Flecks³ reports that the lower dialkylmagnesiums were solids and not liquids, as had been originally indicated in the mid-nineteenth century by Hallwachs

and Schafarik⁴ and by Cahours.⁵ The latter two workers prepared dialkylmagnesium reagents of unknown purity from magnesium metal and the corresponding mercury dialkyls(1), an example of the most venerable of the indirect synthesis techniques in organometallic chemistry.



Also in 1929, Schlenk and Schlenk⁶ discovered their now classical method of preparing the magnesium alkyls, namely, precipitation of the dioxanate complex of the magnesium halide from an ethereal solution of Grignard reagent. From the varying amounts of magnesium halide precipitated by this technique with different Grignard reagents, the authors proposed equilibria (2) and (3), which they felt could exist



in solutions of Grignard reagents. They proposed that ethylmagnesium iodide consisted of $6EtMgI + 4MgEt_2 + 4MgI_2$ in solution and phenylmagnesium bromide of $PhMgBr + 0.115MgPh_2 + 0.115MgBr_2$. Many authors since then have been engaged in attempts to prove or disprove this hypothesis and recent reviews,^{7,8,9,10} of such work are available.

The two indirect techniques, the Schlenks' dioxanate precipitation^{11,12,13,14,15} and the older magnesium-mercury exchange^{16,17,18,19} have been and are still widely employed to prepare dialkylmagnesium reagents in moderate to good yields. There are, however, several disadvantages in these techniques. Mercurials are both poisonous and expensive. If the reaction is effected without an ethereal type solvent, or in the absence of a solvating medium (that is, in the absence of a

Lewis base), the magnesium metal-mercury dialkyl exchange method involves heating these reagents together in sealed tubes at rather high temperatures (115-120°) for extended periods of time (24 hours or longer). Such conditions preclude the synthesis of easily pyrolyzed dialkylmagnesium reagents. In addition, there arises the problem of separating the reagents from by-product mercury, particularly if insoluble dialkylmagnesium reagents are produced. The dioxane method is somewhat more rapid, and less stringent conditions are required, but even so, the specific procedure can not be called convenient. Further, the reagents so produced are solvated. They contain some residual halogen and are always difficult to free of dioxane.¹²

It would, of course, be most convenient if magnesium alkyls could be prepared directly, particularly in a non-solvating medium, e.g., much as solutions of lithium alkyls are prepared by direct reaction of the metal with alkyl chlorides in a hydrocarbon (4). However, direct reaction



of magnesium with an organic halide in a solvating medium has always been considered to give the Grignard reagent, or perhaps as a better description, to give an organomagnesium reagent which contains halogen. Until recently there have been relatively few reports of the direct reaction in hydrocarbon of magnesium metal with alkyl chlorides, but alkylmagnesium iodides were prepared in benzene as long ago as 1904 by Tschelinzeff.²⁰ In 1931 Schlenk²¹ did investigate the preparation of a few different alkylmagnesium halides at room temperature in pure benzene, i.e., without the aid of solvating agents as "activators" or catalysts. Essentially

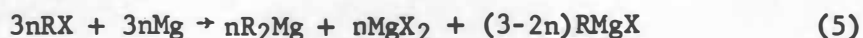
quantitative yields of n-butyl- and n-octylmagnesium iodide, but only a 55 per cent yield of n-butylmagnesium chloride were reported.

A group of Russian workers²² have repeated Schlenk's work and reported that greatly improved yields (80-95 per cent) of alkylmagnesium halides could be obtained from all the various normal alkyl iodides, bromides, and chlorides from methyl to decyl in solvents such as isooctane or dodecane by employing temperatures of 80-100°. By this direct route secondary and tertiary alkylmagnesium halides could not be prepared, presumably because of their thermal lability and the ease with which they undergo side reactions at these temperatures. Bryce-Smith and Cox²³ have reported that Grignard reagents prepared by the direct reaction in benzene contain considerably less than a stoichiometric amount of halide. It appeared to these workers that the products obtained vary in composition from a stoichiometry of R_5Mg_3I (or R_3Mg_2I), for soluble products derived from some n-alkyl iodides, to an almost halide-free hydrocarbon insoluble product, derived from n-butyl chloride. The yield of the n-butylmagnesium reagent was indicated to be 80-85 per cent, based on the alkyl chloride, when an elevated reaction temperature was employed. This butylmagnesium reagent was characterized by slow precipitation of both active base and halide from the initial reaction solution, the latter proceeding more rapidly than the former. For example, a freshly prepared solution of n-butylmagnesium chloride in cumene, having an initial active base to halide ratio of 2.0, slowly precipitated solid on standing. After 19 and 50 hr. at 25°, the active base/halide ratios were 5.0 and 14.6, respectively. The original concentration of magnesium

product in solution decreased from 0.235 to 0.075 g. atom/liter during this time. The authors suggested the occurrence of a gradual change in composition with elimination of insoluble MgCl_2 to give less soluble species until an almost insoluble R_2Mg was obtained.

A particularly interesting n-amylmagnesium compound was reported by Glaze and Selman¹⁹ after the present study was initiated. These workers reacted the n-amyl halides directly with magnesium powder at approximately 85° over a period of several hours. Extraction of the reaction mixture, which was of a "muddy" consistency, with refluxing benzene for two hours left a solid "mud" phase and yielded the organo-magnesium reagent in a very viscous, clear colorless liquid phase. Removal of solvent benzene from the viscous liquid left a solid; addition of more benzene to the solid regenerated the viscous liquid, and the quantity of halogen in the liquid was not changed by this process. In one such liquid phase which contained a total of 0.17M amylmagnesium reagent, the quantity of halogen (chloride) corresponded to only ca. two mole per cent amylmagnesium chloride. When the halogen was bromide, the relative amount in the liquid was greater, and was still greater with iodide.

Thus there are several previous reports which suggest that in the absence of a solvating medium, direct reaction of magnesium with an organic halide (particularly with chloride) can produce a mixture of diorganomagnesium reagent and magnesium halide along with organo-magnesium halide (5).



Another "direct" route to unsolvated dialkylmagnesium reagents involves the addition of MgH_2 (or its precursors, Mg and H_2) to ethylene.^{24,25} Although there is no halide by-product formed in this method, yields of product are low and high pressures and temperatures are required. Other isolated examples of the preparation of solvated dialkylmagnesium reagents have involved reaction of alkyl ~~salts~~ sulfates with magnesium and magnesium iodide,²⁶ and metal-metal exchange between diphenylmagnesium and *n*-butyllithium.²⁷

Some particularly elaborate, but very interesting, techniques have been developed to remove both halogen and complexed solvent from organomagnesium halides. In one process, desolvation of ethylmagnesium chloride by dropwise addition of the Grignard solution in ether to boiling toluene, was followed by admixture of the precipitated EtMgCl with triethylaluminum in hexane to give a halide-free solution. Distillation was then used to remove hexane and finally (at reduced pressure) to remove triethylaluminum and leave diethylmagnesium.²⁸ There is a patented process of electrolysis of alkali metal tetraalkylaluminum solutions using a magnesium anode and separation of the products ($\text{MgR}_2 \cdot 2\text{AlR}_3$) as above, by fractionation under reduced pressure.²⁹ Also, interaction of magnesium with ethyl chloride and NaBEt_4 in diglyme at 115° for one hour, is reported to yield a mixed reagent, $\text{MgEt}_2 \cdot \text{BEt}_3$, which can be separated by fractionation.³⁰

One method of preparing organic derivatives of magnesium is almost conspicuous by its absence. It has been known for many years that organic derivatives of more electropositive metals will undergo metathetical

exchange with halides of metals lower in the electrochemical series, including exchanges involving organomagnesium halides (6).^{31,32,33} For



example, Glaze and co-workers³⁴ reacted n-butylmagnesium iodide prepared in benzene with beryllium chloride to produce di-n-butylberyllium in 7 per cent yield. There are, however, only a few recorded instances of attempts to use this metathesis to synthesize organomagnesium reagents themselves; in each instance the use was highly specific. Nobis and Robinson³⁵ added 1,3-butadiene to a mixture of finely dispersed sodium and anhydrous magnesium chloride in dimethyl ether to produce a "di-Grignard" butadiene dimer adduct. In an unsuccessful attempt to obtain the corresponding optically active dialkylmagnesium compound, Smith³⁶ reacted an optically active s-alkyllithium compound with magnesium bromide. Tzschach and Hackert³⁷ prepared magnesium bis-di-cyclohexylarsenide from lithium dicyclohexylarsenide and magnesium bromide in tetrahydrofuran (THF).

An initial goal of the present study was to develop general techniques by which alkyls of the alkali metals could be caused to exchange with halides of magnesium and by which unsolvated dialkylmagnesium compounds could be obtained, e.g., as illustrated below (7).



During this study it became apparent that further advantage of the Schlenk's equilibrium (2) and of direct reaction (3) could be taken in synthesizing dialkylmagnesium compounds.

B. PROPERTIES OF UNSOLVATED DIALKYL MAGNESIUM COMPOUNDS

The smaller normal dialkylmagnesium compounds (C_1 - C_4) and one branched reagent (diisopropylmagnesium) have been found to be solids and to be essentially insoluble in both aromatic and aliphatic hydrocarbons. There is evidence that longer normal chain reagents might dissolve in aromatic hydrocarbons, but solubility properties of s- and t-dialkylmagnesium compounds (other than diisopropyl) were not determined prior to the present study.

Shown below are quantitative data reported by Strohmeier¹² on the solubilities in benzene of some of the lower homologs. These previously reported solubilities must be considered upper limits because they were determined by simply titrating the total base from hydrolysis of the supernatant benzene taken from excess solid magnesium reagent. Solubilities found this way include dissolved compounds containing magnesium-oxygen bonds (e.g., $ROMgR$) as well as dialkyl reagents. Other data

<u>Reagent</u>	<u>Found in benzene</u>
$(C_2H_5)_2Mg$	0.016M
$(n-C_3H_7)_2Mg$	0.012M
$(iso-C_3H_7)_2Mg$	0.024M
$(n-C_4H_9)_2Mg$	0.024M

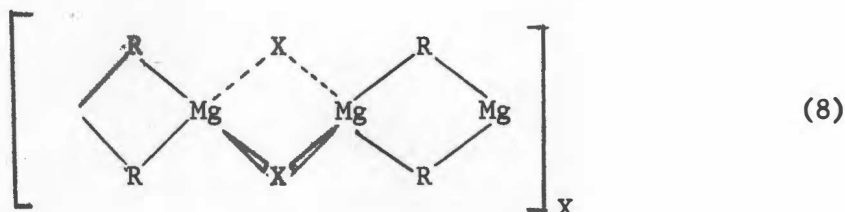
obtained by Strohmeier indicate that these reagents must be even less soluble (by at least an order of magnitude) in an aliphatic hydrocarbon, hexane.

Magnesium alkyls are soluble in ethers and other basic solvents, and, as previously indicated, have not generally been obtained free of

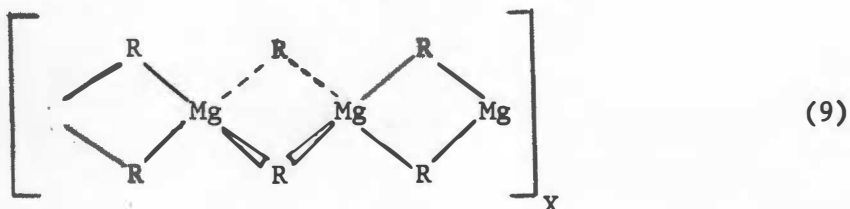
solvation. It is, in fact the difficulty in obtaining magnesium alkyls free of such base which has precluded studies of the solubilities of the unsolvated reagents with branched chain alkyls or with higher homologs of the primary alkyls. For example, Strohmeier had prepared the reagents he studied by the dioxanate precipitation technique.¹² In order to remove dioxane from his reagents it was necessary to heat them under high vacuum over a long period of time. (The isopropyl reagent was heated with a bath temperature of 115° for 15 hours under a "Klebevakuums" produced with a three-stage mercury diffusion pump; other reagents he studied were desolvated at even higher temperatures.) Strohmeier found this desolvation technique was unsuccessful with a branched reagent, (diisobutylmagnesium) and with a higher homolog (di-n-hexylmagnesium); these reagents underwent thermal decomposition before all dioxane had been removed. (In the present study it has been found that di-t-butylmagnesium undergoes thermal decomposition when a desolvation is attempted at temperatures even well below 100°).

The factor of relative instability of reagents due to chain branching, a factor which is well recognized in thermal elimination reactions in general, is an obvious reason for desolvation difficulties with the branched compounds. The reason why a higher homolog (but primary) should be difficult to desolvate is less obvious; they are stable at elevated temperatures (at least to 150° and perhaps higher) for many hours. It is probable though that the longer chain reagents are viscous liquids, whereas the smaller reagents become amorphous solid powders upon desolvation. For physical reasons, removing solvent from a viscous liquid is more difficult than removing solvent from an amorphous solid.

That the longer chain reagents might be soluble in benzene is suggested by the solubilities of the "Grignard reagents" which were prepared directly in that solvent by reactions of alkyl halides and which were found to contain less than a stoichiometric quantity of halide in solution after reaction. Bryce-Smith and Cox²³ as well as Glaze and Selman¹⁹ expressed the belief that the structure of an alkyl-magnesium bromide or iodide in benzene solution is polymeric with an unmixed bridge bonding of the type illustrated in (8). It is known that



in the progression from alkyl iodides to bromides to chlorides, the organo-metallic in solution contained less and less halide. It is therefore natural to assume that in this progression, the structure in solution begins to assume a polymeric, totally alkyl-bridge-bonded type, illustrated in (9). Indeed, from X-ray crystallographic data, Weiss^{38,39}



suggested that the dry residues obtained by removal of solvent from ethereal solutions of RMgX ($\text{R}=\text{CH}_3$, C_2H_5 ; $\text{X}=\text{Cl}$, Br) were actually mixtures of dialkylmagnesiums and magnesium halides. (Earlier Kirmann, Hamelin and Hayes⁴⁰ had studied Grignard solutions by thermogravimetric

techniques and expressed the belief that even in ethyl ether, the organomagnesium halides are not represented by a single compound, RMgX , nor by a simple mixture of MgR_2 , MgX_2 and ether.) The dialkylmagnesium reagents studied by Weiss were reported to be in the form of infinite polymeric chains; in the case of dimethylmagnesium, a complete analysis of crystalline material was reported. The unit cell is orthorhombic with an Mg-Mg distance of 2.73\AA ; the metal atoms are connected by pairs of methyl bridges (Mg-C of 2.24\AA) with an almost tetrahedral arrangement of four methyl groups around each metal atom, cf. (9).

The self associated structures of magnesium alkyls can be classed as typical electron deficient oligomers. (The concept of electron deficient bonding has been extensively considered elsewhere and it is not within the scope of this survey to review that concept.)

All of these observations leave it difficult to rationalize one of the observations of Glaze and Selman on the organomagnesium reagent they prepared from direct reaction of amyl chloride with magnesium. The products of this reaction were refluxed with benzene for about two hours; an upper viscous benzene phase was obtained. With one set of analytical data it was indicated that one viscous benzene phase they obtained contained the equivalent of $0.17\text{M R}_2\text{Mg}$ and very little RMgX (0.01M), as previously indicated. It appeared then to Glaze and Selman that a true solution of diamylmagnesium in benzene was produced. A freezing point depression measurement of the benzene indicated that the contained diamylmagnesium reagent was dimeric. That is the observation which is difficult to rationalize. From the evidence and arguments favoring polymeric self

association of other dialkylmagnesium reagents and of organomagnesium halides containing limited halide, one would also expect an amyl reagent to be extensively associated, rather than a simple dimer. Also, if this reagent is not polymeric, its ability to greatly increase the viscosity of benzene seems somewhat unusual.

Whatever the exact degree of association of magnesium alkyls in the solid state or in hydrocarbon solution, solvation by basic solvents such as ethers and amines depolymerizes the reagents to structures containing just one or two R_2Mg units.

C. SOLVATION AND THE PROPERTIES OF DIALKYL MAGNESIUM COMPOUNDS

In general, just as with preparative studies, much more has been done in considering solvents with Grignard reagents than with diorganomagnesium compounds. Since there is every reason to believe that solvation of the two types of compounds could be analogous, several pertinent findings with the organomagnesium halides will be briefly stated in this section.

In work with ethylmagnesium reagents, Storfer and Becker⁴¹ concluded from colligative property studies, and from reaction kinetics with benzonitrile, that diethylmagnesium (0.5-1M) is dimeric in THF. (Ashby⁴² had indicated earlier that ethylmagnesium halides are monomeric in THF and triethylamine.) Vreugdenhil and Blomberg,⁴³ on the other hand, concluded that at low concentrations (0.01M) diethylmagnesium is monomeric in diethyl ether. If both conclusions are correct, this behavior is somewhat analogous to that found by Ashby and Smith⁴⁴ for Grignard reagents in ether.

Generally, the Grignard reagents were found to be monomeric at low concentrations (0.001-0.01M) and dimeric at higher concentrations (0.2M and above). Recent colligative property studies by Ashby⁴⁶ indicate, however, that dialkylmagnesium compounds in diethyl ether and in THF are less highly associated than are Grignard reagents. Thus, it is difficult to reconcile the work of others with that of Storfer and Becker, and it seems most likely that dialkylmagnesium compounds are monomeric, rather than dimeric, in basic solvents. Smith and Becker have reached the same conclusion.⁴⁵

Scala and Becker showed that a considerable effect on reactivity results from coordination of Grignard reagents by basic solvents.⁴⁷ Reaction of ethylmagnesium bromide with benzonitrile was found to be slower in more basic solvents such as THF and ether solutions containing various amines than in ethyl ether alone. This decelerating effect on rate was especially evident when diglyme was the solvent, the authors ascribing its great effect on reaction rate to the especially stable chelate-coordination between one molecule of the magnesium reagent and two oxygen atoms in the same molecule of diglyme. The authors cited Normant's⁴⁸ belief that success in preparing alkenyl Grignard reagents in THF is due to the greater stability of these reagents in this more basic solvent. From this belief the generalization was made that Grignard reagents are most stable in the more basic solvents. Vink and coworkers⁴⁹ found that the optical activity of (+)(S)-1-ethoxy-2-methylbutane in benzene was greatly enhanced by coordination with ethylmagnesium bromide; THF was found to return

the optical activity of the system to its original value prior to addition of the Grignard, whereas di-n-butyl ether did not effect this change. These findings are easily rationalized with the postulate that the magnesium reagent is specifically coordinated by the ether with the lowest steric requirements in the system.

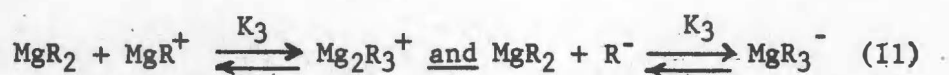
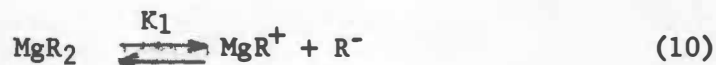
The only complete structural analyses available on crystalline Grignard reagents are on solvated reagents. Stucky and Rundle⁵⁰ found that both ethylmagnesium bromide and phenylmagnesium bromide exist as identifiable monomeric units coordinated to two molecules of ether. The authors were unsuccessful in attempts to remove solvation from their Grignard reagents and retain crystallinity; amorphous solids resulted. These observations, along with others cited earlier,^{28,38,39,40} make it seem logical to define "Grignard reagents" as including solvation, and make it seem promising to further explore techniques of producing isolable dialkylmagnesium compounds by desolvation of Grignard reagents.

Coates and Heslop⁵¹ obtained monomeric complexes (in benzene) of dimethyl- and of diphenylmagnesium with 1,2-dimethoxyethane (monoglyme) and with N,N,N',N'-tetramethylethylene diamine (TMEDA). The $(\text{CH}_3)_2\text{Mg}:\text{TMEDA}$ complex could be sublimed intact at 65-75°/0.01 mm. (m.p. 97-98°C), while the corresponding monoglyme complex did not melt but did decompose by dissociation above 120°. These authors also found that complexes containing two molecules of a monoether such as THF could also be isolated. Zakharkin⁵² isolated volatile monomeric TMEDA complexes of diethyl-, di-n-propyl-, diisopropyl-, and di-n-butylmagnesium. Coates and Ridley⁵³ obtained a crystalline coordination complex of diisopropylmagnesium with

t-butyl cyanide. The low solubility of the dioxanate complex of dimethylmagnesium in diethyl ether has been known for some time.⁵⁴

It has also been known for some time that basic solvents promote some type of ionization of magnesium alkyls. In a relatively recent report on dimethylmagnesium in ether, Vreugdenhil and Blomberg⁵⁵ plotted "molar conductivity" (Λ_{molar}) (found by dividing the specific electrical conductivity by the molarity in magnesium reagent) vs. molar concentration and obtained a direct linear relationship up to a one molar concentration. Above this concentration the linear relationship no longer held and a maximum in Λ_{molar} values was obtained at about 1.7 M. These authors found much lower Λ_{molar} values for these solutions than had Dessy and Jones earlier,⁵⁶ and they ascribed this discrepancy to the presence of oxygen impurities during the earlier work.

Strohmeier and coworkers^{57,58} also measured the equivalent conductivity of dialkylmagnesium compounds in ether and in THF. Their findings were interpreted in terms of the compounds' behaving like monovalent electrolytes, forming "triple ions," as indicated by equilibria (10) and (11). With this interpretation, dissociation constants K_1 in



THF and ether were estimated to be in the range of 10^{-8} to 10^{-9} and 10^{-11} to 10^{-13} , respectively. Values of K_3 were said to be much larger, ca. 10^{-2} in THF. In other words, the extent of ionization of

magnesium alkyls in basic solvents appears to be quite small. Interestingly enough, magnesium bromide, a "salt," showed slightly lower conductivity in these solvents than did magnesium alkyls. The equivalent conductivities of the organomagnesium compounds, measured in dioxane, ether, THF and triethylamine, increased with increasing dielectric constant of the solvent and seemed to Strohmeier to depend on the solvent's electron donor ability. It is noteworthy here that Ebel and Schneider⁵⁹ were able to cause benzylmagnesium chloride to ionize, i.e., give the intense red color of the benzyl anion, by addition of hexamethylphosphoramide to a colorless ethereal solution.

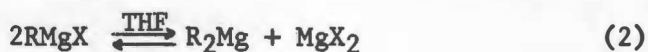
Quite recently, Psarras and Dessy⁶⁰ reported on the polarographic behavior of magnesium alkyls in 1,2-dimethoxyethane and elaborated on the nature of the electrolytic oxidative and reductive processes. It was their conclusion that R_2Mg reagents undergo a two-electron oxidation at a mercury electrode to R_2Hg and Mg^{+2} . A one-electron reduction of the reagents occurred, but only when R was a stable anion precursor such as benzyl or allyl, and appeared to form $R:^-$ and RMg^{\cdot} , which decomposed to R^{\cdot} and magnesium metal.

From NMR studies^{61,62} of organomagnesium reagents, Fraenkel and coworkers concluded that chemical shifts are the same for both the Grignard and the corresponding dialkyl compound. Temperature dependent spectra of reagents with special symmetry properties (2-methylbutyl- and 2-phenyl-3,3-dimethylbutylmagnesium) indicated that inversion at the α -carbon atom (magnesium-bound carbon) occurs fairly rapidly and, according to Fraenkel, by a mechanism involving electrophilic displacement of magnesium (SE^2). Rates of inversion were said to be strongly

solvent dependent. Roberts and coworkers,^{63,64} from NMR work with neohexylmetal compounds, have postulated the inversion mechanism to be unimolecular and of the SE^1 type.

Seitz and Brown⁶⁵ presented proton and 7Li NMR spectral evidence for the existence of intermetallic complexes of methyllithium and dimethylmagnesium in ether, $Li_2Mg(CH_3)_4$ and $Li_3Mg(CH_3)_5$. Exchange of 7Li between methyllithium and the complexes appeared to occur at about the same rate as methyl group exchange.

Salinger and Mosher⁶⁶ studied the IR spectra of methyl, ethyl and phenyl Grignard reagents and the corresponding dialkyl- and diarylmagnesium compounds in ether and THF. It was their conclusion that carbon-magnesium bonding absorption occurred in wide bands between 500 and 535 cm^{-1} ($R=CH_3$, C_2H_5) and between 365 and 383 cm^{-1} ($R=C_6H_5$). Whereas there was no difference in the proton NMR spectra of the Grignard reagents and their corresponding disubstituted magnesium reagents in THF, IR spectra showed noticeable differences in these two reagent types. There was spectral identity between Grignard reagents and synthetic mixtures of dialkylmagnesium reagents and MgX_2 in THF. Additions of excess MgX_2 to these solutions altered the shape of the absorption band in the manner expected for an increase in the concentration of $RMgX$ and a decrease in the concentration of R_2Mg , as would be expected from the Schlenk equilibrium (2).



Because of the real possibility that this equilibrium can be rapidly established and maintained under many reaction conditions, it would seem particularly important to consider the relative reactivity of dialkylmagnesium compounds when consideration is given to the mechanism of Grignard reactions.

D. RELATIVE CHEMICAL REACTIVITY OF MAGNESIUM

ALKYLS AND GRIGNARD REAGENTS

Holm⁶⁷ compared the reactions of n-butyl Grignard reagents with those of di-n-butylmagnesium in ether and in THF with various substrates: acetone, methyl acetate, azobenzene, methyl trifluoroacetate, 1-hexyne, and s-butyl crotonate. . Using ether he found that, except for 1-hexyne, there was in general a ca. 400 fold greater rate of reaction by di-n-butylmagnesium than by n-butylmagnesium bromide toward all the substrates. The bromide reacted four times faster than the iodide, and the chloride, 20-30 times faster than the bromide. Using THF he found reactivity of both types of reagents toward all of the substrates except azobenzene (where the rate was accelerated) was considerably decreased relative to that in ether. In addition, the reactivities of the two reagent types (except for the iodide) were roughly equivalent in THF. It is suggested here that these results can be interpreted as follows. During reactions in ether, the Schlenk's equilibrium was not rapidly maintained; RMgX is less reactive than R_2Mg , so rates with solutions of the latter were faster. During reactions in THF, the Schlenk equilibrium was rapidly maintained, so whichever reagent was put into solution, rates were characteristic of the R_2Mg , which now because of better solvation by THF was less reactive than it was in ether.

The "expected" addition of dialkylmagnesium reagents to ketones is complicated by "side" reduction and enolization of the ketone even more than is the same reaction with Grignard reagents. If the mole ratio of dialkylmagnesium reagent to ketone is 1:2, the reaction rate is much

more rapid during the first 50 per cent of reaction of alkyl groups; the rate is said to follow second-order kinetics up to this half-way point and the rate to decline rapidly thereafter.⁶⁸ It has been proposed that the alkylmagnesium alkoxide formed (12) during the first half of the



reaction is considerably less reactive than the initial dialkylmagnesium reagent.¹⁷ When the molar ratio of R_2Mg to ketone is increased to 1:1 (so that the alkylmagnesium alkoxide formed did not have to react), the evidence is that the ratio of products (from addition, reduction and enolization) is not far from that observed with $RMgX$.⁶⁸ In recent developments, House and Respass⁶⁹ have presented stereochemical evidence for the difference in reactivity of alkylmagnesium alkoxides in these systems, and several alkylmagnesium alkoxides have been synthesized by workers in England.^{70,71}

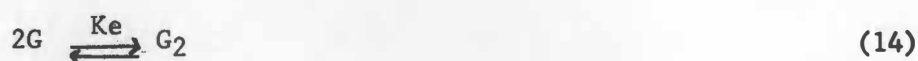
House and Traficante⁷² postulated that although $MgBr_2$ does not catalyze the addition of alkylmagnesium reagents to carbonyl functions, it does suppress the tendency of ethylmagnesium alkoxides to give the side products resulting from enolization and reduction. They felt that a basic alkoxide molecule would be removed from the reaction medium by the presence of the Lewis acid, $MgBr_2$. Another interesting opinion they expressed concerned a transient yellow color observed during reactions of magnesium alkyls with ketones, which they speculated might represent a charge transfer complex (formed from the ketone and the organomagnesium compound) and which might be a true intermediate. The authors could not maintain the transient yellow color long enough to measure spectral properties of the species responsible. In a similar view, Guthrie, Spencer

and Wright⁷³ obtained an intense red color on mixing benzoin in benzene with an excess of solid ether-free dimethylmagnesium. No significant amounts of side products were formed; work up gave a 92 per cent yield of 1,2-diphenyl-1,2-propanediol (the expected addition product) and only 8 per cent of enolization product. From the same reactants in basic ethereal solvents, they obtained less of the former and more of the latter products.

While no one appears to have obtained specific spectral characteristics of intermediate complexes formed during reactions of dialkylmagnesium reagents with ketones, several workers have reported on such complexes from Grignard reagents. For example, S. G. Smith⁷⁴ obtained direct spectroscopic evidence for the formation of complexes between some highly hindered diaryl ketones and methylmagnesium bromide in ether. A new band (in addition to the ketone band) appears in the ultraviolet spectrum of the mixture, but both bands disappear rapidly at 25°. These results led Smith and Su⁷⁵ to postulate a mechanism (13) in which ketone reacts with monomeric Grignard compound in a fast step to produce a complex, which then rearranges in a first-order process to produce the product.

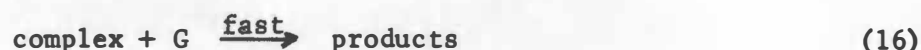


The following reactions, involving an association complex, have also been represented as a mechanism for addition of Grignard reagents to ketones. This specific representation, (14), (15), and (16), is that of Ashby and Smith,⁴⁴ but the general concepts, and many details, have often been presented by others.

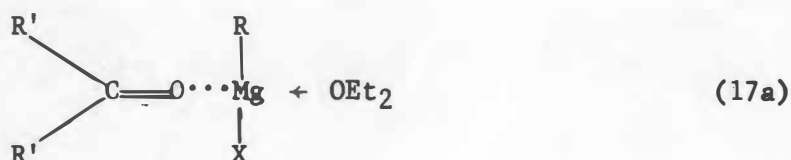


G = monomeric Grignard species, e.g., R_2Mg , $RMgX$

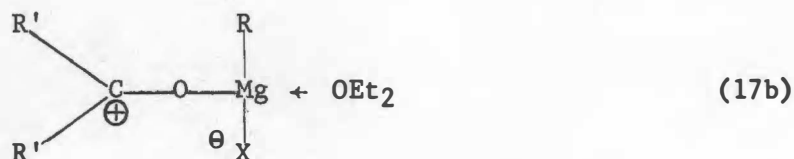
G_2 = dimeric species, e.g., $R_2Mg \cdot MgX_2$, $(RMgX)_2$



The rate determining step (15) is thought by Ashby and Smith to be displacement by the ketone of one of the strongly solvated ether molecules attached to the magnesium atom. The authors describe the complex so formed either as one involving polarization of the carbonyl group (17a) or as one derived from coordinate covalent bond formation and



having ionic character (17b); such a distinction would seem to have



little physical meaning, to the present writer. They explain the lower reactivity of $RMgX$, relative to that of R_2Mg , with ketones as being due to the Grignard reagent's greater Lewis acidity, which leads to stronger bond formation with ether of solvation and thus slower formation of the association complex. An interesting point to consider in this explanation is that the actual difference in acidity between $RMgX$ and R_2Mg seems never to have been measured.

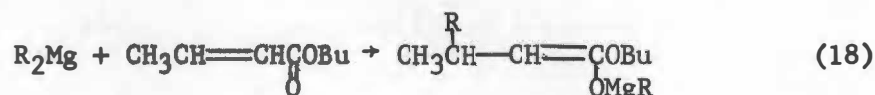
It would seem somewhat more logical to presently assume that R_2Mg is more reactive than $RMgX$ in a general way, including their relative reactivity toward complexation by bases, i.e., until there is contrary evidence there is no need to assume that R_2Mg is more acidic than $RMgX$. Sufficiently basic solvents might actually tend to stabilize the R_2Mg reagent (as already suggested, cf. page 13), while similar solvents could possibly even enhance $RMgX$ reactivity by facilitating maintenance of the Schlenk equilibrium.

This latter possibility has been realized by Wotiz and coworkers,⁷⁶ who found that halogen-free diethylmagnesium reacts three times faster in ether with 1-hexyne than does ethylmagnesium bromide. Use of triethylamine as a solvent increases the rate of reaction of $EtMgBr$ with 1-hexyne, but not the rate of Et_2Mg .⁷⁷

Again, the postulate being stressed here is that in some cases, reactions of Grignard reagents can actually be those of dialkylmagnesium reagents made available by the Schlenk equilibrium. This is not a new postulate.

House and Thompson⁷⁸ studied the effect of adding only the first alkyl group of Et_2Mg on the ratio of conjugate to normal addition to α,β -unsaturated ketones. They found that the order of both reactions in R_2Mg and ketone is the same and that the presence of $MgBr_2$ slightly enhanced normal addition. (With long reaction times and a large excess of R_2Mg , di-addition to the ketones resulted, presumably due to reaction of the enolate salt derived from conjugate addition with Et_2Mg .) Conjugate addition of magnesium alkyls also occurs with α,β -unsaturated esters.

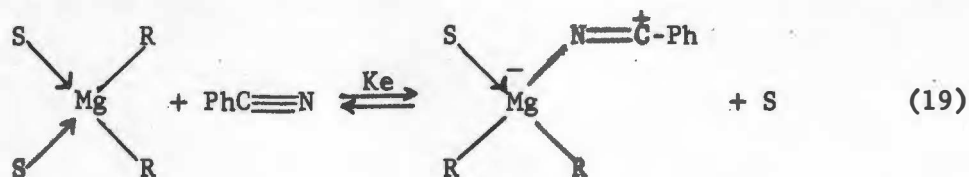
An interesting study was made of conjugate addition (18) of dibutylmagnesium to the hindered ester s-butyl crotonate.⁷⁹ Use of butylmagnesium bromide instead of dibutylmagnesium lowered the yield of

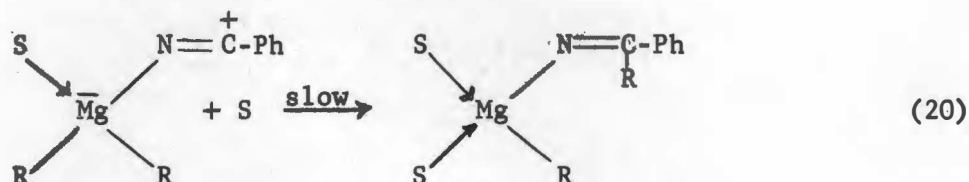


s-butyl-3-methyl-heptanoate obtained from reaction of the ester. .

Addition of $MgBr_2$ to the Grignard reagent lowered the yield still further. The authors postulated that the mechanism of conjugate addition to an α,β -unsaturated carbonyl compound should involve only the dialkylmagnesium moiety from the Grignard reagent.

Contrary to the later results obtained by others with ketones, Gilman and Brown⁸⁰ reported in 1930 that nitriles react faster with Grignard reagents than with their corresponding diorganomagnesium compounds. Much more recently (1963) Citron and Becker⁸¹ made a rate study with various *p*-substituted benzonitriles and diethylmagnesium in THF, but did not compare rates with Grignard reagents. They found that a second order rate equation, rate proportional to $[Et_2Mg][\text{nitrile}]$, best fit their data. The linearity of a Hammett plot, with a positive rho value (+1.57), obtained from this study suggested that the same mechanism, (19) and (20), is operative in all the examples studied. The rate determining step suggested (20) involves a dipolar species and is represented as involving transfer of R from R_2Mg in a complex to carbon of the nitrile group. Storfer and Becker had already reported





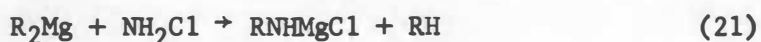
that, as was the case in reactions of R_2Mg with ketones, only one-half of the available alkyl groups are readily utilized in reactions of R_2Mg with nitriles.⁴¹ Schiff bases also add R_2Mg via a process which readily utilizes only half of the available R groups.⁸²

Reaction with epoxides probably provides the clearest example of the dialkylmagnesium compound being the better reagent. Side products obtained along with the expected addition products (alcohols) on reaction of Grignard reagents with substituted epoxides include halohydrins and their hydrolysis products. Only the expected addition products are obtained on reaction of dialkylmagnesium reagents with these epoxides.^{15,83,84,85} On the other hand, Reeves and Fine⁸⁶ did observe that both reagents reacted with 3,3,3-trichloro-1,2-epoxypropane to produce the product from halogen-metal interconversion, no expected addition product being formed.

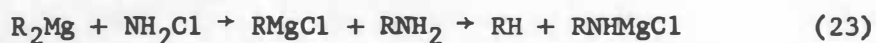
Another specific example of the Grignard reagent being less useful was found in carbonation of some alkynyl reagents. Gilman⁸⁷ discovered that 1-hexynylmagnesium halides gave low yields of acidic product on carbonation (<5 per cent) whereas dihexynylmagnesium (from Et_2Mg and hexyne-1) gave a 73 per cent yield of 2-heptynoic acid. While it would be a mistake to generalize that the magnesium alkyls are superior for carbonation, the following is another example which can be so interpreted. Apparently, after finding poor results from conventional carbonation of

an ethereal solution of (+)(S)-2-methylbutylmagnesium chloride, Lardicci⁸⁸ obtained a 71 per cent yield of (+)(S) acid product on carbonation of the suspension obtained by slow addition of the Grignard reagent in ether to boiling xylene followed by continuous distillation until the distillate was ether-free. There can be little doubt that the indicated removal of ether converted the Grignard reagent to a mixture of magnesium bromide and dialkylmagnesium.

A particularly interesting reaction was studied by Coleman and Blomquist.⁸⁹ These workers obtained 90-100 per cent yields of n-butylamine and no ammonia on reaction of $(\text{Bu})_2\text{Mg}$ with ClNH_2 . When BuMgX was used, less amine was formed, ammonia was obtained, and the yield of amine decreased according to X in the order $\text{Cl} > \text{Br} > \text{I}$. Formation of amine (21) apparently involves a coupling process (22) followed by metallation. If



such coupling is restricted to the dialkyl reagent, then only to the extent that the Schlenk's equilibrium produces R_2Mg could RMgX produce amine (23).

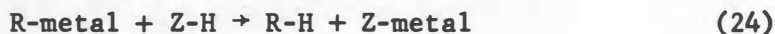


Coupling of Grignard reagents with organic halides has not been widely employed, and coupling of the dialkyls, even less. Zakharkin and coworkers^{90,91} showed that although interaction between organomagnesium compounds and alkyl halides in ethers of high solvating power results mainly in the formation of typical Wurtz reaction products, suggesting a heterolytic reaction process, the same reactants in non-solvating

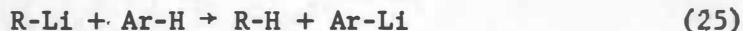
media, cumene, resulted in the formation of large amounts of bicumene, suggesting a free-radical process.

E. METALLATION AND POLYMERIZATION BY MAGNESIUM ALKYL

In the past most of the chemistry of the simple organometallic reagents, e.g., lithium alkyls and Grignard reagents (i.e., not π -complexed metals), has been classified as "carbanion" chemistry. Such reagents, R-metal, have been looked upon as salts of very weak acids, R-H, and as sources of very strong bases, R^- , carbanions. Relative kinetic and thermodynamic stabilities of these simple organometallics have been thought to be a function of relative carbanion stability. Foremost amongst the reactions which characterize these organometallics as "carbanionic" has been the hydrogen-metal interchange with various substrates, which reaction has been variously called "metallation," "active hydrogen reaction," "solvolysis," "Zerewitinof reaction," etc. The process can be represented with a general substrate, Z-H, as follows (24).



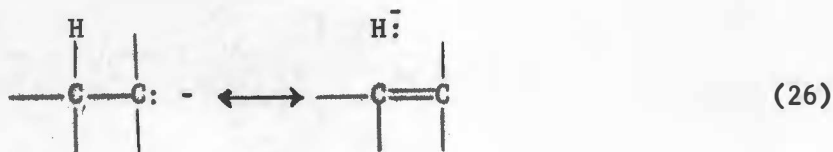
Probably the most useful of these exchanges is that of aromatic hydrogen with lithium alkyls, commonly called simply Metallation (25).



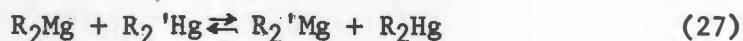
This type of metallation, which has been widely employed for syntheses of lithium aryls, has never been observed with magnesium reagents, presumably because the latter are not sufficiently "carbanionic" to react with an "acid" as weak as Ar-H.

Diorganomagnesium compounds are known to react readily with many such active-hydrogen containing compounds as amines,⁵¹ arsines,³⁶ alcohols,⁷¹ and silanes.⁹² The latter reaction with silanes leads to the formation of RMgH. The cleavage of ethers by organometallic reagents also probably involves metallation. Podall and Foster⁹³ reported that diethylmagnesium underwent cleavage reactions with diethyl ether, diglyme, and other ethers much more readily than does MgH₂. On the other hand, it appeared to Bauer⁹² that RMgH cleaves diethyl ether more rapidly than does R₂Mg. Products from ether cleavage by magnesium alkyls have not been fully studied, and the reaction has apparently served no useful purpose. (A useful cleavage of dimethyl ether by lithium alkyls was found in the present study.)

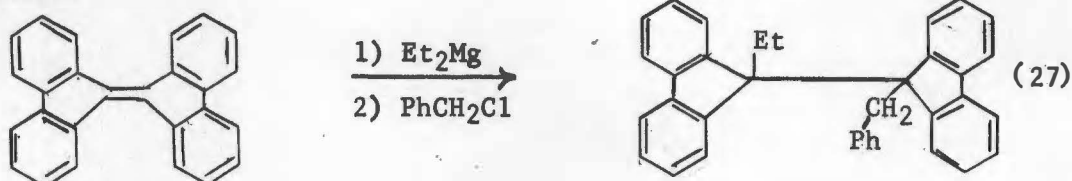
Alkynes are probably the weakest acids for which magnesium alkyls have served as useful metallating agents. Podder and coworkers⁹⁴ expressed the reactivities of R₂Mg with 1-hexyne in terms of rate constants corresponding to a two-step, competitive, consecutive, second order mechanism with the first half of the alkyl groups again being more reactive than the second half. Reactivities of alkyl groups were found to be in the order isopropyl > ethyl > n-propyl > methyl. Since this order correlated with the number of β-hydrogens on the alkyl groups, "anionic hyperconjugation" was suggested⁹⁴ to increase the reactivity of R₂Mg (26)!



In a more conventional attempt to rationalize the relation of structure to reactivity, Dessy and coworkers⁹⁵ suggested that a four-center, non-ionic transition state could be postulated for dialkylmercury-dialkylmagnesium exchange reactions (27) in ethereal solvents. Salinger and Dessy⁹⁶ applied a study of equilibrium positions in this metathetical reaction to the determination of carbanion stabilities. They reported an order of decreasing stability to be phenylethynyl, phenyl, methyl, ethyl, isopropyl, and said that this order would be expected from consideration of inductive (+I) effects.



Polymerizations initiated by organometallic reagents are also generally considered to involve carbanion chemistry. Apparently the first use of a magnesium alkyl for polymerization of ethylene came in 1958; Podall and Foster reported the following observations.⁹³ Diethylmagnesium in hexane or heptane reacts quantitatively with ethylene at 100° and ca. 700 p.s.i. to produce (after quenching with water) liquid hydrocarbons ranging from C₁₀ up and a small quantity of solid polymer, expected products from addition polymerization. Ether retards addition (the chain growth processes) with diethylmagnesium, while the ethyl Grignard reagent does not add at all to ethylene or other simple olefins. Diethylmagnesium was also found to react (27) with bis-(diphenylene)-ethylene in ether-dioxane at 25°C to give after reaction with benzyl chloride, 1-ethyl-2-benzyl-bis-(diphenylene)-ethane. Again, Grignards failed to undergo this addition.



More recently Langer⁹⁷ stated in a patent that he had polymerized ethylene to solid polyethylene with a catalyst prepared by reacting equimolar quantities of di-n-butylmagnesium and N,N,N',N'-tetramethylethylenediamine. He also used heptane as diluent and a temperature of 100°C, and a pressure of ca. 700 p.s.i. After a reaction time of three hours, a yield of twenty grams of polymer per gram of di-n-butylmagnesium was reported by Langer. He also reported that EtMgCl, Et₂Zn, and Et₃Al did not give solid polyethylene under the same conditions. Most recently (1966) Fontanille and Sigwalt^{98a} polymerized styrene, *d*-methylstyrene, and 2-vinylpyridine, in the presence of diphenylmagnesium in hexamethylphosphoramide. Yields of polymers were quantitative. The electronic absorption spectrum of the reaction mixtures during polymerization indicated the reaction took place through polystyrene carbanions ("living polymer").

CHAPTER II

RESULTS AND DISCUSSION

A. PREPARATION OF DIALKYL MAGNESIUM REAGENTS

The preparative techniques developed in the present study involve (1) exchange reactions of alkyllithium reagents with alkylmagnesium chlorides and with magnesium chloride, and (2) direct reaction of magnesium metal with alkyl chlorides in a hydrocarbon or in a hydrocarbon-ether solution.

1. Preparation of R_2Mg by Metal-Metal Exchange between RLi and $RMgCl$ or $MgCl_2$

Alkyllithium reagents were found to react readily with alkylmagnesium chlorides or with magnesium chloride in ethereal media to yield the corresponding dialkylmagnesium reagents in solution and precipitated



lithium chloride. Table I shows the compounds produced (1) from Grignard reagents when the main solvent was diethyl or di-n-butyl ether; yields were essentially quantitative. Diethylether was removed from the initial reaction solutions by continuous codistillation with hydrocarbon solvents, i.e., hydrocarbon solutions were prepared by "desolvation" of ethereal solutions.

Ether-free solutions of magnesium alkyls were also prepared by exchange (2) of magnesium chloride with lithium alkyls directly in hydrocarbons. With commercially available anhydrous magnesium chloride, the

TABLE I
PREPARATIONS OF DIALKYL MAGNESIUM COMPOUNDS FROM
GRIGNARD REAGENTS

Compound Prepared	Reactants						Product, R ₂ Mg		
	RMgCl			RLi			Orig. conc. in ether	After Desolvation	
	R	Solvent	Milli-moles	R	Solvent	Milli-moles		Solvent	Conc.
(<u>n</u> -Bu) ₂ Mg	<u>n</u> -Bu	Bu ₂ O	84	<u>n</u> -Bu	heptane	84	0.84M	benzene	1.0M ^b
(<u>iso</u> -Bu)MeMg	<u>iso</u> -Bu	Et ₂ O	81	Me	Et ₂ O	82	0.76M	benzene	0.72M
(<u>s</u> -Bu) ₂ Mg	<u>s</u> -Bu	Et ₂ O	90	<u>s</u> -Bu	C ₆ H ₁₂	89	0.78M	cyclohexane	0.92M
(<u>s</u> -Bu) ₂ Mg	<u>s</u> -Bu	DME ^a	100	<u>s</u> -Bu	hexane	98	0.46M	hexane-cyclohexane	0.68M ^c
(<u>iso</u> -Bu) ₂ Mg	<u>iso</u> -Bu	Et ₂ O	78	<u>iso</u> -Bu	Et ₂ O	77	0.42M	cyclohexane	0.1M ^d
(<u>t</u> -Bu) ₂ Mg	<u>t</u> -Bu	Et ₂ O	48	<u>t</u> -Bu	pentane	79 ^e	0.82M	benzene	--- ^f

^aSolvent was 5 per cent dimethyl ether in cyclohexane.

^bSolution contained di-n-Bu₂O.

^cFrom this solution there was obtained a 1.35M (s-Bu)₂Mg solution in benzene by vacuum distilling the hexane cyclohexane and redissolving the residual viscous liquid in benzene.

TABLE I (CONTINUED)

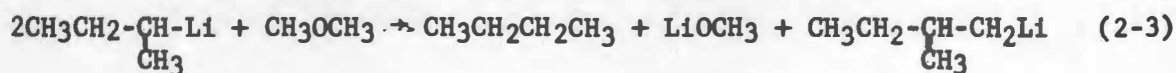
^dWhite precipitate formed; N.E. 66, calculated for (iso-Bu)₂Mg, 69.

^eThis amount of t-butyllithium added to react with t-BuMgCl and with solid by-product MgCl₂ present.

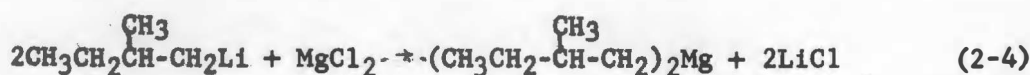
^fSolution contained ethyl ether. Heating to 80°C caused thermal decomposition with the formation of a black precipitate.

exchange is slow and incomplete. Addition of ether to the reaction mixture apparently "activates" the magnesium chloride and definitely facilitates the exchange reaction. After exchange, the ether which had been added could be removed by distillation of the hydrocarbon solutions. For the exchange to proceed to completion, addition of at least two equivalents of diethyl ether per mole of alkyllithium and attritional stirring of the hydrocarbon reaction mixture was required. Tables II and III show the results of some alkyllithium-MgCl₂ exchange runs.

If the ether employed for activation is dimethyl ether and the reaction is carried out at room temperature without high speed stirring, a side reaction can occur. Methylene insertion into secondary or tertiary alkyllithium reagents occurs, forming a homologous primary reagent (2-3). These new primary alkyllithium reagents then react with MgCl₂ in the usual manner (2-4). The homologization process is discussed further



the usual manner (2-4). The homologization process is discussed further



in part G. following.

Several processes were tried for activating commercial magnesium chloride so that it would exchange with lithium reagents in the absence of an ether. Some success was realized in treating the salt with an ether or an alcohol or some other "activating" agent, followed by a complete desolvation. (These processes are described in detail in the experimental section, Chapter III.) Some activating agents are rather tightly held, such as the "active ethers," e.g., dimethyl ether (DME)

TABLE II
PREPARATION OF DIALKYL MAGNESIUM COMPOUNDS FROM COMMERCIAL
MAGNESIUM CHLORIDE

Compound Prepared	Reactants					Reaction Time (hr.)	Reaction Temp. (°C)	Per Cent ^d Yield R ₂ Mg	Final ^s Conc. R ₂ Mg (m/l)
	MgCl ₂		R	RLi					
	Amount (moles)	Solvent		Amount (moles)	Solvent				
(<u>s</u> -Bu) ₂ Mg	0.22 ^a	none	<u>s</u> -Bu	0.36	<u>n</u> -hexane ^b	16 ^c	10	77 ^d	1.68 ^e
(<u>s</u> -Bu) ₂ Mg	0.49 ^a	none	<u>s</u> -Bu	0.80	<u>n</u> -hexane ^f	27	25-35	65 ^g	2.33
(<u>s</u> -Bu) ₂ Mg	1.16 ^a	none	<u>s</u> -Bu	1.94	<u>n</u> -hexane ^h	22	0-25	55 ^g	---
(<u>n</u> -Bu) ₂ Mg	0.27 ^a	none	<u>n</u> -Bu	0.11	benzene ^j	2	0-10	90 ^k	0.2
(Neopentyl) ₂ Mg	0.137 ^a	none	Neopentyl ^l	0.07	<u>n</u> -pentane	2	0-10	79 ^s	0.27 ^e
(<u>s</u> -Bu) ₂ Mg	0.15 ^m	cyclohexane	<u>s</u> -Bu	0.11	cyclohexane	16	25	21 ⁿ	0.05
(<u>s</u> -Bu) ₂ Mg	0.5 ^o	benzene	<u>s</u> -Bu	0.026	cyclohexane	16	25	61	0.13
(<u>s</u> -Bu) ₂ Mg	0.07 ^p	toluene	<u>s</u> -Bu	0.11	<u>n</u> -hexane	4	30	76	0.15
(<u>s</u> -Bu) ₂ Mg	0.2 ^q	tetralin	<u>s</u> -Bu	0.12	<u>n</u> -hexane	20	25	77 ^r	0.22
(2-MeBu) ₂ Mg	--- ^p	toluene	2-MeBu	0.07	benzene	2	40	95	0.13

^aAnhydrous powdered MgCl₂.

TABLE II (CONTINUED)

^bDME, 0.44 mole, added.

^cHigh speed stirring employed.

^dUnless otherwise indicated, yields were based on analyses of aliquots of supernatant reaction solutions for total base, active alkyl and magnesium.

^eEther of complexation present in quantities equivalent to R_2Mg .

^fDME, 0.46 mole, added at start; then an additional 0.45 mole DME added after 4 hours.

^gRepresents a mixture of 2-butyland 2-methylbutyl products due to some homologization.

^hDME, 2.1 moles, added.

ⁱYield based on ratio of n-butane to 2-methylbutane obtained on hydrolysis (VPC).

^j100 ml. ether added.

^kOnly 50 per cent of product soluble.

^lPrepared by homologization of t-butyllithium with DME.

^mAnhydrous lump $MgCl_2$ ball-milled in 100 ml. cyclohexane.

ⁿPer cent of total alkalinity represented by magnesium containing compounds.

^oAnhydrous powdered $MgCl_2$ stirred vigorously overnight with ethyl ether; then desolvated with benzene.

^pBall-milled lumps treated with isopropyl alcohol; then desolvated with toluene.

TABLE II (CONTINUED)

^qMgCl₂·6H₂O dehydrated with isoamyl alcohol; then desolvated with tetralin.

^rPer cent of total alkalinity represented by active alkyl content.

^sConcentration after distillative desolvation.

TABLE III
PREPARATION OF DIALKYL MAGNESIUM COMPOUNDS FROM
SYNTHETIC MAGNESIUM CHLORIDE

Compound Prepared	Reactants					Reaction Time (hr.)	Reaction Temp. (°C)	Per Cent ^b Yield R ₂ Mg	Final ^k Conc. R ₂ Mg (m/l)
	MgCl ₂		R	RLi					
	Amount (moles)	Solvent		Amount (moles)	Solvent				
(<u>s</u> -Bu) ₂ Mg	0.25 ^a	benzene	<u>s</u> -Bu	0.40	cyclohexane	2	25-35	90	0.5 ^c
(<u>s</u> -Bu) ₂ Mg	0.05 ^d	benzene	<u>s</u> -Bu	0.26	cyclohexane	0.25	25-35	95	0.55
(<u>t</u> -Bu) ₂ Mg	0.08 ^e	benzene	<u>t</u> -Bu	0.12	<u>n</u> -pentane	2	25	95	0.5 ^c
(<u>s</u> -Bu) ₂ Mg	0.09 ^f	benzene	<u>s</u> -Bu	0.026	cyclohexane	0.25	25-35	95 ^g	0.5
(<u>t</u> -Bu) ₂ Mg	0.14 ^h	benzene	<u>t</u> -Bu	0.18	benzene	0.75	25-35	70	0.42
(<u>n</u> -Bu)(<u>t</u> -Bu)Mg	0.14 ^h	benzene	<u>t</u> -Bu <u>n</u> -Bu	0.07 0.07	benzene	0.75	25-40	80	0.5
(<u>s</u> -Bu) ₂ Mg	0.6 ⁱ	cyclohexane	<u>s</u> -Bu	0.89	<u>n</u> -hexane	5	40	83 ^j	0.4

^aWashed solid by-product from direct reaction of s-BuCl and Mg in benzene-DME.

^bUnless otherwise indicated, yields were based on analyses of aliquots of supernatant solutions for total base, active alkyl and magnesium.

^cEther of complexation present in quantities equivalent to R₂Mg.

TABLE III (CONTINUED)

^dWashed solid by-product from direct reaction of n-AmCl and Mg in benzene.

^eWashed solid by-product from direct reaction of iso-PrCl and Mg in benzene-DME.

^fWashed solids from distillation under vacuum of ether from s-BuMgCl in ether.

^gBased on negative Gilman Color Test IIa at end of reaction period.

^hDesolvated solid product from reaction of s-BuMgCl with benzyl chloride.

ⁱDesolvated solid product from reaction of s-BuMgCl with Cl₂.

^jBased on per cent of total alkalinity represented by magnesium containing compounds.

^kConcentration after distillative desolvation.

or tetrahydrofuran, and require higher distillation temperatures for removal than ethyl ether requires. For example, distillation with benzene will not effect the removal of DME from the crystal structure of MgCl_2 , whereas it rapidly removes ethyl ether.

No activating process produced a magnesium chloride which is as active or which reacts as completely with alkyllithium reagents in ether-free hydrocarbons as that magnesium chloride obtained as a solid by-product from reaction or preparation of an organomagnesium reagent, e.g., from reaction of a Grignard reagent with benzyl chloride. It would appear that a salt with a particular crystal structure is the most important factor in reactivity toward the exchange (2). X-ray analysis of these "active" MgCl_2 residues from reactions would no doubt supply some interesting information in this regard.

Reaction of an alkyllithium reagent in a hydrocarbon with an "active" magnesium chloride is the most important of the techniques used to produce unsolvated dialkylmagnesium reagents. This rapid, low temperature exchange technique has permitted the preparation of hydrocarbon-soluble, but relatively thermally unstable reagents such as di-s- and di-t-butylmagnesium in excellent yields. Thus, one may react directly with an alkyllithium reagent, the MgCl_2 produced as a by-product of a direct magnesium alkyl preparation, or that produced by reaction of a Grignard reagent with a reactive chlorine-containing compound (see Table III), or less desirably, that produced by ether-activation of commercially available anhydrous MgCl_2 (see Table II) without removal of the complexed ether in the MgCl_2 . If an unsolvated dialkylmagnesium

reagent is desired, either the MgCl_2 must be further treated to desolvate it by continuous distillation with a hydrocarbon solvent prior to exchange with alkyllithium, or the magnesium alkyl must be similarly desolvated after exchange. Desolvation of the magnesium chloride is preferable because it is not as sensitive to pyrolysis as are the dialkylmagnesium reagents. Actually, reaction of unsolvated activated MgCl_2 with t -butyllithium is the only route to unsolvated di- t -butylmagnesium, since this latter reagent decomposes readily during the desolvating distillation procedure.

If one employs the MgCl_2 produced (2-5) as a by-product of the



direct preparation of a hydrocarbon-soluble primary dialkylmagnesium reagent (see following paragraph), there is no ether present in the process to begin with, and desolvation techniques may be dispensed with entirely. Use of MgCl_2 produced in such a manner (2-5) for the exchange reaction (2-2) in effect allows preparation of two different unsolvated dialkylmagnesium reagents utilizing the same initial magnesium source. There is considerable versatility in this exchange procedure; it would appear to be amenable to the synthesis of a variety of dialkylmagnesium reagents.

2. Direct Preparation of R_2Mg from Magnesium Metal and Alkyl Chlorides

A variety of techniques were employed to remove magnesium chloride from dialkylmagnesium reagents prepared by direct reaction (2-5) of magnesium with alkyl halides. Some of the results are summarized in

Table IV. One technique developed was the use, as solvent for this direct reaction, a hydrocarbon containing a limited amount of an ether. When diethyl ether was used under those circumstances, magnesium chloride stayed in solution. However, its precipitation could be forced by removal of ether through codistillation with a hydrocarbon solvent, or by vacuum stripping to dryness and redissolving the R_2Mg in hydrocarbon. If, instead of diethyl ether, dimethyl ether was employed in the hydrocarbon solvent for reaction of magnesium with an alkyl chloride, $MgCl_2$ did precipitate almost completely (>90 per cent) during the reaction (2-5). The remaining soluble portion of the $MgCl_2$ could be precipitated during a distillation desolvation step. It thus appears that ethers other than dioxane may cause reversible formation (and precipitation) of $MgCl_2$ from $RMgCl$ solutions.

Another technique was developed to separate $MgCl_2$ and R_2Mg after direct preparations in hydrocarbon solvents with no ether present. For example, preparation of di-n-butylmagnesium in benzene from magnesium and n-butylchloride was readily carried out. Both products of the reaction are insoluble. The organometallic product, however, was dissolved preferentially by passing gaseous dimethyl ether into the slurried reaction mixture. Desolvation was then effected by the usual method of continuous codistillation with benzene until the residual mixture was free of DME.

It has been found that yields of R_2Mg are generally improved when ethers are employed as cosolvents in these direct preparations, especially when magnesium in the form of turnings is used. Elevated

TABLE IV
DIRECT PREPARATION OF DIALKYL MAGNESIUM COMPOUNDS
FROM ALKYL CHLORIDES

Compound Prepared	Reactants				Reaction Time Hr.	Reaction Temp. °C	Final Conc. R ₂ Mg	Final Solvent	Per Cent Yield ¹
	RCl, Amount mole	Mg, Amount g. atom	Solvents						
			Hydrocarbon	Ether					
(<u>s</u> -Bu) ₂ Mg	0.1	0.1	Cyclohexane	DME ^a	2 Days	25	0.39M	Cyclohexane-DME ^d	79
(<u>s</u> -Bu) ₂ Mg	0.4	0.4	none	Et ₂ O	4	35	0.85M	Benzene-ether ^e	79
(<u>s</u> -Bu) ₂ Mg	0.39	0.415	Benzene	Et ₂ O ^b	3	77	0.3M	Benzene-ether ^f	79
(<u>iso</u> -Pr) ₂ Mg	6.4	0.4	Benzene	DME ^c	3	35-45	0.7M	Benzene-DME	80
(<u>n</u> -Bu) ₂ Mg	0.1	0.1	Cyclohexane	none	5	80	0.29M	Cyclohexane-DME ^g	60
(<u>n</u> -Amyl) ₂ Mg	0.1	0.11	none	none	2	108	0.31M	Benzene ^h	35
(<u>n</u> -Bu) ₂ Mg	0.19	0.1	none	Et ₂ O	3.5	35	0.30M	Ether	60

^a100 ml. DME used as first solvent for reaction. This DME gradually displaced by 100 ml. cyclohexane, but not completely.

TABLE IV (CONTINUED)

^bAmount of ether, 0.48 mole.

^cAmount of DME, 0.94 mole.

^dSolution contained approximately 1-2 molar equivalents of DME per mole of R_2Mg .

^eBenzene added to residue (after evaporation under vacuum) containing $MgCl_2$ and R_2Mg .
Final molar Ether: R_2Mg ratio = 0.7.

^fMolar ratio of ether to RMg compounds was 2:1 after distillation of 50 per cent of solvent; molar ratio of $RMgCl$: R_2Mg was 4:1.

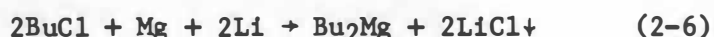
^gDME bubbled into a slurry of $(n-Bu)_2Mg$ and $MgCl_2$ in cyclohexane until solution complete.

^hTwo volumes of 50 ml. each of benzene added with stirring and refluxing for 1 and 2 hr., respectively.

ⁱUnless otherwise indicated, yields were based on analyses of aliquots of supernatant solutions for total base, active alkyl and magnesium.

reaction temperatures also shorten reaction time and give improved yields of R_2Mg . Commercially available magnesium powder is not reactive at all, but undoubtedly it could somehow be activated prior to reaction with alkyl halide. It has been suggested that the magnesium be freshly powdered prior to use and Mendel⁹⁹ describes such a preparation from regular Grignard turnings. As Bryce-Smith and Zakharkin observed, it was found in the present study that secondary and tertiary alkyl halides did not react (2-5) with magnesium in hydrocarbon solvents alone and required the presence of ethereal cosolvents to form the desired products.

In one attempt at another technique for the direct preparation, one which is actually a modification of the exchange reaction, n-butyl chloride was caused to react (2-6) with a mixture of lithium and magnesium metal in ether to afford a 60 per cent yield of di-n-butylmagnesium.



B. PHYSICAL PROPERTIES OF DIALKYL MAGNESIUM REAGENTS

As indicated in Chapter I, knowledge about the physical properties of dialkylmagnesium reagents is limited. Previously measured solubilities of dialkylmagnesium compounds in hydrocarbons were listed on page 31; in all of those cases, the dialkylmagnesiums investigated were infusible solids which possessed extremely low solubilities in hydrocarbon solvents. It is known that these compounds can be polymerically associated, and this factor may influence the nature of their physical state as well as their solubility characteristics in some cases.

For example, it is known that n-butyllithium and s-butyllithium are liquids at room temperature and are completely miscible in hydrocarbon solvents. Although the analogous di-n-butylmagnesium is an infusible solid at room temperature, and reportedly possesses a low order of solubility in hydrocarbon solvents, the present study has shown that di-s-butylmagnesium is a liquid and is, like s-butyllithium, miscible in all proportions with hydrocarbon solvents. Di-t-butylmagnesium is also extremely soluble in hydrocarbon media.

Utilizing the C-Mg and Mg-Mg bond distances reported by Weiss³⁸ and using tetrahedral configurations around each Mg atom, it was noted that although it is possible to construct models of polymeric diisopropylmagnesium, di-n-butylmagnesium, or diisobutylmagnesium, it is not possible to construct associated forms of di-s- or di-t-butylmagnesium beyond the dimer state (cf. Fig. 1). This restricted ability to self-associate is apparently due to the steric hindrance imposed by the presence of α - and β -methyl groups in the former compound and three α -methyl groups in the latter. Dimeric magnesium alkyls would correspond in molecular size to the tetrameric oligomers previously found for s-butyllithium and t-butyllithium. Presumably the ability of magnesium to form tetracoordinate structures permits the ready formation of polymers as soon as steric hindrance is relieved, and this condition prevails in the n-butyl and isobutyl structures.

Table V shows some solubilities of symmetrical dialkylmagnesium compounds observed in the present study. Although Glaze has found that di-n-amylmagnesium is somewhat soluble in benzene (and we corroborated

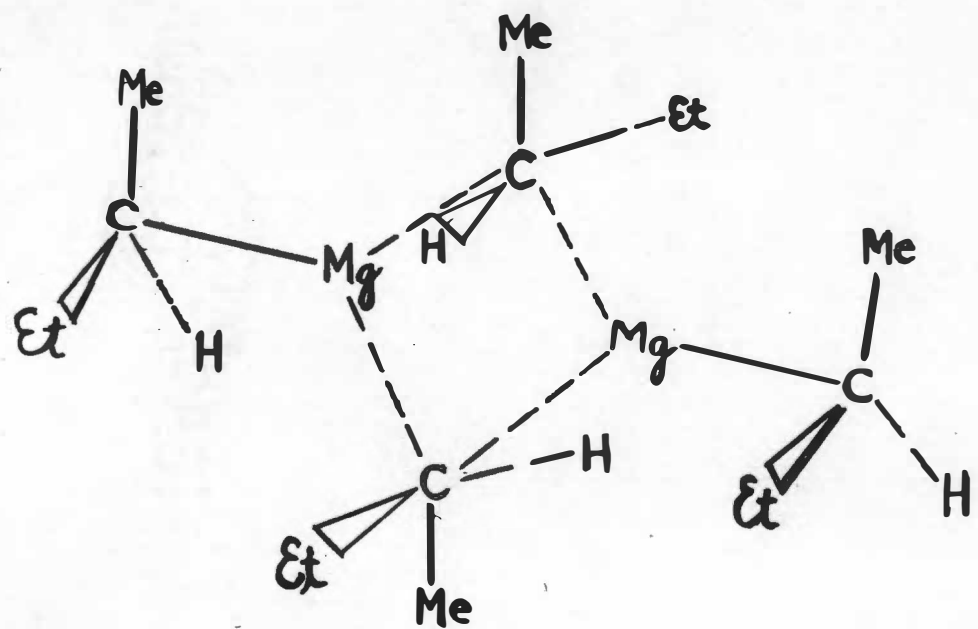


Figure 1. Simplified structure of di-s-butylmagnesium dimer.

TABLE V
SOLUBILITY DATA ON SYMMETRICAL DIALKYL MAGNESIUM COMPOUNDS

R_2Mg	Solvents		Observed Concentrations moles/liter	Comments
	Hydrocarbon	Ether		
$(\underline{s}\text{-Bu})_2Mg$	Benzene	none	0.43 ^a	Compound is a liquid and exhibits infinite solubility in these solvents
	<u>n</u> -Hexane	none	0.39 ^a	
$(\underline{n}\text{-Bu})_2Mg$	Benzene	none	0.06	Compound is a solid.
	Cyclohexane	Trace Et ₂ O	0.22 ^b	
	none	Ethyl Ether	0.38 ^a	
$(\underline{n}\text{-Am})_2Mg$	Benzene	none	0.13 ^a	Glaze ¹⁹ shows figure of 0.22M
$(\underline{t}\text{-Bu})_2Mg$	Benzene	none	0.77 ^a	
$(\underline{i}\text{so-Bu})_2Mg$	Cyclohexane	none	0.09	
$(\underline{i}\text{so-Pr})_2Mg$	Benzene	none	0.1	Compound is a solid.
$(2\text{-Mebutyl})_2Mg$	Toluene	none	3.8 ^a	
$(\text{Neopentyl})_2Mg$	<u>n</u> -Pentane	DME	0.28 ^a	
$((CH_2)_4Mg)_x$	None	Ether	0.07	Analogous Li compound is very soluble (>2M)

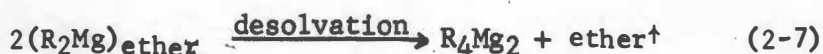
^aNot necessarily upper limit of solubility.

^bMetastable system.

this finding), in our hands, the solution as first obtained was quite viscous, but it thinned out on standing for a period of from 16 to 24 hours. Since Glaze reported that di-n-amylmagnesium was dimeric, it seems probable that the solid product when first dissolved in benzene is of a higher associative order, but that these oligomers gradually "break up" and "dissolve" to form dimers. There is somewhat more steric hindrance to the formation of polymeric chains in this compound than in di-n-butylmagnesium. Probably of greater importance, however, is the lower van der Waals' energy between polymeric chains in di-n-amylmagnesium due to the progressively more random distribution of side chains in the polymer as the carbon number increases.

A metastable solubility of di-n-butylmagnesium was found during its ether desolvation with cyclohexane. When this reagent was prepared in the absence of ether, it was found to be a solid of low solubility in hydrocarbon. Ether does affect solubilization of this reagent in a hydrocarbon, just as it does other insoluble magnesium alkyls studied. However, as a di-n-butylmagnesium cyclohexane solution containing ether was distilled, and the ether content was reduced to only traces, the reagent stayed in solution. Eventually the solid reagent did come out of solution, very slowly, but at one stage the cyclohexane was over 0.2 M in di-n-butylmagnesium.

It now seems safe to assume that with sufficient solvation, magnesium alkyls are monomeric, and that desolvation (2-7) in a



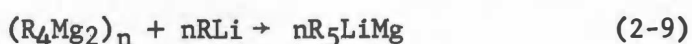
hydrocarbon can produce a soluble dimer. The process of polymeric association (2-8) produces an insoluble reagent. From the above



observations on diamyl and di-n-butylmagnesium, it appears that the polymerization process (2-8) of magnesium alkyls is not necessarily a fast one, and that the structure of the alkyl groups determines rates as well as positions of equilibrium in this process.

Although bis(2-methylbutyl)magnesium was previously reported to be insoluble in hydrocarbon solvents,⁶² in our hands it was found to be extremely soluble in toluene and to form a quite fluid solution. This compound, as well as di-neopentylmagnesium, probably prefers to exist as a dimer, again due to steric hindrance to further association. Perhaps not surprisingly, tetramethylenemagnesium has a low order of solubility even in ethereal media, although its lithium counterpart is quite soluble.

It was found that hydrocarbon-insoluble dialkylmagnesium compounds could be readily solubilized by solutions of organolithium reagents in hydrocarbon solvents. This must result from formation of intermetallic complexes. The complexes did appear to have a preferred stoichiometry. For example, n- and s-butyllithium dissolved enough di-n-butylmagnesium (in the presence of excess undissolved magnesium reagent) to form 1:2 complexes, i.e., to have the composition (n-Bu)₅Mg₂Li and (n-Bu)₄(s-Bu)Mg₂Li in solution. Disruption of the tetracoordinate polymeric structure of the magnesium reagent by the alkyl lithium reagent takes place (2-9) leading to lower molecular



weight, soluble oligomers. Presumably electron-deficient three-center bonds take part in the intermetallic structures.

Another interesting discovery was that mixing a soluble dialkylmagnesium with an insoluble dialkylmagnesium resulted in a hydrocarbon soluble complex containing both types of alkyl groups. The stoichiometry in this case is not as clear-cut as in the intermetallic complexes. Ratios of alkyl groups in the complexes were sometimes found close to 1:1, but often were not found in ratios of whole numbers. The mixed dialkylmagnesium compounds may be formed by simply mixing a hydrocarbon solution of the soluble R_2Mg with the insoluble solid one (e.g., t-butyl-isobutyl reagents) or, they may be formed (2-10) by reacting a



Grignard reagent having one type of alkyl group with an organolithium reagent possessing the other group. Since the reaction is usually carried out in an ethereal medium, desolvation with a hydrocarbon solvent must be carried out.

It was discovered, rather surprisingly, that reaction of isobutylmagnesium chloride with methyllithium followed by filtration to remove lithium chloride and desolvation of the filtrate with benzene to remove ether resulted in a somewhat viscous solution of the mixed methylisobutylmagnesium. It is known that neither of the two individual magnesium alkyls is soluble in benzene. On cooling, a clear glassy second layer separates; warming redissolves the glass. An explanation for this behavior can once again be found, not so much in steric hindrance in the mixed alkyl to the formation of polymers, for there is none apparent

in methylisobutylmagnesium, but rather in the ability of the polymeric chains to align themselves to form high molecular weight crystalline solids. This "loose" structure permits solvent attack to break down the chains into smaller, more soluble oligomeric units. The methylisobutylmagnesium solution maintains its viscosity with time (unlike di-n-amylmagnesium); the reagent is obviously in a higher state of association than dimeric.

Table VI shows some data on mixed magnesium alkyls. Another indication of the formation of mixed organomagnesium compounds was obtained when, upon metallation of resorcinol dimethyl ether in benzene-cyclohexane solution, an insoluble crystalline compound formed (2-11)



containing equivalent quantities of 2,6-dimethoxyphenyl and s-butyl groups. Metallation is discussed in part D following.

Listed in Table VII are NMR chemical shifts in the "organo-metallic region" for a number of reagents examined in the present study. The shifts, given in cps relative to benzene, lie in the region six to eight ppm upfield from benzene, where signals from protons on carbon geminal to metal or in methyl groups vicinal to metal generally are found. Chemical shifts of mixed magnesium reagents, as well as those of symmetrical reagents, and of lithium alkyls are shown from both hydrocarbon and basic media. The signals from basic media always appear upfield from those in hydrocarbons, and the shift is much greater with magnesium alkyls than with lithium alkyls. This particularly effective shielding by base of the magnesium reagents is entirely consistent

TABLE VI

PREPARATION OF HYDROCARBON-SOLUBLE ORGANOMETALLIC COMPLEXES DIALKYL MAGNESIUM COMPOUNDS

Approximate Complex Prepared	Reactants				Complex	
	R ₂ Mg (Amount)	Solvent (Amount)	R'Li or R' ₂ Mg (Amount)	Solvent (Amount)	Final Conc. m/l	Molar Ratio R:R' Groups in complex
(<u>n</u> -Bu) ₅ Mg ₂ Li	(<u>n</u> -Bu) ₂ Mg (3 mmole)	Benzene (5 ml.)	<u>n</u> -BuLi (1 mmole)	<u>n</u> -Hexane cyclohexane (0.825 ml.)	0.77N	---
(<u>n</u> -Bu) ₄ (<u>s</u> -Bu)Mg ₂ Li	(<u>n</u> -Bu) ₂ Mg (3 mmoles)	Benzene (5 ml.)	<u>s</u> -BuLi (1 mmole)	Cyclohexane (0.825 ml.)	0.81N	4.0
(<u>iso</u> -Bu) ₂ Mg- (<u>s</u> -Bu) ₂ Mg	(<u>iso</u> -Bu) ₂ Mg (2.5 mmoles)	none	(<u>s</u> -Bu) ₂ Mg (3.4 mmoles)	<u>n</u> -Hexane- cyclohexane	0.78M	1
(<u>iso</u> -Bu) ₂ Mg- (<u>t</u> -Bu) ₂ Mg	(<u>iso</u> -Bu) ₂ Mg (5.4 mmoles)	none	(<u>t</u> -Bu) ₂ Mg	Benzene	1.3M	1
(<u>n</u> -Bu) ₂ Mg · (<u>t</u> -Bu) ₂ Mg	2 <u>n</u> -BuLi + MgCl ₂ — 35 mmoles (<u>n</u> -Bu) ₂ Mg	Benzene (19 ml.)	2 <u>t</u> -BuLi + MgCl ₂ — (35 mmoles- (<u>t</u> -Bu) ₂ Mg)	Benzene (90 ml.)	0.52M	0.8 ^a
(<u>iso</u> -Bu) ₂ Mg · (Me) ₂ Mg	<u>iso</u> -Bu-MgCl 0.18 moles	Ether	MeLi 0.18 moles	Ether	0.72M ^b	0.8

^aSome loss of (t-Bu)₂Mg probably occurred due to heat of reaction of MgCl₂ and t-BuLi.^bSolution in benzene. Reaction mixture in ether desolvated by continuous codistillation with benzene.

TABLE VII
PMR CHEMICAL SHIFTS IN SELECTED ORGANOMETALLIC REAGENTS

Reagent	Solvent	Chemical Shifts (cps from Benzene)			
		CH ₃	RCH ₂	R ₂ CH	(CH ₃) ₃ C
(<u>n</u> -Bu) ₂ Mg	Cyclohexane	----	406	----	----
(<u>n</u> -Bu) ₂ Mg	THF/TED ^b	----	474	----	----
(neoPent) ₂ Mg	Pentane/DME ^c	----	447	----	360 ^d
(2-MeBu) ₂ Mg	Benzene	----	425 ^e	----	----
(<u>s</u> -Bu) ₂ Mg	Cyclohexane	----	----	436	----
(<u>s</u> -Bu) ₂ Mg	THF/TED ^b	----	----	455	----
(<u>iso</u> -Pr) ₂ Mg	Benzene/Et ₂ O ^f	----	----	432	----
(<u>t</u> -Bu) ₂ Mg	Benzene	----	----	----	365.5
(<u>t</u> -Bu) ₂ Mg	THF/TED	----	----	----	380.5
(<u>iso</u> -Bu)(Me)Mg	Benzene	470.5	425	----	----
(<u>iso</u> -Bu)(Me)Mg	THF/MTED ^b	543	469	----	----
(<u>iso</u> -Bu)(<u>t</u> -Bu)Mg	Benzene	----	447.5	----	355.5
(<u>iso</u> -Bu)(<u>t</u> -Bu)Mg	THF/MTED ^b	----	469	----	384
(<u>iso</u> -Bu) ₃ MgLi	Benzene	----	450	----	----
(<u>t</u> -Bu) ₄ MgLi ₂	Benzene	----	----	----	366.5
(<u>t</u> -Bu)(<u>n</u> -Bu)Mg	Benzene	----	442	----	356
(<u>t</u> -Bu)(<u>n</u> -Bu)Mg	THF/TED ^b	----	470	----	377
(<u>n</u> -Bu) ₃ MgLi	Cyclohexane	----	442	----	----
(<u>s</u> -Bu)MgCl	Benzene/Et ₂ O ^f	----	----	426	----

TABLE VII (CONTINUED)

Reagent	Solvent ^a	Chemical Shift (cps from Benzene)			
		CH ₃	RCH ₂	R ₂ CH	(CH ₃) ₃ C
(γ -Picolyl) ₂ Mg	Cyclohexane	----	327	----	----
(2,6-Dimethoxyphenyl)THF (<u>s</u> -Bu)Mg ^g		----	----	457	----
(Phenyl)(<u>t</u> -Bu)Mg	THF	----	----	----	381
MeLi	THF	553	----	----	----
MeLi	THF/MTED	556	----	----	----
<u>n</u> -BuLi	Cyclohexane	----	482	----	----
<u>n</u> -BuLi	THF	----	493	----	----
<u>n</u> -BuLi	THF/MTED ^b	----	497	----	----
<u>iso</u> -BuLi	Benzene	----	480	----	----
<u>iso</u> -BuLi	THF	----	491	----	----
neoPenLi	Benzene	----	483	----	362 ^d
<u>s</u> -BuLi	Benzene	----	----	493	----
<u>iso</u> -PrLi	Benzene	----	----	485	----
<u>iso</u> -PrLi	Benzene/Et ₂ O ^f	----	----	490	----
<u>t</u> -BuLi	Benzene	----	----	----	372.5

^aSymbols: THF, tetrahydrofuran; TED, triethylenediamine; MTED, methyltriethylenediamine; DME, dimethylether.

^bTED/or MTED/organometallic reagent ratio of one.

^cDME/R₂Mg ratio of four.

^dt-Bu group separated from metal by methylene group.

TABLE VII (CONTINUED)

^eBroad unsymmetrical multiplet.

^fEt₂O/organometallic reagent ratio of two.

^gProton para to Mg, 22 cps downfield from benzene.

with the process of solvation, the reverse of the process represented in equation (2-7), being one which dissociates oligomeric reagents.

The presence of the Lewis acid MgCl_2 leads to a downfield shift in the proton resonance of a group adjacent to magnesium. Even in the presence of ether (a Lewis base), the methine proton in s-butylmagnesium chloride (or di-s-butylmagnesium- MgCl_2) dissolved in benzene resonates 10 cps lower than it does in di-s-butylmagnesium-benzene solutions alone.

The signals from the mixed compounds corroborate the conclusion, based on solubility studies, that the magnesium alkyls form true inter-metallic compounds, i.e., not simply mixed solutions in which each reagent retains its structural integrity. It can be noted that in the n-butyllithium-di-n-butylmagnesium system, $(\text{n-Bu})_3\text{MgLi}$, only one methylene triplet appeared, centered 446 cps from benzene. Also, only one singlet appeared for the t-butyl protons in the t-butyllithium-di-t-butylmagnesium system, $(\text{t-Bu})_4\text{MgLi}_2$. These results indicate either that there is a rapid exchange of all alkyl groups in the complex in solution, or that there is only one environment for each alkyl group in the mixed compound. In either case, there must be a new environment provided by a mixed compound, because the one signal it provides is not at the average position provided by the separate reagents. For example, if the signal from $(\text{n-Bu})_3\text{MgLi}$, found at 442 cps, were the average from $(\text{n-Bu})_2\text{Mg}$ and n-BuLi it would have been found at 431 cps.

Similar evidence for compound formation is seen in comparing the two chemical shifts from the unsymmetrical dialkylmagnesium reagents with those from the corresponding symmetrical reagents. For example, there is an upfield shift of 36 cps for the protons on the methylene group adjacent to Mg on replacing half of the n-butyl groups in di-n-butylmagnesium with t-butyl groups. These shifts suggest an increased shielding of the methylene protons due to inductive effects in the t-butyl group. As might be expected, there is a concomitant decrease of 10 cps in the chemical shift of the t-butyl group from its normal position in di-t-butylmagnesium.

C. COMPLEXES OF DIALKYL MAGNESIUM REAGENTS

WITH BRIDGEHEAD DIAMINES

Table VIII shows some of the results obtained from reactions of triethylenediamine (TED) and methyltriethylenediamine (MTED) with various symmetrical and mixed dialkylmagnesium compounds. Both reagents could cause precipitation of complexes. The triethylenediamine complexes were only slightly soluble in hydrocarbon solvents while the methyltriethylenediamine complexes were moderately soluble and could be easily recrystallized. The TED complexes all melted above 200° (with decomposition) while the MTED complexes melted considerably lower. All of the complexes tested, however, decomposed on melting. For example, the TED derivative of di-s-butylmagnesium melted at 201-203° (dec.), while the MTED derivative melted at 160°C (dec.). With TED and MTED, di-s-butyl- and di-t-butylmagnesium formed only insoluble 1:1 complexes, while with TED,

TABLE VIII

COMPLEXES OF DIALKYL MAGNESIUM COMPOUNDS WITH TRIETHYLENEDIAMINE (TED)
AND METHYLTRIETHYLENEDIAMINE (MTED)

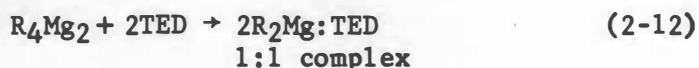
R ₂ Mg		Amine			Complex			m.p. (dec.)	Ratio ^a Amine:R ₂ Mg
Reagent	Amount, mmoles	Solvent	Reagent	Amount, mmoles	Solubility in Medium	NE Found	NR Theory		
(s-Bu) ₂ Mg	2.13	Cyclohexane	TED	2.07	Low	248	250	201-203°	1.0
	2.33	Cyclohexane	MTED	2.38	High	----	----	160°	1.0
(t-Bu) ₂ Mg	3.0	Benzene	TED	3.0	Low	----	----	----	1.0
	2.5	Benzene	MTED	2.5	High	309	264	163-165°	1.0
	2.2	Cyclohexane	TED	2.1	Low	----	----	----	1.0
(n-Bu) ₂ Mg	1.3	Cyclohexane	TED	0.65	Low	----	----	----	0.5
	1.0	Cyclohexane	MTED	1.0	No Insoluble Complex Formed				.
(n-Am) ₂ Mg	1.0	Benzene	TED	0.5	No Insoluble Complex Formed				
(iso-Bu)(Me)Mg	2.8	Benzene	MTED	2.9	High	----	----	115-270°	0.5 ^b
(iso-Bu)(t-Bu)Mg	1.52	Benzene	MTED	1.52	High	----	----	140-165°	1.0 ^c

^aRatios determined by analysis of NMR spectrum of complex dissolved in THF.

^bRatio Me to iso-Bu groups = 3:2.

^cRatio iso-Bu to t-Bu groups = 3.2:2

di-n-butylmagnesium formed insoluble 1:1 and 1:2 complexes, amine:reagent mole ratio. Such results are taken to indicate that sufficient amine dissociates oligomeric reagents and precipitates the monomer, as illustrated in equation (2-12), but that with a limited amount, the intact dimeric reagent is complexed, as illustrated in equation (2-13).



No insoluble complex was formed between di-n-butylmagnesium and MTED or between di-n-amylmagnesium and TED.

The mixed alkyls of methyl-isobutylmagnesium and isobutyl-t-butylmagnesium reacted with MTED to form non-stoichiometric materials with wide melting point ranges; slow decomposition occurred throughout this range. The MTED-methyl-isobutylmagnesium product contained a high ratio of alkyl groups to MTED (average of 4 alkyl groups to 1 MTED) while the isobutyl-t-butylmagnesium product contained a ratio of about one alkyl group to one MTED. However, in both cases there was less of the isobutyl group than either methyl or t-butyl groups. It is probable that both the isobutylmagnesium and the methylmagnesium moieties act like di-n-butylmagnesium with TED in that a 1:2 amine: R_2Mg complex may be formed. It would also appear that, like the di-n-butylmagnesium-MTED case, the di-isobutylmagnesium-MTED complex is more soluble than either the dimethylmagnesium- or di-t-butylmagnesium-MTED complexes. The results obtained support the conclusion that a mixed dialkylmagnesium reagent does not necessarily form a mixed dialkylmagnesium-amine complex, but instead the amine may disproportionate the

reagent and form symmetrical dialkylmagnesium-amine complexes. Rapid interchange of alkyl during complexation by the amine must allow this result, which is apparently caused by precipitation of the least soluble complex as it is formed during this rapid interchange of alkyl groups. It certainly could be expected that the least soluble complexes would indeed be the most symmetrical ones.

D. METALLATIONS WITH DIALKYL MAGNESIUM REAGENTS

Metallations of several different substrates were attempted with dialkylmagnesium reagents. Tables IX and X show the general conditions employed and the results obtained with some aromatic substrates. It is apparent that the magnesium compounds do not metallate aromatics with the facility that lithium reagents do (as was known), but the results obtained unequivocally demonstrate that the metallation by magnesium alkyls does occur. These results, illustrated in the following equations, would seem to be the first reported metallations of aromatic and hetero-aromatic substrates by magnesium reagents.

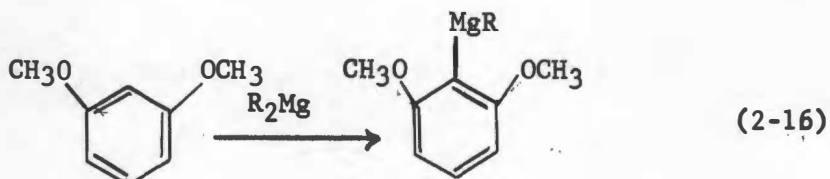
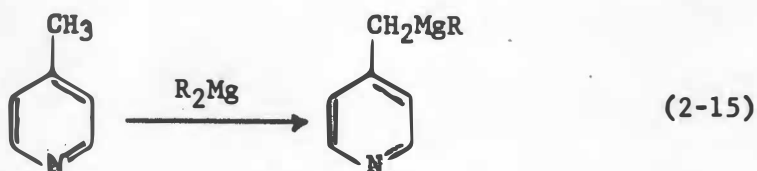


TABLE IX
METALLATION OF AROMATIC SUBSTRATES BY DIALKYL MAGNESIUM REAGENTS

Reagent	Source ^a	Solvent	Substrate	Catalyst	Reaction Time(hr.)	Reaction Temp.(°C)	Apparent Metallation Product	Yield (%)
(<u>s</u> -Bu) ₂ Mg	I	Toluene ^b	Toluene	TMEDA ^c	2	112	BenzylMgR ^d	22
(<u>s</u> -Bu) ₂ Mg	II	Toluene ^e	Toluene	TMEDA ^c	16 16	75 112	None ⁿ	0
(<u>s</u> -Bu) ₂ Mg	I	Benzene ^f	Benzene	TMEDA ^c	4	80	BenzylMgR ^d	14
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	RDE ^g	None	16	75	2,6-Dimethoxyphenyl-MgR ^h	50
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	RDE ^g	THF ¹	16 16	25 75	None ^j	0
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	RDE ^g	THF + K-(O <u>t</u> -Bu) ^k	1	25	2,6-Dimethoxyphenyl-K ⁿ	57
(<u>p</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	RDE ^g	TMEDA ^c	16	75	None ^j	0
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	RDE ^g	TMEDA + Li-(O <u>t</u> -Bu) ¹	16	75	2,6-Dimethoxyphenyl-Li ^{n,m}	>90

^aI - Reaction of s-butyllithium with commercial anhydrous MgCl₂ in hexane-dimethyl ether solution, followed by partial or complete desolvation.

TABLE IX (CONTINUED)

II-Reaction of s-butyllithium with synthetic "active" desolvated MgCl_2 (from (s-BuMgCl + Cl_2)) in hexane-cyclohexane.

^bPartially desolvated di-s-butylmagnesium solution in hexane further desolvated by codistillation with toluene. Some pyrolysis with formation of white precipitate was noted.

^cTwo moles TMEDA per mole of di-s-butylmagnesium.

^dProduct analyzed by NMR assay of dried ethereal solution of mixture of acids obtained on carbonation.

^eHexane and cyclohexane distilled under vacuum, toluene added. No pyrolysis observed.

^fHexane distilled and replaced by benzene. Some pyrolysis noted.

^gResorcinol Dimethyl Ether.

^hNMR analysis showed no organomagnesium compounds in solution and the insoluble crystalline product (dissolved in THF) to consist of an equivalent amount of 2,6-dimethoxy-phenyl- and s-butyl-groups linked to magnesium.

ⁱTwo moles THF per mole di-s-butylmagnesium present during first 12 hours; six moles THF per mole present during next 16 hours.

^jNMR analysis showed no loss of di-s-butylmagnesium and no appearance of metallated resorcinol dimethyl ether.

^kRun number 6 to which was added 2 moles potassium t-butoxide per mole di-s-butylmagnesium.

^lRun number 8 to which was added at least 2 moles lithium t-butoxide per mole di-s-butylmagnesium.

TABLE IX (CONTINUED)

^mNMR analysis showed absence of (s-Bu)₂Mg in product.

ⁿProduct analyzed by NMR assay of D₂O solution of mixture of salts of acids obtained on carbonation (Na₂CO₃) added to aid solubilization).

TABLE X

METALLATION OF HETEROAROMATIC SUBSTRATES BY DIALKYL MAGNESIUM REAGENTS

Reagent	Source ^a	Solvent	Substrate	Catalyst	Reaction Time (hr.)	Reaction Temp. (°C)	Apparent Metallation Product	Yield (%)
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	γ -Picoline	None	2-3	25	γ -PicolyLMg-R ^b	~75
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	Thiophene	None	20	25	None ^c	0
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	Thiophene	None	20	75	2-ThienylMgR ^d	~33
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	Thiophene	THF ^e	1) 12 2) 16	75 25	None ^c	0
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	Thiophene	THF ^e K-(Ot-Bu) ^f	<1	25	2-Thienyl-K ^g	~90
(<u>s</u> -Bu) ₂ Mg	III	Cyclohexane	Thiophene	TMEDA ^h	Few. Min.	25	None ⁱ	0
(<u>s</u> -Bu) ₂ Mg TED complex	IV	THF	Thiophene	TED	24	70	None ^c	0
(<u>t</u> -Bu) ₂ Mg TED complex	V	THF	Thiophene	TED	24	70	None ^c	0
(<u>n</u> -Bu) ₄ (<u>s</u> -Bu)Mg ₂ Li	VI	Benzene-cyclohexane	Thiophene	TMEDA	5 days	20	2-ThienylLi ^j	~20

TABLE X (CONTINUED)

^aI - Reaction of s-butyllithium with commercial anhydrous MgCl_2 in hexane-dimethyl ether solution followed by partial or complete desolvation.

II - Reaction of s-butyllithium with synthetic "active" MgCl_2 (from (s-BuMgCl + Cl_2)) in hexane-cyclohexane.

III - Reaction of magnesium turnings and s-butyl chloride in cyclohexane-ether, followed by desolvation.

IV - Reaction of s-butyllithium with synthetic "active" MgCl_2 (from s-butylMgCl + benzyl-chloride) in cyclohexane, followed by precipitation with triethylenediamine.

V - Reaction of t-butyllithium with synthetic "active" MgCl_2 (from s-butylMgCl + benzyl-chloride) in cyclohexane, followed by precipitation with triethylenediamine.

VI - Solution formed by addition of s-butyllithium in C_6H_{12} to a slurry of (n-Bu) $_2\text{Mg}$ in benzene.

^bNMR analysis indicated a 3:1 ratio of metallated to unmetallated γ -picoline. Product identified by derivatization with benzoyl chloride to γ -phenacetylpyridine.

^cNMR analysis showed no loss of di-s-butylmagnesium and absence of metallated thiophene.

^dNMR analysis showed no (s-Bu) $_2\text{Mg}$ and presence of metallated thiophene in supernatant solution; NMR analysis of D_2O solution of salts of acids obtained on carbonation of the reaction mixture showed a 2:1 ratio of the salts of 2-methylbutyric and 2-thienoic acids.

^eTwo moles THF per mole di-s-butylmagnesium present during first 12 hours; six moles THF per mole present during next 16 hours.

^fPrevious run with THF to which was added 2 moles of potassium t-butoxide per mole of di-s-butylmagnesium.

TABLE X (CONTINUED)

^gProduct analyzed by NMR assay of the D₂O solution of the mixture of salts obtained on carbonation (Na₂CO₃ added to aid solubilization).

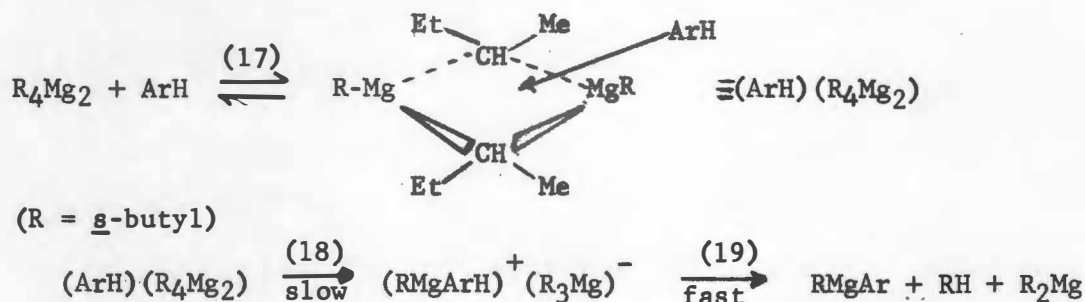
^hTwo moles TMEDA per mole of R₂Mg.

ⁱNMR showed absence of 2-thienoic acid on workup of acids derived from carbonation of product.

^jNMR showed presence of n-butyl- and 2-thienyl-, but no s-butyl-organometallics.

Unlike metallations carried out by alkyllithium reagents, which are catalyzed by Lewis bases such as THF and tetramethylethylenediamine (TMEDA), metallations by dialkylmagnesium reagents are actually suppressed by these bases. This observation is particularly clear in results obtained with thiophene and with resorcinol dimethyl ether. Both are metallated by di-s-butylmagnesium in refluxing hydrocarbon solutions; neither is metallated if excess THF or TMEDA is present in the solutions.

These results are not consistent with interpretation of magnesium reagent reactivity in the simple terms of carbanionic character. Surely polar basic solvents should facilitate release of a carbanion from R_2Mg , so the fact that such solvents do not facilitate metallation tends to mitigate against any simple nucleophilic proton abstraction process as a mechanistic pathway for metallation with these reagents. It does seem possible that metallation could involve dimeric reagent and nucleophilic displacement on one magnesium of the bridging alkyl group by the species to be metallated. As illustrated below, this process could proceed through formation of a π -complex (2-17), rearrangement to an ion-pair (2-18), and elimination of hydrocarbon (2-19).

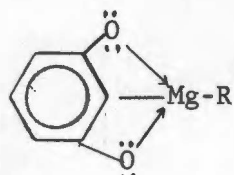


Such a process is made more plausible by the known rapid interchange of alkyl groups as well as by the high degree of nucleophilicity of the magnesium reagent. This process would be inhibited by electron-donating reagents such as THF and TMEDA, which complex readily with the monomeric magnesium reagent and thereby stabilize it, i.e., remove electron-deficient dimer from the reaction medium. In short, the electron-deficient character or π -acidity of dimeric magnesium alkyls seems to provide a better basis of interpreting reactivity than does carbanionic character.

While the mechanism speculated on above is illustrated, steps (17), (18), and (19), as involving the maintenance of paired electrons, this is done for simplicity, and because illustration of any further details would be even more speculative. However, the possibility should be considered that charge transfer does occur during this reaction, possibly in forming the initial complex, step (17). If this is so, then single electron transfer (SET) processes do not require basic solvents; as has been previously suggested.¹⁰⁶

The results shown in Table IX suggest that the second alkyl group is not normally displaced from the metallated product initially formed. This is probably due, not only to steric hindrance, which is obvious in the case of the metallation product of resorcinol dimethyl ether, but also to stabilization by π -electron donation from the aromatic ring to metal in the product. In the case of resorcinol dimethyl ether (DMR), additional internal stabilization of the metallated product is afforded

by the presence of adjacent methoxy groups. This added stabilization prevents pyrolytic decomposition of the species; this product remained unchanged even during extended reflux at 70-80°, used to attempt utilization of the second alkyl group in metallation.



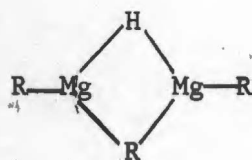
The same stabilizing effect was found to be true for solutions of the dialkylmagnesium reagents themselves in the presence of added Lewis bases such as THF, TED, and TMEDA. Thus even after extended refluxing at 70-80°, di-t-butyl- and di-s-butylmagnesium did not eliminate olefin in the presence of these bases. However, in the absence of bases (or of readily metallatable substrates) the t-butyl reagent decomposed readily even at room temperature, while solutions of di-s-butylmagnesium pyrolyzed slowly at reflux temperatures of 70-80°. Stabilization of R_2Mg by solvating base is almost surely some function of the quantity of base. In the desolvation of hydrocarbon solutions by distillation, decomposition was not observed until the concentration of base present was reduced to the same molar level as the R_2Mg present. Then, with further distillation, it was apparent that elimination set in, presumably according to the following equation.



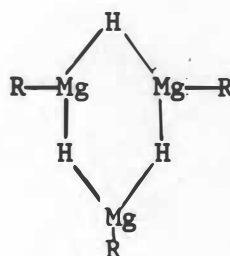
Di-s-butylmagnesium which has partially undergone this thermal elimination (pyrolysis) possesses the ability to effect some metallation of toluene, even in the presence of Lewis bases. If pyrolysis

of the dialkylmagnesium reagent had not previously been effected, metallation of toluene could not be realized in the presence of bases. Benzene was also partially metallated when desolvated (partially pyrolyzed) di-s-butylmagnesium in benzene containing two equivalents of TMEDA was heated to reflux for 4 hours. These results are particularly interesting because benzene and toluene are relatively unreactive substrates.

A possible explanation for these results, which show an enhanced reactivity of pyrolyzed R_2Mg , lies in formation (2-20) of a soluble alkylmagnesium hydride which can retain some self-associated form even in the presence of basic solvents. It is a fact that metal hydrides and alkylmetal hydrides are often more strongly associated and less affected by base than are metal alkyls. A good example of this fact is the trimeric existence of R_2AlH when R_3Al is monomeric, e.g., when R is isobutyl.¹⁰⁷ Another example is the retention of B_2H_6 in its dimeric form even in basic solvents.¹⁰⁸ Some metal hydrides, e.g., LiH and MgH_2 , are not even sufficiently solvated by base to be soluble therein.¹⁰⁹ Tentatively it is postulated that structures such as (2-21) and (2-22) can be formed by pyrolysis of magnesium alkyls. It is further postulated that these structures represent hydrocarbon soluble



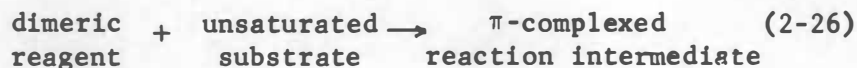
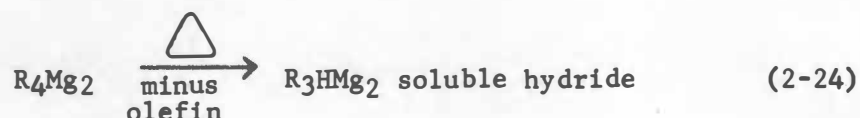
(2-21)



(2-22)

reagents which may retain their self-associated form, at least in some finite equilibrium concentration, even in the presence of base.

These postulates, and related phenomena previously discussed, are reiterated with the illustrative equations shown below, where B represents an ether or tertiary amine. The equations show some probable states of association and solvation and are not intended to represent all possible (or even probable) states.



While the postulates concerning oligomeric alkylmagnesium hydrides are quite speculative if based only on the present experimental results, they do have rather good analogies, and they are amenable to future experimental tests. It seems most probable that solution processes which completely dissociate electron deficient oligomers e.g., σ -complexation of monomers as in (2-23), decrease the reactivity of metal alkyls and metal hydrides. It is because of their electron deficient structures that species like R_4Mg_2 or R_3HMg_2 can initiate metallation through π -coordination of ArH , as in (2-26).

Solvation of these self-associated species intact, as in (2-25) might even promote their reaction, as does solvation of self-associated lithium alkyls.

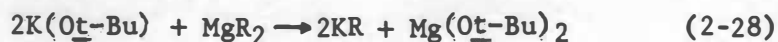
Observations made with hydrogenolysis reactions provide interesting evidence both that lithium alkyl solvation increases reactivity (π -complexation) and that magnesium alkyl solvation removes reactivity (σ -complexation). Hydrogenolysis of lithium alkyls, which can be looked upon as a metallation of hydrogen (2-27), requires base. In the present study, magnesium alkyls were found to resist hydrogenolysis



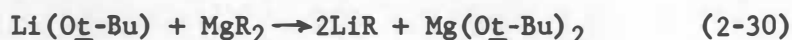
with or without base. In an earlier study Screttas obtained rapid and complete hydrogenolysis of s-butyllithium in the presence of very small catalytic quantities of a Lewis base, such as 0.01 molar equivalent of TMEDA.^{100b} Surprisingly, it was found in the present study that s-butyllithium would not undergo hydrogenolysis in the presence of a 0.5 molar equivalent of TMEDA and 1.0 molar equivalent of di-s-butylmagnesium.

Since s-butyllithium undergoes very rapid hydrogenolysis (2-27) in the presence of this much TMEDA, it appears that the di-s-butylmagnesium coordinates more strongly with TMEDA than does s-butyllithium. The coordination which occurs in the case of the dialkylmagnesium reagent is different from that of the alkyllithium reagent; it is known that a 1:1 ratio of TMEDA (and other bases) to dialkylmagnesium reagent is normally found in these complexes, cf. equation (2-23), but that only the dimeric form of alkyllithium reagents coordinates (1:2 complex) with TMEDA. The 1:1 R_2Mg -Lewis base complex, a chelate, has been studied by Zakharkin⁵² and indicated to be quite stable.

Another interesting illustration of the mechanistic difference in the metallations effected by alkyllithium and dialkylmagnesium reagents arose with alkoxide promoted metallations. It was found that when two equivalents of potassium t-butoxide was added to the non-reactive mixture of dialkylmagnesium, substrate (RDE) and Lewis base (THF or TMEDA) rapid metallation occurred, presumably via metal-metal exchange (2-28, 2-29). An intense dark-red color developed immediately

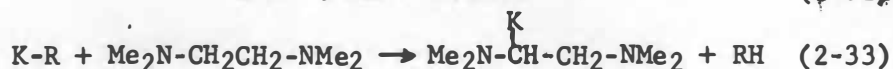


on mixing the reagents at room temperature. When lithium t-butoxide was employed in place of the potassium alkoxide in the mixture, metallation also occurred, although much more slowly (refluxing required) and with less intense color formation. Again, metal-metal exchange probably occurred as a first step, followed by metallation of the substrate (2-30, 2-31).

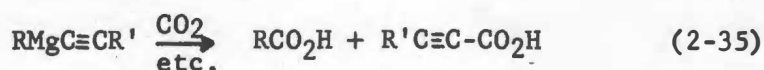


In hopes that an exchange between dialkylmagnesium reagents and potassium t-butoxide might allow hydrogenolysis to occur, the metal-metal exchange reaction was carried out both in the presence and absence of Lewis bases prior to the admittance of hydrogen gas to the system. No hydrogenolysis occurred, and furthermore, the resulting insoluble product subsequently did not promote the metallation of DMR or thiophene. Thus it appears that the metal-metal exchange must be allowed to take place in the presence of all of the reactant in

order for metallation or occur. Possible explanations for this lack of metallation are rather rapid thermal degradation of the resulting s-butylpotassium (2-32), or metallation of the Lewis base by the potassium alkyl (2-33).



Dialkylmagnesium reagents in the absence of Lewis bases were found to metallate a number of other substrates, including -picoline, dimethyl sulfoxide, and various alkynes such as acetylene, 3-methyl-1-butyne, and 4-methyl-1-pentyne (cf Table XI). Although metallation of alkynes had previously been carried out with dialkylmagnesium reagents in ethereal media, no metallations (in fact, few reactions in general) had previously been carried out with these reagents in hydrocarbon solvents. (This has, of course, been due mainly to the lack of solubility of the normal C₁-C₄ dialkylmagnesium reagents readily obtainable heretofore in an ether-free state.) It was found that the metallations of the two substituted alkynes with equimolar quantities of R₂Mg proceeded rapidly at room temperature with the formation of soluble metallation products (2-34). Carbonation of these solutions in each case yielded a mixture of the two expected products (2-35). Metallation of



acetylene (in large excess) by di-s-butylmagnesium in a mixed hydrocarbon

TABLE XI

METALLATION OF ACYCLIC SUBSTRATES BY DIALKYL MAGNESIUM REAGENTS

Reagent	Source ^a	Solvent	Substrate	Catalyst	Reaction Time (hr.)	Reaction Temp. (°C)	Apparent Metallation Product	Yield (%)
(<u>s</u> -Bu) ₂ Mg	I	<u>n</u> -Hexane-Benzene	Dimethyl sulfoxide	None	Essent. Instant.	25	Bis-(Methylsulfinyl-methyl)Mg ^b	Essent. Quant.
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	Acetylene	None	Essent. Instant.	25	60% MgC ₂ + 40% Mg(C ₂ H) ₂ ^c	Essent. Quant.
(<u>s</u> -Bu) ₂ Mg	II	Hexane-cyclohexane	3-Methyl-1-butyne	None	5-10 mins.	25	3-Me-1-butyneMgR (R=3-Me-1-butyne or <u>s</u> -butyl) ^d	50-100
(<u>t</u> -Bu) ₂ Mg	III	Benzene	4-Methyl-1-pentyne	None	5-10 mins.	25	4-Me-1-pentyneMgR (R=4-Me-1-pentyne or <u>t</u> -butyl) ^e	~50

^a I - Reaction of s-butyllithium with commercial anhydrous MgCl₂ in hexane-dimethyl ether solution followed by partial or complete desolvation.

II - Reaction of s-butyllithium with synthetic "active" MgCl₂ (from (s-BuMgCl + Cl₂)) in hexane-cyclohexane.

III - Prepared by reaction of t-butyllithium in benzene with synthetic "active" MgCl₂ (from s-BuMgCl + benzyl chloride).

TABLE XI (CONTINUED)

^bProduct formed by reaction of "dimsyl"-magnesium with trimethylchlorosilane (TMCS) analyzed by VPC and NMR and compared with dimsyllithium-TMCS product. Absence of DMSO in product solution.

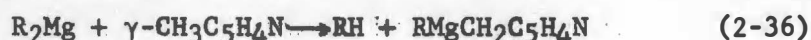
^cVPC of deuterolyzed products on triethylamine column at -78°C.

^dNo (s-Bu)₂Mg found by NMR analysis.

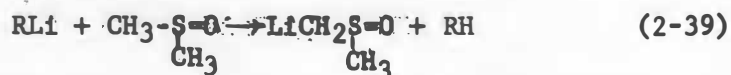
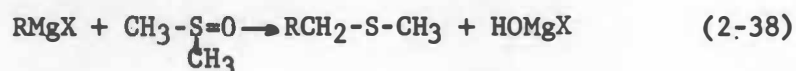
^eNMR showed presence of alkynyl- and t-butyl groups in D₂O solution of salts obtained on carbonation. Na₂CO₃ added to aid solubilization.

medium yielded a mixture of magnesium carbide and magnesium acetylide, neither of which were hydrocarbon soluble.

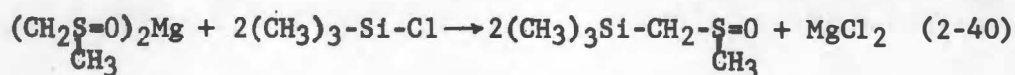
γ -Picoline has not previously been metallated by organomagnesium reagents, although it is known to be readily metallated by alkyllithium reagents but only in an ethereal solvent.¹¹⁰ Thus, it is of interest that metallation by the magnesium reagent takes place readily in hydrocarbon solvents at room temperature. A deeply colored red solution is obtained during the reaction. The product was characterized by derivatization with benzoyl chloride to the known solid γ -phenacylpyridine (2-37).



Grignard reagents are known to form sulfides on reaction with dimethyl sulfoxide^{99b} (2-38), whereas alkyllithium reagents metallate DMSO to form "dimesyllithium"^{100a} (2-39). In the present study, hydrocarbon-soluble dialkylmagnesium reagents were found to react readily



with DMSO to give the corresponding di-dimesylmagnesium reagent, identified by its reaction with trimethylchlorosilane to give a trimethylsilyl derivative identical to that obtained with dimesyllithium (2-40).



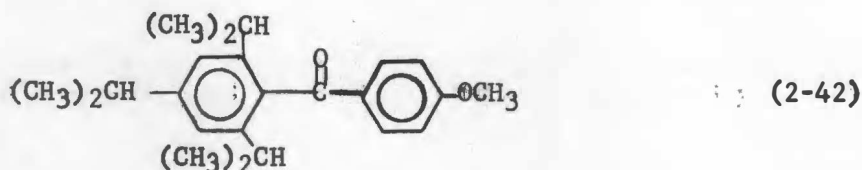
It seems likely that the anomalous reaction (2-38) obtained with the Grignard reagent is due to prior or simultaneous reaction of DMSO with MgX_2 .

E. REACTIONS OF DIALKYL MAGNESIUM REAGENTS WITH BENZOPHENONE

In essentially all modern studies of the system, a Grignard-ketone complex is proposed to form as a first step (2-41) in the



addition reaction. For example, Smith⁷⁴ has recently presented evidence for the presence in ether solution of as much as 25 per cent of the complex between the hindered ketone (2-42) and methylmagnesium bromide when the reactants were mixed in a 1:1 ratio.



Reaction in this system was slow and permitted study of the complexation by ultraviolet techniques. Actually, evidence for such complexes was presented as long ago as 1939 by Pfeiffer and Blank.¹⁰¹ These authors first advanced the hypothesis that addition is effected by interaction of the complex with a second molecule of Grignard reagent. They reported that the mixing of one equivalent of EtMgBr with benzophenone in ether solution resulted in the formation of a "dirty" white precipitate which quickly coalesced into an oily insoluble lower layer. The oily product, on treatment with water, was found to regenerate most of the benzophenone originally present. When the experiment was repeated with two (or more) equivalents of EtMgBr, the alcoholate derived from normal addition was formed. Utilization of an intermediate Grignard-ketone complex in mechanistic interpretations of their addition reaction was reviewed in Chapter I.

While essentially no specific experimental work has been reported for dialkylmagnesium reagent-ketone complexation, it is apparent that most workers reason that these analogous complexes do form and should serve as addition reaction intermediates. In the present study, branched chain dialkylmagnesium compounds in hydrocarbon solvents were reacted in different proportions with benzophenone and the products studied by NMR and ESR spectroscopy. Evidence for relatively stable dialkylmagnesium reagent-ketone complexes has been found, but the intermediacy of these complexes in the addition reaction is left open to question. The findings reported below must be considered preliminary and, for the most part, inconclusive, but these findings would seem to make the further study of these complexes quite promising.

Rapid mixing of one molar equivalent of di-t-butylmagnesium with two molar equivalents of benzophenone (called hereafter the "1:2 solution") gives a persistent (2-3 days) deep brown color which is interpreted as indicating the presence of some type of relatively stable charge transfer complex. NMR examination of this 1:2 solution showed the presence of benzophenone although its amount could not be accurately ascertained because of absorption by the solvent employed, benzene. A t-butylmagnesium species was also present, although the t-butyl proton signals were shifted downfield from their normal position by ca. 0.3 ppm. Addition of another mole equivalent of di-t-butylmagnesium, to give a "1:1 solution," caused the simultaneous disappearance of the brown color and the typical benzophenone signal and an increase in the t-butyl proton signal. That this t-butyl proton signal was made

up from t-butyl protons of a magnesium reagent, as well as from a product carbinol derivative, was determined by NMR analysis after hydrolysis of the 1:1 solution. The hydrolysis of the reaction solution caused loss of the organometallic t-butyl signal, but retention of the signal from the product carbinol. The product carbinol was, as expected, mostly the normal addition product.

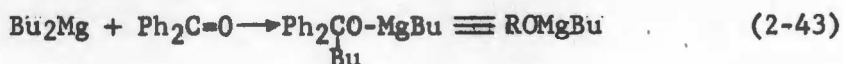
An ESR spectrum was also obtained with another 1:2, brown colored benzene solution of di-t-butylmagnesium and benzophenone. The spectrum which was intense and well-resolved, showed at least 44 lines. Both the color and the spectrum disappeared after about one hour in the sample tube used in the spectrometer.

Rather analogous observations were made with di-s-butylmagnesium. When the secondary reagent in hexane-cyclohexane solution was added to two molar equivalents of benzophenone in cyclohexane a green, sticky curdy precipitate formed. (Perhaps this insoluble complex precipitated from the 1:2 solution was similar to that observed by Pfeiffer and Blank.)¹⁰¹ The green precipitate could be dissolved in benzene (but not in ether) with the formation of a green solution which displayed an ESR spectrum, not as well resolved as that from the brown 1:2 solution produced using di-t-butylmagnesium. An NMR spectrum of this green solution showed no trace of the s-butyl methine proton signal in its normal region for the magnesium reagent, but benzophenone was present.

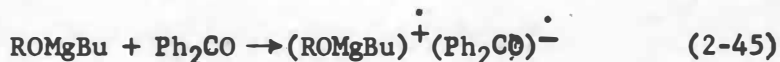
The ESR spectra from the highly colored 1:2 solutions described above (brown and green with di-t- and di-s-butylmagnesium, respectively)

have not been fully analyzed, but most probably the basic structural unit giving rise to these spectra is that of a benzophenone radical anion. An interesting point is that these spectra show hyperfine splitting, despite the fact that the solvent employed was hydrocarbon. These would seem to be the first resolved ESR spectra of ionic species ever obtained in a hydrocarbon medium.

From what is known about dialkylmagnesium reagent reactivity (Chapter I), there can be little doubt that in the 1:2 reagent:ketone solutions, there is an insufficiency of reagent to cause an addition reaction with all of the ketone. That is, when the initial equivalent of butyl groups is consumed by an addition (2-43), the second equivalent of



butyl groups (in the initial adduct, ROMgBu) reacts quite slowly, leaving unreacted ketone in the 1:2 solution. This excess ketone apparently then is reduced to a radical anion by the initial adduct, ROMgBu, which is both a magnesium alkoxide salt and an organomagnesium reagent. Russell, Janzen, and Stromm¹⁰² have previously demonstrated the general ability of an alkoxide (RO^-) to reduce a single electron acceptor (Z), as represented in equation (2-44). Tentatively then, radical anions in the 1:2 solutions are represented as arising in the manner illustrated in equation (2-45).



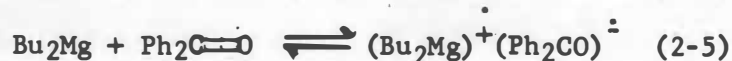
Just as observed with the brown colored 1:2 solution produced with the t-butyl reagent, color could be caused to disappear from the

green solution by addition of sufficient di-s-butylmagnesium to give a 1:1 solution. However, the rate of addition of s-reagent had to be controlled to produce a solution free of color. Relatively slow (drop-wise) addition of di-s-butylmagnesium solution to benzophenone solution resulted in the generation of heat indicating reaction. A green color (with a transient violet cast before thorough mixing) was present throughout the addition, until addition of a molar excess of di-s-butylmagnesium over the 1:1 ratio caused the green color to disappear. At this point reaction of the ketone was apparently complete, i.e., there was no reducible substrate left to accept the electron transfer suggested in equation (2-45). After hydrolysis, the product ratio of benzhydrol (reduction product) to normal addition product obtained in the case of di-s-butylmagnesium and benzophenone in benzene solution was about 3:1. This can be compared with a ratio of only 0.7:1 obtained with the corresponding Grignard reagent and benzophenone in diethyl ether.

The most interesting result in the present study stemmed from the observation of a transient violet cast when the di-s-butylmagnesium was added slowly to benzophenone. When an excess of the reagent was mixed rapidly with benzophenone in benzene or hexane-cyclohexane, the solution became violet colored and the color was stable for an indefinite period. In other words, if the dialkylmagnesium reagent is added slowly to the ketone, perceptible heat is evolved and a green colored solution (or precipitate) is formed until a 1:1 molar ratio is achieved, when color disappears and there is no evidence for further reaction, but if the reagent is added rapidly to the ketone so as to give quickly at

least a ca. 2:1 molar ratio of reagent to ketone, a relatively stable violet-colored solution is produced. The following two additional observations were made concerning the violet solution. (1) It showed an NMR signal from the methine proton in di-s-butylmagnesium; no such NMR signal from the green solution appeared. (2) It showed an intense well-resolved ESR spectrum which was different from that of the green solution. The spectrum from the violet solution, which is shown in Figure 2, is unquestionably that of the benzophenone radical anion.

Again any interpretation must be highly tentative, but the facts concerning the violet solution show clearly that benzophenone, in the form of its radical anion in a hydrocarbon medium, can survive unreacted for an indefinite but long period of time in the presence of a large excess of magnesium reagent. A possible interpretation for these facts is that the large excess of magnesium reagent complexes the ketone in such a manner that none is free for additional reaction, and that the species so produced is a type of charge transfer complex, as suggested in equation (2-5). In the presence of limited magnesium reagent, or



probably in an ethereal solvent, reversibility of the reagent-ketone complexation (2-5) would be sufficient to always leave ketone free for other reactions.

If the above interpretation is valid, then the idea that the addition reaction requires complexation of a ketone with a magnesium reagent becomes somewhat less attractive. In other words, the above



Figure 2. E.S.R. spectrum-excess-(*s*-butyl)₂Mg plus benzophenone in hydrocarbon solution (violet color).

interpretation is that complexation (2-5) may be a reversible side reaction, which under some circumstances actually can leave no ketone free to be added to.

F. MISCELLANEOUS REACTIONS WITH DIALKYL MAGNESIUM REAGENTS

1. Attempted Addition of Dialkylmagnesium Reagents to Ethylene

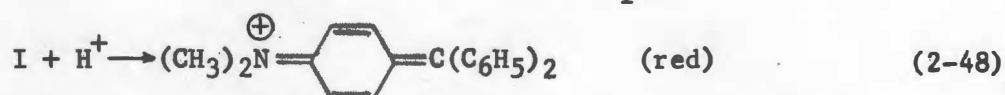
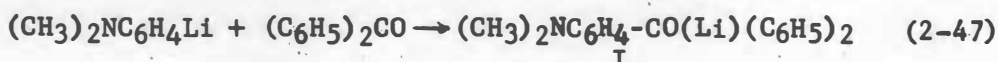
Comparable results to those obtained in the metallation and hydrogenolysis experiments were obtained when attempts were made to add di-s-butylmagnesium to ethylene in a hydrocarbon solvent. No uptake of ethylene by the reagent occurred in the presence of TMEDA (alone) or in the presence of potassium t-butoxide (alone or in combination with THF or TMEDA). Under conditions which caused the absorption of ethylene in the presence of s-butyllithium to be too fast to measure,^{102,104} an equimolar mixture of s-butyllithium and di-s-butylmagnesium did not absorb any significant quantity of ethylene. These runs were made with ethylene at atmospheric pressure; magnesium alkyls are known to add to ethylene at elevated temperature and pressure.

2. Attempted Reaction of di-s-Butylmagnesium Reagents with Phenyl-dimethylchlorosilane in Ethyl Ether

No reaction could be caused to occur between di-s-butylmagnesium and phenyldimethylchlorosilane in diethyl ether-hydrocarbon mixtures even after prolonged reflux. The chlorosilane reacts readily with s-butyllithium.

3. Effect of Dialkylmagnesium Reagents on the Halogen-Metal Interconversion Reaction with Alkylolithium Reagents

It was found that dialkylmagnesium reagents inhibit the halogen-metal interconversion reaction between alkylolithium reagents and *p*-bromodimethylaniline. When a 2:1 molar mixture of *s*-butyllithium and di-*s*-butylmagnesium (in hydrocarbon solution) was treated with *p*-bromodimethylaniline under the conditions of Gilman Color Test IIa,⁷ only a faintly positive test was obtained. A strongly positive test was obtained with a solution of comparable concentration in *s*-butyllithium, no magnesium reagent present. The reactions involved in obtaining a positive test, shown below, involve first a halogen-metal interconversion.

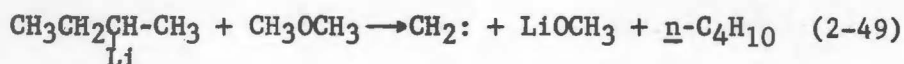


Proof that inhibition of the halogen-metal interconversion (2-46) was occurring when the mixture of the two organometallics was used was obtained by carbonation of appropriate reaction mixtures and NMR examination of D₂O solutions of the carboxylic acid salts so obtained. When *s*-butyllithium alone was allowed to react with *p*-bromodimethylaniline, carbonation indicated that all of the alkylolithium exchanged to *p*-dimethylaminophenyllithium. In the case of the mixed lithium-magnesium alkyl, only an insignificant amount of exchange occurred and mainly carbonation products from the unchanged *s*-butyl reagents were obtained.

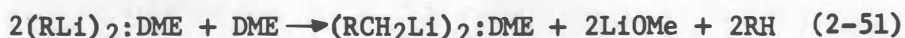
These results, those from hydrogenolysis experiments, from solubility studies and from NMR spectral measurements, all indicate that mixed magnesium-lithium alkyls constitute a new group of complex structures. They would seem to be new hydrocarbon-soluble structures in which one electron-deficient member of the oligomeric unit has simply been replaced by a different organometallic molecule possessing like properties. The minimum molar ratio of alkyllithium to dialkyl-magnesium reagent in such complexes appears to be 1:2, but it is not known what the upper limit might be. Indeed, it may vary widely, and should be the subject of further research. The halogen-metal inter-conversion reaction might be a useful diagnostic test to determine this limit.

G. HOMOLOGIZATION OF ALKYLLITHIUM REAGENTS

During an attempted preparation of di-s-butylmagnesium from exchange of s-butyllithium with MgCl_2 in the presence of dimethyl ether, it was observed that some of the s-butyllithium reacted with the dimethyl ether. A homologization product, 2-methylbutyllithium was formed, in addition to the exchange product. The homologization product is also formed in the absence of MgCl_2 . Its formation can be formally represented (2-49, 2-50) as involving a carbene insertion



process. One can conceive of this reaction as proceeding by metallation of DME to yield an intermediate "carbenoid," e.g., $\text{CH}_3\text{OCH}_2\text{Li}$, which causes the insertion. It is known that $\text{CH}_3\text{OCH}_2\text{MgCl}$ gives carbene-type reactions.¹⁰³ The overall stoichiometry of this insertion process can be represented as consuming two solvated dimers and one free DME molecule (2-51). For the purpose of discussion of the equation (2-51), the DME which is free or uncomplexed by dimeric alkyllithium reagent is called "effective DME," DME_{eff} .



t-Butyllithium also reacts with dimethyl ether and is homologized to produce neopentyllithium. The insertion products have been identified by NMR analysis and by conversion to the lithium salts of the expected carboxylic acids on carbonation. The experimental procedure for this homologization constitutes a new, rapid means of converting secondary and tertiary alkyllithium compounds to their corresponding branched-chain normal homologues containing one more carbon atom. Yields are essentially theoretical; two moles of RLi produce one of RCH_2Li .

The kinetics of the homologization reaction were examined with s-butyllithium in hydrocarbon media using two types of experimental conditions: runs involving only the reactants shown in equation (2-51), designated as "ordinary runs," and runs having tetramethylethylenediamine present designated as "TMEDA-catalyzed runs."¹¹¹

1. Two Ordinary Runs

The first two kinetic runs were carried out at 40° in cyclohexane with just reactants present. In one, only the amount of DME

corresponding to the stoichiometric amount depicted in equation (2-51) was employed. In the other run, an excess of DME was employed, which insured that the effective DME present would remain essentially constant throughout the run. The reactions were allowed to proceed to over 50 per cent completion and in each case samples were withdrawn periodically, reacted with excess trimethylchlorosilane and the product solutions assayed for g-butyl- and 2-methylbutyltrimethylsilane by gas chromatography. The fraction of unreacted g-butyllithium (c) was treated as the reaction variable and various plots involving c versus time (t) were made for each run, including c vs. t, log c vs. t, 1/c vs. t, and 1/c² vs. t. Figure 4 depicts the results from the stoichiometric DME run and Figure 6, the results from the excess DME run. (cf. also Figures 3 and 5 for 0-5°C data).

With a stoichiometric amount of DME, a plot of 1/c² vs. t appeared to fit the data best (Figure 4), with excess DME, a plot of 1/c vs. t fit the data best (Figure 6). These observations are consistent with the kinetic order of the reaction, being, somewhat surprisingly, exactly the same as the stoichiometry represented in equation (2-51). That is, the process is third order overall, second order in solvated dimer reagent, and first order in the free or effective DME as indicated in equation (2-52).

$$\text{rate} = k_r [(\text{RLi})_2\text{DME}]^2 [\text{DME}]_{\text{eff}} \quad (2-52)$$

In order to calculate the rate constant (k_r) for the run with excess DME, equation (2-52) can be rewritten as in (2-53) in which the

$$\text{rate} = k_r [\text{DME}]_{\text{xs}} \left(\frac{[\text{RLi}]_i}{2} \right)^2 c^2 \quad (2-53)$$

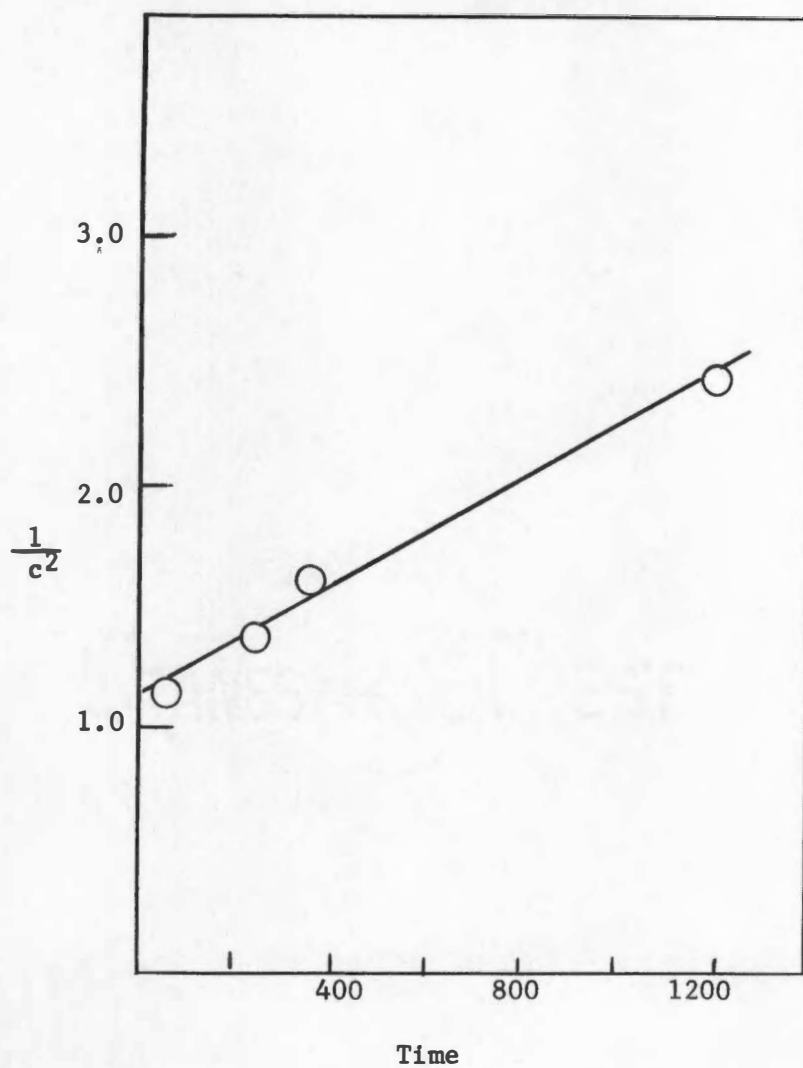


Figure 3. Homologization of s-butyllithium with stoichiometric dimethyl ether at 0°C. $1/(\text{fraction unreacted } \underline{s}\text{-butyllithium})^2$ versus time (minutes).

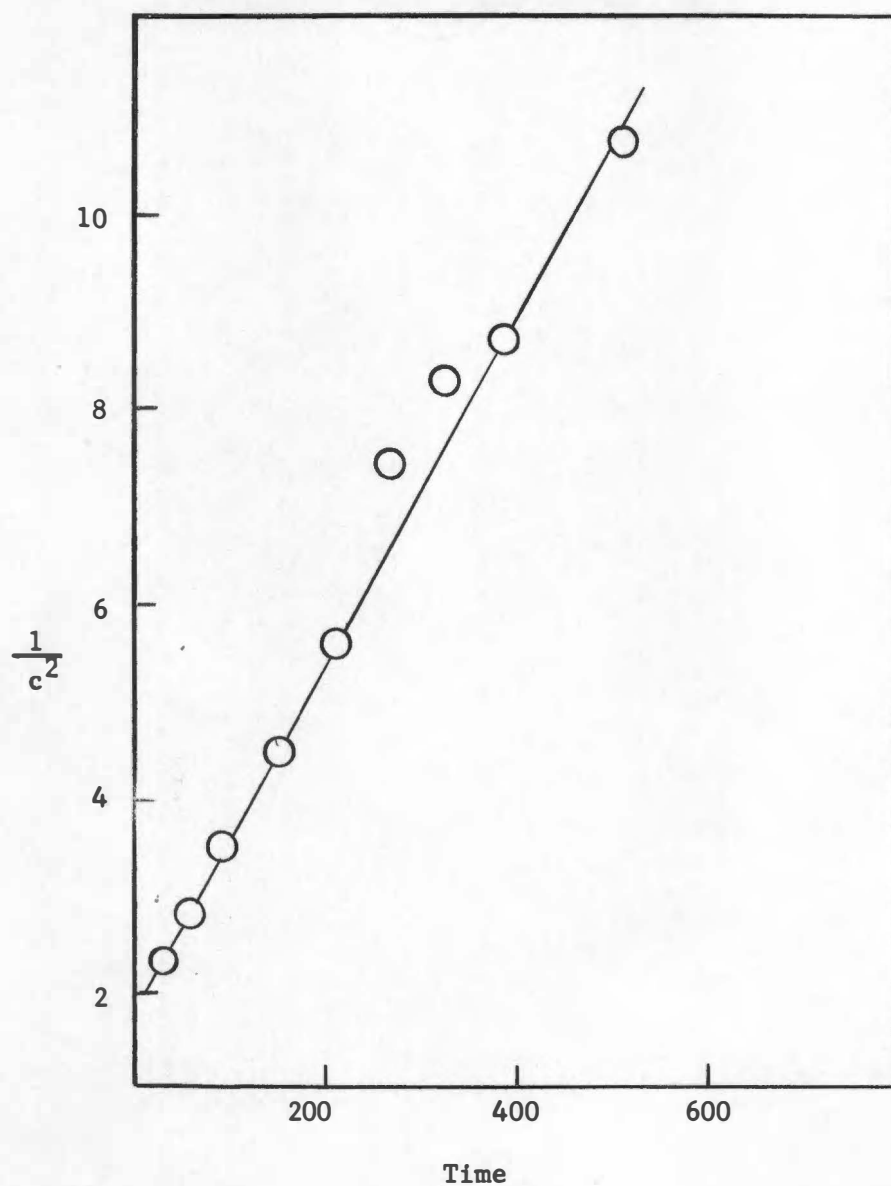


Figure 4. Homologization of s-butyllithium with stoichiometric dimethyl ether at 40°C; $1/(\text{fraction unreacted } \underline{s}\text{-butyllithium})^2$ versus time (minutes).

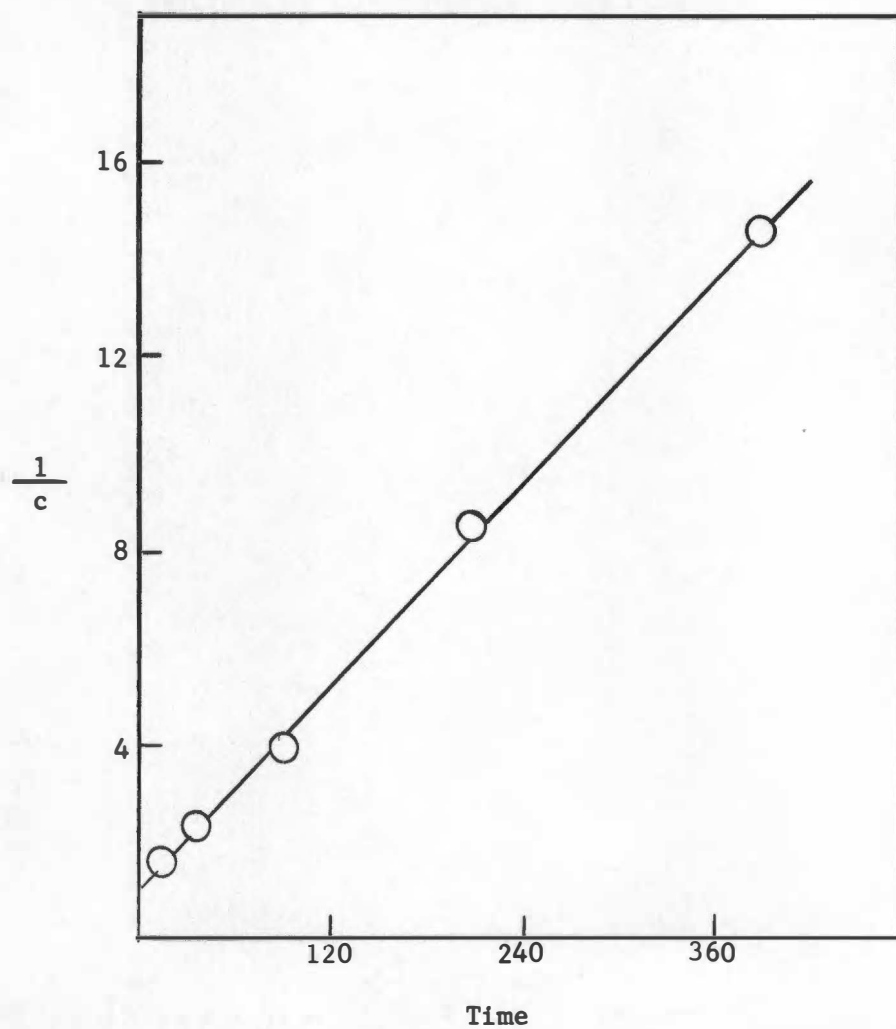


Figure 5. Homologization of *n*-butyllithium with excess dimethyl ether at 5°C; $1/(\text{fraction unreacted } n\text{-butyllithium})$ versus time (minutes).

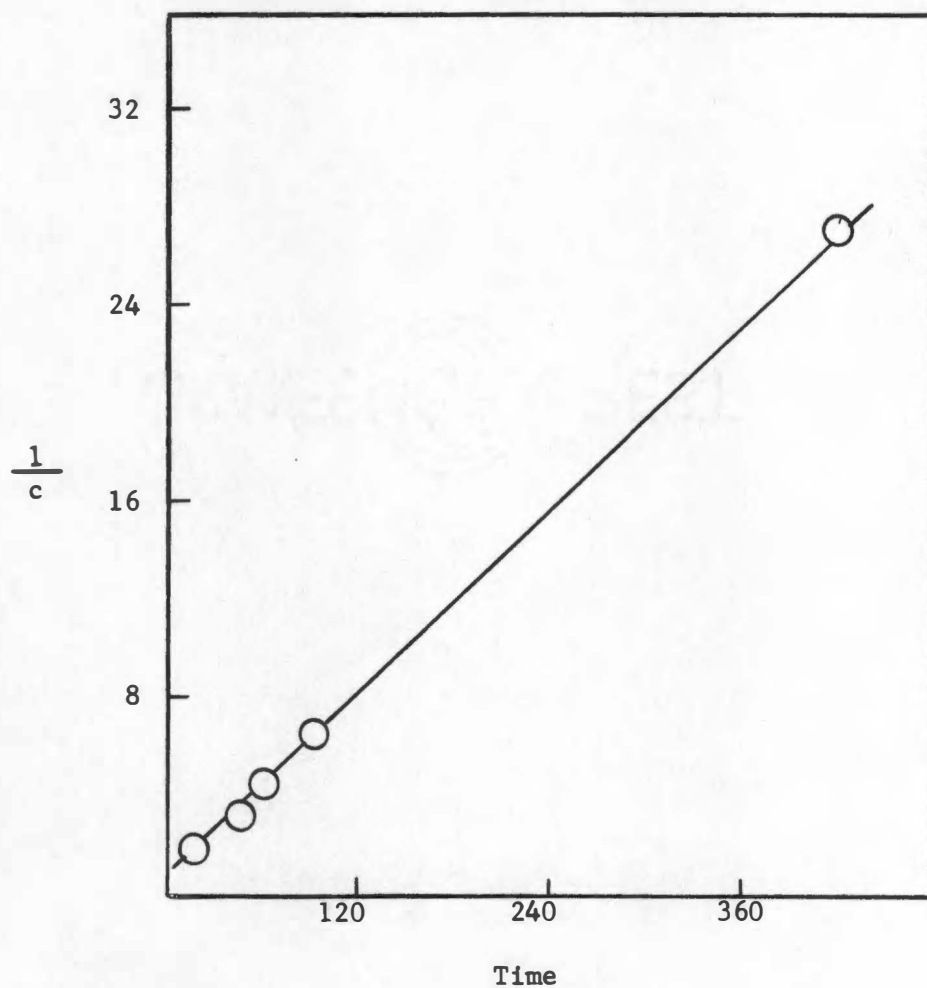


Figure 6. Homologization of *s*-butyllithium with excess dimethyl ether at 40°C; $1/(\text{fraction unreacted } \underline{s}\text{-butyllithium})$ versus time (minutes).

initial solvated dimer concentration is given as $[RLi]_i/2$, and the effective DME concentration is expressed as $[DME]_{xs}$, because it is in such excess over that required stoichiometrically as to be a reaction constant. Under the circumstances the only variable is c . On integrating equation (2-53), equation (2-54) is obtained, which shows that a value of k_r in the run with excess DME can be obtained using the slope of the $1/c$ vs. t plot in Figure 6. Doing this, one obtains a value for k_r of $0.134 \text{ l. mole}^{-1} \text{ min.}^{-1}$ at 40° .

$$1/c = k_r [DME]_{xs} \left(\frac{[RLi]_i^2}{4} \right) t + \text{constant} \quad (2-54)$$

The rate constant for the reaction with stoichiometric DME can be derived as follows. In this case, $[DME]_{eff}$ is always just one-half the unreacted solvated dimer concentration, so the rate expression may be written as in (2-55). Integration gives equation (2-56), with

$$\text{rate} = k_r \left(\frac{[RLi]_i}{2} \right)^3 c^3 \quad (2-55)$$

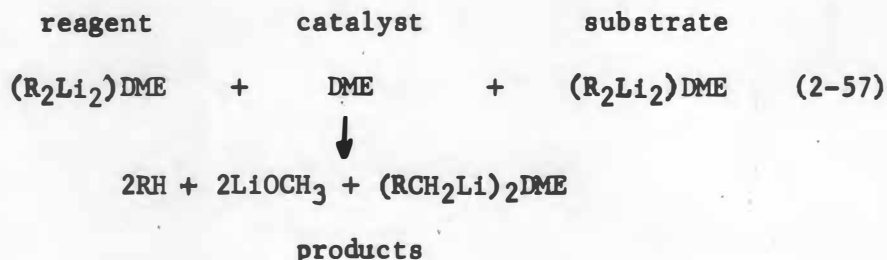
$$\frac{1}{c^2} = k_r \left(\frac{[RLi]_i^3}{16} \right) t + \text{constant} \quad (2-56)$$

which, and the slope obtained from the $1/c^2$ vs. t plot (40° data, Figure 4), one obtains a value for k_r of $0.151 \text{ l}^2 \text{ mole}^{-2} \text{ min}^{-1}$.

The agreement between values of k_r (0.14 ± 0.01) obtained from these two runs is remarkably good. The conclusion is that in these runs the order of the homologization reaction follows the stoichiometry shown in equation (2-51), i.e., the insertion process is third order. Two solvated dimer units as well as the free base, $(DME)_{eff}$, are involved before the rate determining step. This result is consistent

with the concept that the free base is a catalyst, a concept previously suggested by Screttas^{100b} for reactions of lithium reagents with other substrates.

The involvement of the two solvated dimers does not seem to be consistent with formation of any free carbene, or even a carbenoid. From the stoichiometry and kinetics, it seems possible that one solvated dimer unit is the "reagent" and is acting on a second as the "substrate," causing the second to undergo the insertion reaction. An attempt to represent this general idea is shown below. Quite possibly the primary action of the one solvated dimer on the other is charge transfer and this transfer process is catalyzed by the free DME.



2. Four TMEDA-Catalyzed Runs.

Two kinetic runs were carried out at low temperatures with equal catalytic amounts of TMEDA but with differing amounts of excess DME. Two other runs were carried out at 0°C with differing amounts of TMEDA and the DME present in stoichiometric amount. The data from these catalyzed runs were plotted as c vs. t , $1/c$ vs. t , $1/c^2$ vs. t , and $\log c$ vs. t . The best fits for the runs with excess DME were obtained

by plotting $\log c$ vs. t and are shown in Figure 7. The best fit for the runs with stoichiometric DME were also obtained by plotting $\log c$ vs. t and are shown in Figure 8. In other words, the reaction is no longer third order; all of the TMEDA-catalyzed runs appeared to be first order reactions.

The result that the overall reaction appears as first order in the presence of catalytic amounts of TMEDA is analogous to results found by Screttas^{100b} in his study on the catalysis of hydrogenolysis of RLi reagents by various bases. He observed that with most monofunctional bases, such as tertiary amines and ethers, hydrogenolysis occurred at a moderate rate and was kinetically dependent (first order) on RLi reagent concentrations even with excess base. With difunctional bases such as TMEDA as catalysts, RLi hydrogenolysis rates were too high to study with excess base. Measurable rates obtained by Screttas^{100b} with low TMEDA concentrations showed no kinetic dependence on the RLi reagent concentration, although the rates obtained did show kinetic dependence on catalyst (base) concentration. Selvidge¹⁰⁴ later showed that the TMEDA-catalyzed hydrogenolysis does show a kinetic dependence also on the concentration of substrate, hydrogen. Thus, it is not surprising that the TMEDA-catalyzed homologization reaction, wherein solvated dimer acts as both the substrate and the RLi reagent, should be only first order in solvated dimer.

The loss of two kinetic orders observed (in going from ordinary runs with stoichiometric DME to TMEDA-catalyzed runs) is due to free DME, as well as one solvated dimer unit, no longer playing kinetic roles in

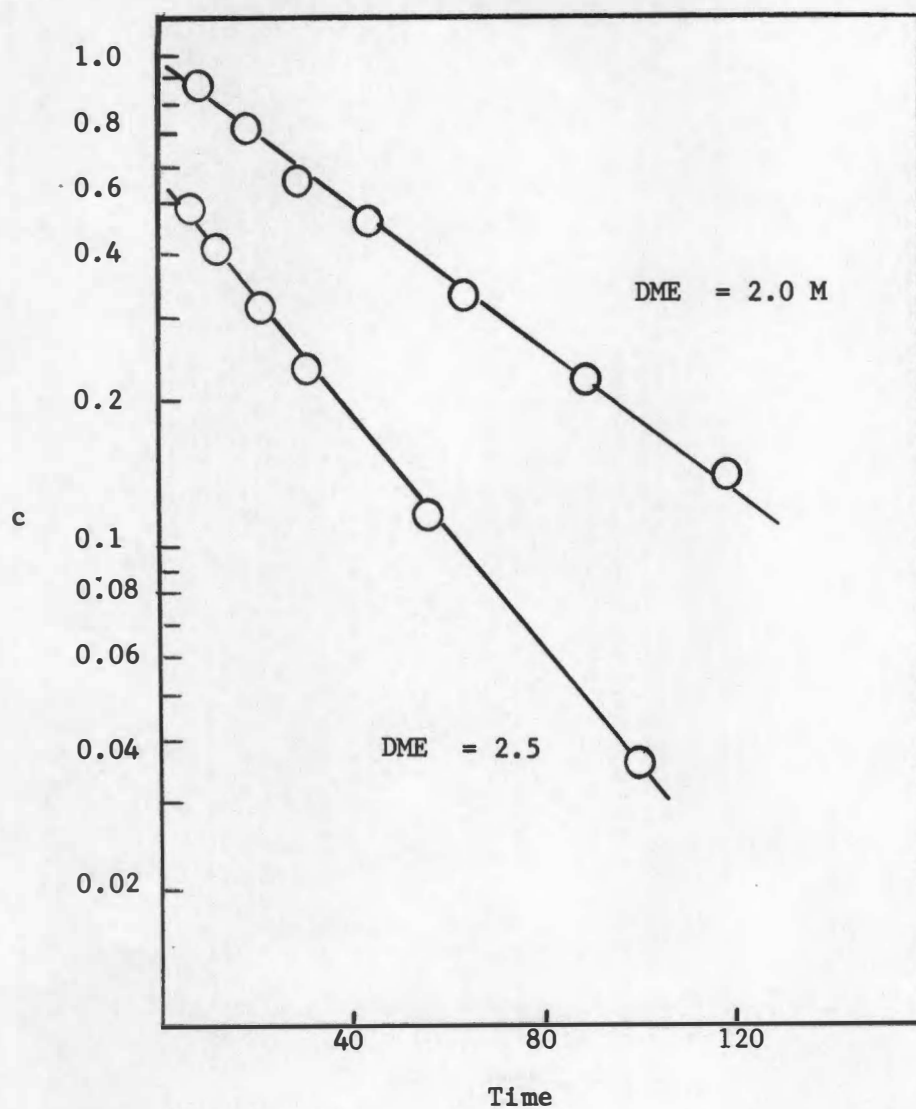


Figure 7. Homologization of *s*-butyllithium with excess dimethyl ether catalyzed by TMEDA (0.0134M); fraction unreacted *s*-butyllithium versus time (minutes).

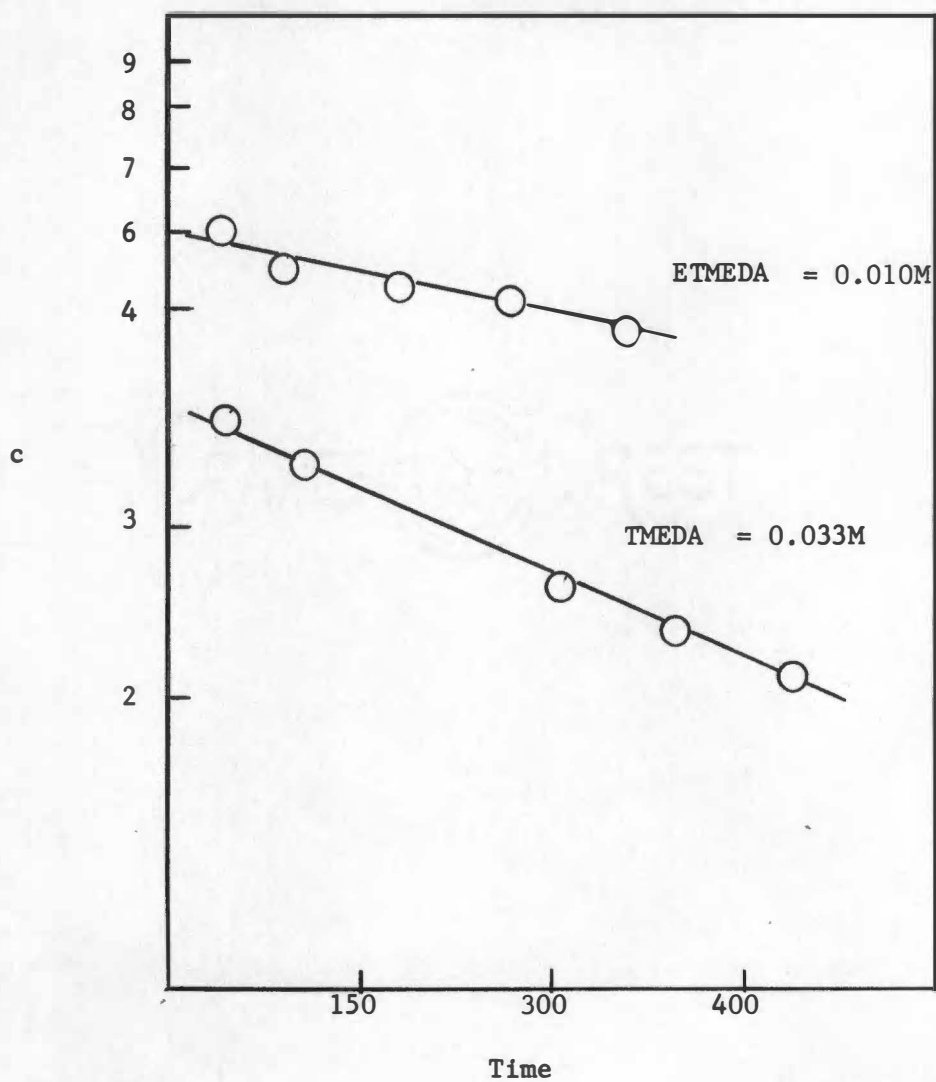


Figure 8. Homologization of s-butyllithium with stoichiometric dimethyl ether catalyzed by TMEDA at 0°C; fraction unreacted s-butyllithium versus time (minutes).

the reaction. That there is loss of kinetic dependence on the free DME concentration in the TMEDA-catalyzed runs is corroborated by the fact that there was no change in the apparent order of the reaction in the presence or absence of excess DME, although there was such a change in ordinary runs. This loss almost surely is a consequence of the TMEDA being a much better catalyst than DME. From the work of Settle¹⁰⁵ on steric effects in RL1 solvation, it is safe to assume that the dimeric RL1 units present would be preferentially solvated by DME, rather than TMEDA. The point is, it is free TMEDA concentration which promotes catalyzed runs, and even in the ordinary runs, free DME was just a base acting as catalyst and was not the substrate. The substrate in all runs was dimer solvated with DME, which was caused to react with the reagent, another solvated dimer, by one base or the other acting as a catalyst.

It follows that the overall rate in the TMEDA-catalyzed runs was probably a two-term function, equation (2-58), the first of which was

$$\text{rate} = (k_r)_{\text{DME}} [\text{DME}]_{\text{eff}} [\text{R}_2\text{Li}_2:\text{DME}]^2 + (k_r)_{\text{TMEDA}} [\text{TMEDA}]_{\text{eff}} [\text{R}_2\text{Li}_2:\text{DME}]^2 \quad (2-58)$$

insignificant in magnitude to the second. Hence the integrated function could be written as in equation (2-59). From the log c vs. t

$$\log c = (k_r)_{\text{TMEDA}} [\text{TMEDA}]_t \frac{1}{2} [\text{RLi}]_t + \text{constant} \quad (2-59)$$

plots, slopes yielded the rate constants for TMEDA-catalyzed runs which are shown in Table X. For corroboration that the proper rate function was used, it can be seen that while runs 7 and 8 differed both in [TMEDA] and [RLi]_t, the rate constants were essentially the same, 1.0±0.1.

3. t-Butyllithium Run

One kinetic run was made employing t-butyllithium and excess DME, but no TMEDA. The best fit for the t-butyllithium-excess DME reaction data was a first order plot ($\log c$ vs. t) shown in Figure 9, which is in contrast with the fits of a second order plot for s-butyllithium-excess DME runs.

Again, analogous contrasting results were found in the hydrogenolysis study. Other RLi reagents (i.e., n- and s-reagents) and monofunctional bases gave data showing kinetic dependency on the RLi concentration, but t-butyllithium was kinetically independent of that reagent even with the monofunctional basic catalyst. Thus, t-butyllithium with DME acts like s-butyllithium with TMEDA; there is a washing out of one kinetic order with respect to solvated dimer. Perhaps this is due to the fact that t-butyllithium is a better electron source than is s-butyllithium.

The bright yellow color, clearly observable during the t-butyllithium-DME reaction, (but absent or only faint in the s-butyllithium-DME reaction) is thought to be evidence for a charge transfer complex or a radical ion intermediate and thus to support some electron-transfer process. This coloration disappears when the reaction is essentially complete. An ESR spectrum (Figure 10) of the yellow solution showed a weak, but definite signal.

The rate function for this t-butyllithium reaction would be that in equation (2-60), where $(\text{DME})_{\text{eff}}$ is again essentially a reaction constant

$$\text{rate} = k_r [\text{DME}]_{\text{eff}} [\text{R}_2\text{Li}_2:\text{DME}] \quad (2-60)$$

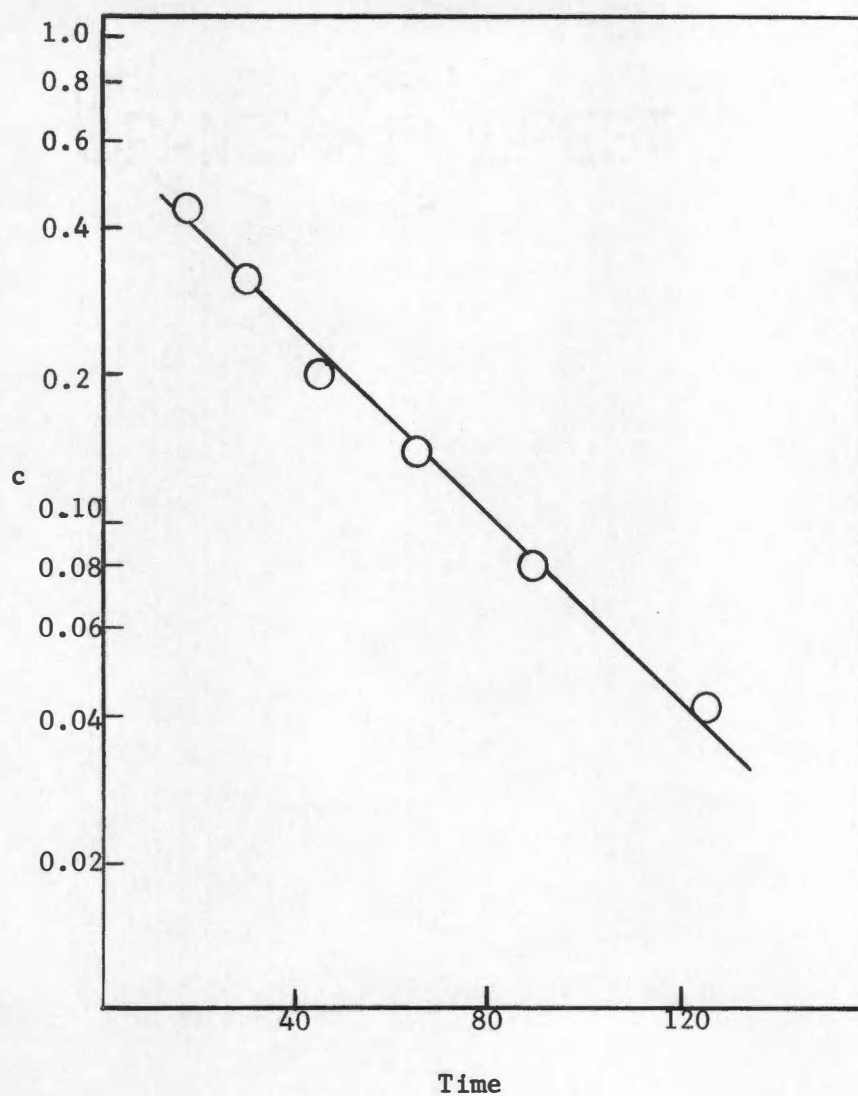


Figure 9. Homologization of *t*-butyllithium with excess dimethyl ether at 0°C; fraction unreacted *t*-butyllithium versus time (minutes).



Figure 10. ESR spectrum-t-butyllithium plus excess DME 77°K.

equal at any time to one-half the unreacted solvated dimer concentration plus the excess DME concentration, i.e., that above stoichiometric. The k_r value found, 1.5×10^{-2} , for the t-butyllithium run, and those for other runs, are shown in Table XII. From estimates of the experimental error, the rate constants shown in Table XII are considered to be no more accurate than about ± 10 per cent of each value shown.

4. Summary

Comparison of the rate constants shown in Table XII does not constitute a particularly useful comparison of homologization kinetics under the various conditions employed. The primary reason for this is the fact that these values are mixtures of second and third order constants. Even this fact that the homologization kinetic order changes in going from one experimental condition to another has not been really rationalized with a reaction mechanism, although analogous changes in another reaction (hydrogenolysis) have been cited, along with the idea that the kinetic role of base (its catalytic activity) is played as a charge transfer agent. In this connection it has recently been pointed out that while the general concept of base support of charge transfer has obvious utility in rationalizing diverse phenomena, elucidation of detailed steps in reaction mechanisms may prove difficult.¹⁸⁶ For the present, our elucidation of the homologization reaction consists mainly of the two kinetic expressions written below.

$$\text{rate} = k_r \underset{\text{reagent}}{[R_2Li_2:DME]} \underset{\text{catalyst}}{[base]} \underset{\text{substrate}}{[R_2Li_2:DME]} \quad (2-61)$$

$$\text{rate} = k_r \underset{\text{catalyst}}{[base]} \underset{\text{substrate}}{[R_2Li:DME]} \quad (2-62)$$

TABLE XII
KINETIC DATA-REACTION OF s-BUTYLLITHIUM WITH DIMETHYL ETHER

Run No.	Temp. °C	[TMEDA]	[DME] _{xs}	[RLi] _i	k _r
1.	40	--	1.1	1.3	0.13 ^b
2. ^a	40	--	-	1.24	0.15 ^c
3.	5	--	1.1	1.31	7.4x10 ⁻² ^b
4. ^a	0	--	-	1.24	9.6x10 ⁻³ ^c
5.	2.5	0.0134	1.0	1.31	0.8 ^d
6.	4	0.0134	1.5	1.31	1.4 ^d
7.	0	0.010	-	0.80	1.1 ^d
8.	0	0.033	-	0.59	0.9 ^d
9. ^f	-7	--	0.8	1.75	1.5x10 ⁻² ^e

^aArrhenius activation energy calculated from data on runs 2. and 4. is 2.9 kcal/mole.

^bFunction for k_r(calc'd) = $\frac{(\text{slope})(4)}{[\text{DME}]_{\text{xs}}[\text{RLi}]_i^2}$; units = liter² mole⁻² min⁻¹ (third order).

^cFunction for k_r(calc'd) = $\frac{(\text{slope})(16)}{[\text{RLi}]_i^3}$; units = liter² mole⁻² min⁻¹ (third order).

^dFunction for k_r(calc'd) = $\frac{(\text{slope})(2)}{[\text{TMEDA}][\text{RLi}]_i}$; units = liter mole⁻¹ min⁻¹ (second order).

^eFunction for k_r(calc'd) = $\frac{(\text{slope})(2)}{[\text{DME}]_{\text{xs}}[\text{RLi}]_i}$; units = liter mole⁻¹ min⁻¹ (second order).

^ft-Butyllithium used in run instead of s-butyllithium.

The substrate in the homologization reaction is the same species as the reagent. With s-butyllithium as reagent and DME as catalyst, equation (2-61) is followed; there is kinetic dependence on both reagent and substrate. With the s-reagent and TMEDA as catalyst, equation (2-62) is followed; there is no kinetic dependence on reagent. The latter is true with t-butyllithium even with DME as catalyst. The greater reactivity, i.e., loss of kinetic dependence, with t-butyllithium and with s-butyllithium-TMEDA, quite likely results from greater facility in charge transfer.

Values which do constitute a useful comparison of homologization kinetics under the various conditions are shown in Table XIII. The numbered entries there correspond to those in Table XII, but the rate values shown are calculated absolute initial rates ($-dc/dt$) which would have obtained had each of those runs been initiated with $RLi = 1M$. For example, from these values one comparison available (runs 4 and 7, Table XIII), is that addition of just 10^{-2} mole equivalents of TMEDA to a stoichiometric mixture of s-butyllithium and DME causes a ten-fold increase in their reaction rate.

TABLE XIII
INITIAL HOMOLOGIZATION RATES OF 1M RL1 WITH DME

Run No. ^a	Temp.	[TMEDA]	[DME] _{xs}	Initial Rates ^b	Relative Rate
1.	40°	-	1.1	0.036	60
2.	40°	-	-	0.009	15
3.	5°	-	1.1	0.020	35
4.	0°	-	-	0.0006	1
5.	2°	0.013	1.0	0.005	8
6.	4°	0.013	1.5	0.009	15
7.	0°	0.010	-	0.006	10
8.	0°	0.033	-	0.015	25
9.	-7°	-	0.5	0.006	10

^aAll runs with s-butyllithium except Run 9. with t-butyllithium.

^bValues calculated from rate constants in Table IX.

CHAPTER III

EXPERIMENTAL

A. INTRODUCTORY INFORMATION

1. Reagents

n-Butyllithium in n-hexane and benzene solutions and s-butyllithium in n-hexane and cyclohexane solutions were obtained from Foote Mineral Company. t-Butyllithium in n-pentane and methyl-lithium in ether were obtained from Lithium Corporation of America. Lithium (containing 2 per cent sodium) as a 30 weight per cent dispersion in mineral oil, and as 1/8 inch wire was also obtained from Lithium Corporation of America. t-Butyl-, isopropyl-, and cyclohexyl-magnesium chloride in ether solution were obtained from Matheson, Coleman, and Bell; phenylmagnesium chloride in tetrahydrofuran was obtained from Mallinckrodt Chemical Company. Anhydrous magnesium chloride in powder form was obtained from Alfa Inorganics, Inc. and in lump form from the Dow Chemical Corporation. Anhydrous triethylenediamine (TED), m.p. 158-160°, and methyltriethylenediamine, a liquid, were obtained from Houdry Process and Chemical Company. N,N,N',N'-tetramethylethylenediamine (TMEDA) was obtained from Rohm and Haas Company. The TMEDA was distilled from lithium aluminum hydride and stored over Linde 4A molecular sieves; otherwise, the reagents indicated above were used without refinement.

Other critical solvents and reagents (benzene, toluene, cyclohexane, thiophene, resorcinol dimethyl ether, γ -picoline, etc.) were reagent grade (e.g., Baker's Analyzed Reagent, Mallinckrodt Analytical Reagent, Eastman White Label) and generally were dried with activated alumina and stored over Linde Molecular Sieves 4-A (MS-4A). Benzene and cyclohexane used for desolvation of dialkylmagnesium reagents and for active alkyl analyses were specially treated; these solvents were refluxed for at least 8 hours over lump barium oxide and then distilled into bottles (previously dried at 125°) containing Linde MS-4A sieves and a few pieces of sodium metal. Ether and tetrahydrofuran were refluxed over lithium aluminum hydride and distilled into amber bottles containing Linde MS-4A sieves and sodium.

Nitrogen was a high purity grade obtained from Welding Gas Products Company, was passed through two drying columns, the first containing indicating drierite and the second, Linde MS-4A Molecular Sieves. Dry hydrogen gas, also from Welding Gas Products Company, was passed through a wash-bottle containing concentrated sulfuric acid. Ethylene and dimethyl ether were obtained from the Matheson Gas Company; each was indicated to be at least 99.5 per cent pure and was used without further purification.

2. Instrumentation and Analytical Techniques

Magnesium analyses were carried out using a conventional complexometric titration involving an ethylenediamine tetraacetic acid di-sodium salt solution as titrant and "calmagite" obtained from the G. F. Smith Chemical Company as indicator. Chloride ion was determined by the standard Mohr procedure. Total alkalinity analyses were carried out

by adding a known amount of standard aqueous acid (in excess) and back-titrating dropwise (with vigorous shaking) with standard aqueous base. Each of these titrations was done on hydrolyzed samples of organometallic solutions.

Active alkyl analyses were done by direct titration of the organometallic solution samples using the procedure of Watson and Eastham.^{98b}

Gilman Color Test I, which is sensitive to the presence of both organolithium and organomagnesium compounds, involved the addition of 0.5-1.0 ml. of the organometallic solution to be tested to an equal volume of 1 per cent Michler's ketone in dry benzene, followed by hydrolysis with 1 ml. of water and addition of several drops of a 0.2 per cent solution of iodine in glacial acetic acid. A greenish-blue color was considered positive indication of the presence of C-Li or C-Mg containing compounds. Gilman Color Test IIa was used to differentiate between alkyllithium and dialkylmagnesium compounds and involved the addition of a 0.5-1.0 ml. of the organometallic solution to an equal volume of a 15 per cent solution of *p*-bromodimethylaniline in dry benzene, followed by 1.0 ml. of a 15 per cent solution of benzophenone in dry benzene. After a few seconds, the mixture was hydrolyzed with water and acidified with hydrochloric acid. A red coloration indicated the presence of an alkyllithium compound. Since it was found in this work that dialkylmagnesium compounds interfere in this test, the absence of alkyllithium reagent as determined by this test was in most cases verified by magnesium and total base analyses.

NMR spectra were obtained with the Varian A-60 Spectrometer. Vapor phase chromatographic analyses (VPC) were performed with the Perkin-Elmer Model 154-D Vapor Fractometer. Details of typical VPC analytical procedures are given on page 159. ESR spectra were obtained with the Varian 4500 with 100 KC Modulation (frequency adapted). Melting points were determined with a "Mel-Temp" apparatus and are reported uncorrected.

B. PREPARATION OF DIALKYL MAGNESIUM REAGENTS FROM GRIGNARD
AND ORGANOLITHIUM REAGENTS

1. Preparation of Di-*t*-butylmagnesium

A weight of 2.43 g. (0.1 g. atoms) of magnesium powder (40 mesh) and a few crystals of iodine were placed in a 500 ml. round-bottom 4-neck flask equipped with a mechanical (Hershberg) stirrer, reflux condenser, thermometer, and 100-ml. graduated dropping funnel. The flask was heated to vaporize the iodine and then allowed to cool. Three to four milliliters of a solution of 9.3 g. (0.1 mole) of *t*-butyl chloride in 25 ml. of anhydrous ethyl ether was added to the flask in one portion. Reaction commenced almost immediately. After adding 25 ml. of ether to the reaction mixture in the flask, addition of the remainder of the halide solution was continued with refluxing and stirring. After addition of 10 ml. of the halide solution, the remainder of the halide solution was diluted with 20 ml. of additional ether and addition continued over a period of 1 hour with vigorous stirring. A 3-ml. aliquot of the clear solution was analyzed for total alkalinity

and found to contain 0.94 meq. per ml. of solution. The total 59 ml. of solution thus contained a total of ca. 56 meq. of t-butylmagnesium chloride, i.e., the yield was 56 per cent.

By means of a syringe, 35 ml. of a 1.44N solution of t-butyllithium in n-pentane was added rapidly to the stirred solution of Grignard reagent. Some heat was evolved and formation of a light gray precipitate of lithium chloride was noted. After it was stirred for a few minutes, the mixture was allowed to settle. Aliquots of the clear supernatant solution were withdrawn for chloride and total base analyses, which showed 0.50 meq. of chloride and 1.47 meq. of total base per ml. of solution. By means of a syringe, an additional 20 ml. of 1.44N t-butyllithium solution was added rapidly to the stirred mixture and stirring was continued for another hour. After allowing the mixture to settle, analyses of aliquots from the clear colorless supernatant solution showed 0.016 meq. of chloride, 0.016 meq. of lithium, 1.62 meq. of magnesium, 1.62 meq. of active alkyl, and 1.63 meq. of total base per ml. of solution. The yield of di-t-butylmagnesium solution thus obtained was essentially quantitative, based on t-butylmagnesium chloride.

This solution could not be freed of base (ethyl ether) by codistillation with added hexane solvent at atmospheric pressure, apparently due to facile decomposition to MgH_2 and butene-1. It could not be freed of base at ordinary temperatures by vacuum distillation at 0.1 mm. pressure.

2. Preparation of Methylisobutylmagnesium

A solution of Grignard reagent was prepared from 0.2 g. atoms of magnesium (turnings) and 0.2 mole of isobutyl chloride in 200 ml. of

anhydrous ethyl ether (92 per cent yield). To this solution was added as rapidly as possible with stirring, 200 ml. of a 0.92N solution of methyllithium in ethyl ether. The mixture was stirred for 2 hours and then allowed to settle overnight. The clear supernatant solution (analysis of which showed a ratio of Mg:Li:Cl of 16:1:3) was distilled and the ether solvent replaced with benzene. The residual solution was centrifuged and the clear viscous supernatant solution on analysis showed a 1.45N total base, a 1.41N active alkyl and less than 0.01 in chlorine content. Both VPC and NMR indicated an excess of methyl over isobutyl groups, ca. 1.2-1.3 methyls to one isobutyl.

3. Preparation of Methyl-s-Butylmagnesium

To a volume of 77 ml. of 2.20N s-butylmagnesium chloride in ether, prepared routinely, was added 134 ml. of 1.23N methyllithium solution in ether. Some heat was generated and a precipitate formed. After stirring overnight, the mixture was allowed to settle. The clear, colorless supernatant solution was analyzed and found to be 1.64 N in total base and 0.057N in chloride ion. NMR analysis of the solution showed the ratio of s-butyl to methyl groups in the organometallic to be one.

4. Preparation of t-Butylphenylmagnesium

To 50 ml. of a 1.44N solution of t-butyllithium in n-pentane was added as rapidly as possible and with vigorous stirring, 29 ml. of a 2.4-2.5N solution of phenylmagnesium chloride in THF. Boiling of the pentane occurred, but the reaction subsided quickly after all of

the PhMgCl had been added. After it was stirred for 2 hours, the mixture was allowed to settle, yielding two liquid layers besides the white solid LiCl . After distillation to remove most of the n-pentane, only one clear liquid layer remained. NMR analysis of this layer showed the ratio of t-butyl to phenyl groups in the organometallic to be 1.1.

5. Preparation of Diisobutylmagnesium

To a solution of Grignard reagent prepared from 2.43 g. (0.1 g. atom) of magnesium turnings and 9.3 g. (0.1 mole) of isobutyl chloride in 100 ml. of ethyl ether (90 per cent yield) was added 90 ml. of an 0.96N solution of isobutyllithium in ethyl ether prepared from 1.4 g. (0.2 g. atom) of lithium metal wire (containing 0.8 per cent sodium) and 9.3 g. of isobutyl chloride in 100 ml. of ethyl ether (87 per cent yield). The mixture was refluxed for 5-10 minutes and was allowed to stir for 5-10 minutes longer and then to settle. Analysis of the supernatant solution showed 0.84N total base, 0.02N chloride, 0.88N Mg, and 0.02N Li. The clear supernatant solution was transferred to a distillation unit, and the ethyl ether was distilled while cyclohexane was added until the ether concentration in the distillate was 20-30 ppm. A white precipitate formed during the distillation. The mixture was allowed to cool and the white solid was filtered onto a sintered glass (M) filter funnel under nitrogen. The solid was washed with dry n-pentane, blown dry with argon, and transferred to a weighed vial (fitted with a septum) in a dry box. Analyses of the solid for

total base and ethyl ether (VPC) content showed it to possess a neutral equivalent of 66 (theory 69) and no ethyl ether. It had a solubility in benzene of 0.135 meq./ml.

6. Preparation of Di-n-butylmagnesium from Simultaneous Preparation of n-Butyllithium and n-Butylmagnesium Chloride

A crystal of iodine and 5 ml. of a solution of 17.5 (0.19 moles) of n-butyl chloride in 25 ml. of ether were added to 150 ml. of ether and 2.4 g. (0.1 g. atom) of magnesium (turnings) in a 500 ml. 3-neck flask equipped with reflux condenser, mechanical stirrer, and dropping funnel. After reaction began, a weight of 4.7 g. of lithium dispersion (30 weight per cent in mineral oil) containing 1.4 g. lithium metal (0.2 g. atom) was added. There was a slight heat of reaction evident on mixing the reagents. The remainder of the n-butyl chloride solution was added over a 1 hour period, while the mixture was refluxed, and the mixture was stirred for 15-20 minutes longer. It was then cooled to room temperature and allowed to settle. Analysis of the supernatant solution showed 1.04N total base, 0.39N Li, 0.60N Mg, and 0.02N Cl content. The yield of di-n-butylmagnesium was 61 per cent (based on n-butyl chloride).

C. PREPARATION OF DIALKYL MAGNESIUM REAGENTS FROM ORGANOLITHIUM
REAGENTS AND ANHYDROUS MAGNESIUM CHLORIDE

1. Preparation of Di-s-butylmagnesium

a. From dimethyl ether-solvated by product $MgCl_2$. The magnesium chloride used in the following preparation was produced as a solid by-product in the direct reaction of isopropyl chloride and magnesium turnings

in a benzene solution containing dimethyl ether (DME) following the procedure given on page 130 for the direct preparation of diisopropylmagnesium.

To a stirred slurry of about 24 g. (0.25 moles) of magnesium chloride in 125 ml. of benzene was added 150 ml. of a 1.3N s-butyllithium (0.2 moles) solution in cyclohexane. The temperature of the mixture rose to 35°C and then slowly dropped to below 30°. After further stirring overnight, Gilman Color Test IIa on the supernatant solution was negative. NMR analysis showed a ratio of 1.8 moles of DME to 1 mole of di-s-butylmagnesium. Another volume of 77 ml. of 1.3N s-butyllithium (0.1 moles) solution was added to the stirred reaction mixture and after several hours, Color Test IIa was again negative. A third charge of 77 ml. of s-butyllithium solution (0.1 mole) was added and after stirring for ca. 2 hours, Color Test IIa was negative. Decantation yielded 365 ml. of a 0.98N (0.36 moles, 90 per cent yield) solution of di-s-butylmagnesium. Analysis of the solution for concentrations of total base, active alkyl and magnesium content showed the concentrations to be equivalent to each other within experimental error. Essentially no chlorine(<<0.01N) could be found in the solution.

b. From ether-desolvated by-product MgCl₂. The solids in the slurry from the desolvation experiment described on page 127 were washed several times with benzene, which left the MgCl₂ free of ethyl ether. These solids were then successfully reacted with s-butyllithium in cyclohexane exactly as just described above to give directly a solution of di-s-butylmagnesium free of ether.

c. From ether-desolvated MgCl_2 by-product from reaction of a Grignard reagent with chlorine. A Grignard reagent was prepared from 24.3 g. (1.0 g. atom) of magnesium turnings and 92.5 g. (1.0 mole) of s-butyl chloride in 500 ml. of anhydrous ethyl ether. Chlorine gas, diluted with argon, was bubbled into the vigorously stirred solution for 3 hours. During the passage of chlorine, intermittent bright flashes of light appeared (chemiluminescence) every one to two seconds. Toward the latter part of the reaction, a grey-black vapor was noted in the flask and condenser. Chemiluminescence has been previously observed on reaction of Grignard reagents with oxygen.⁷

The solvent refluxed spontaneously, and a thick, porridge-like mass formed in the flask. Analysis of the supernatant solution for total base showed that a 70 per cent consumption of s-butylmagnesium chloride had occurred. After 300 ml. of benzene was added to the flask, most of the ether was removed by distillation. The residual mixture was filtered and the solids washed three times with benzene on a sintered glass funnel. The salts were transferred as a slurry in benzene to a distillation unit and the ether was distilled with the aid of benzene and then cyclohexane. Distillation was continued until a hydrolyzed sample of the slurry showed the presence of less than 1 mole per cent ethyl ether compared to MgCl_2 . Fifty milliliters of the slurry was reacted with 50 ml. of 1.3N s-butyllithium in cyclohexane. Heat was noted and after 2 minutes, Color Test IIa was negative. All properties (NMR, VPC and Cl, Mg, Li, and total base contents) of the resultant solution were those of di-s-butylmagnesium free of ethereal solvation.

d. From dimethyl ether-solvated commercial anhydrous MgCl_2 .

Two hundred ninety milliliters of a clear filtered solution was obtained from a reaction of 360 ml. of 1.0N s-butyllithium in n-hexane with 20.8 g. (0.22 moles) of powdered anhydrous MgCl_2 and 20 g. (0.44 moles) of dimethyl ether. This solution, which was 0.86N in total base, was placed in a 500-ml. 3-necked round-bottom flask equipped with an 18-inch Vigreux column attached to a distillation head, condenser, and distillate receiver. After distillation of 200 ml. of solvent, an equal volume of fresh hexane was added to the flask. Thereafter, five 40-ml. fractions of solvent were distilled consecutively. The per cent DME in these five cuts were, respectively, 1.8, 1.1, 0.83, 0.65 and 0.12, as determined by VPC. A one milliliter sample of the residual solution (76 ml.) in the distilling flask was solvolyzed by adding it slowly (via a syringe) to 3 ml. of isopropyl alcohol at 0° contained in a centrifuge tube fitted with a rubber septum. After centrifugation, the clear supernatant solution was analyzed by VPC for DME and n-butane. This analysis indicated a molar ratio of n-butane:DME of 12:1 or an initial molar ratio of di-s-butyl magnesium to DME of 6:1.

Ten milliliters of the above residual solution was further desolvated by distillation from a smaller flask attached to a Vigreux column and fractionating head. During the distillation, the hexane solvent was replaced with benzene. After distillation of about 50 ml. of solvent, some decomposition or cracking of the product began to be apparent and distillation was discontinued. NMR analysis of the residual solution showed the absence of DME.

e. From ethyl ether-activated, desolvated commercial anhydrous MgCl_2 . About 150 g. of powdered anhydrous MgCl_2 and 250 ml of anhydrous ether were placed in a 500-ml. Morton flask equipped with a Stir-O-Vac high speed stirrer and reflux condenser. After the mixture had been stirred vigorously for several hours, it thickened appreciably and could no longer be stirred effectively. Benzene was added and distillation was carried out to remove ethyl ether. As the ether was being removed, the mixture became thinner and was more readily stirred. After distillation of 400 ml. of benzene, the mixture was allowed to cool and settle. VPC analysis showed only a trace of ether present in the supernatant (ca. 0.01%).

Forty milliliters of the mixture (as a slurry) was centrifuged, the supernatant drawn off and 20 ml. of 1.3N s-butyllithium in cyclohexane was added to the residual MgCl_2 . The mixture was shaken by hand and a heat of reaction noted. After shaking until the mixture became cool to the touch, Color Test IIa was positive. More of the slurry was added and the mixture stirred overnight. Color Test IIa was then negative. Active alkyl analysis, total base, and a magnesium analysis all indicated that the supernatant solution was 0.6 M in di-sec-butylmagnesium.

f. From unsolvated by-product MgCl_2 . To 10 ml. of a slurry of 4.8 g. (0.05 moles) of MgCl_2 (see following paragraph) in benzene contained in a centrifuge tube fitted with a rubber septum was added 20 ml. of 1.3N s-butyllithium solution in cyclohexane. The mixture became warm on initial mixing of reagents, then cooled while it was shaken

thoroughly by hand for 10-15 minutes. The mixture was centrifuged and the supernatant, upon analysis, showed a negative Color Test IIa, 1.10N total base, 1.02N active alkyl, 1.09N magnesium, and 0.03N chloride content. NMR showed the expected sextet of lines centered 435 cps. upfield from benzene indicative of the methine proton, and VPC analysis of a sample of the hydrolyzed product (organic layer) showed n-butane as the only major hydrocarbon resulting from hydrolysis. No alcoholic impurities were found.

The MgCl_2 used above was formed as a solid by-product of the reaction between n-amyl chloride and magnesium powder in benzene following the procedure of Glaze and Selman.¹⁹ After withdrawal of the supernatant di-n-amylmagnesium solution in benzene, the MgCl_2 residue was washed four times with benzene in the centrifuge tube prior to reaction with s-butyllithium.

g. From unsolvated ball-milled lump commercial anhydrous MgCl_2 . A weight of 386 g. of lump anhydrous MgCl_2 was partially ground with a mortar and pestle under nitrogen. It was then transferred to a 1-quart capacity jar containing smooth stones (1/2 to 1 inch diameter); approximately 400 ml. of cyclohexane was added and the jar was sealed, all under nitrogen. The mixture was rolled mechanically overnight on a jar mill. The finely ground portion of the mixture was poured into 100-ml. amber bottles under nitrogen,

To the contents of one of these bottles (100 ml., 14 g. MgCl_2) was added 85 ml. of 1.3N s-butyllithium in cyclohexane. The mixture was stirred overnight. Color Test IIa was positive. The supernatant

solution on analysis, showed a 0.11N magnesium and 0.53N total base content. Thus, the extent of exchange based on total alkalinity was 21 per cent.

h. From alcohol-activated, desolvated commercial anhydrous MgCl_2 .

(1) Activation of commercial anhydrous MgCl_2 with isopropyl alcohol. The remainder of the ball-milled cyclohexane slurry of anhydrous MgCl_2 (40 g.) described above was treated with 150-200 ml. of isopropyl alcohol in a 500-ml. 3-necked round-bottomed flask equipped with a Hershberg stirrer and jacketed Vigreux column with a variable take-off fractionation head. (Lumps, 1/4 inch in diameter, of anhydrous MgCl_2 may be successfully substituted for the ball-milled slurry; these lumps readily break up to form a powder on trituration with isopropyl alcohol.) Much heat was evolved and a considerable thickening of the mixture occurred on addition of the alcohol. After about 1 hour of vigorous stirring, 100 ml. of toluene was added and distillation was begun to remove isopropyl alcohol as its toluene azeotrope. Successive portions of toluene were added to the residue to replace the solvent distilled. After distilling about 450 ml. of toluene, a sample of residual slurry was hydrolyzed. Analysis showed 1.1 moles MgCl_2 per ml. of slurry and 5 mole per cent isopropyl alcohol relative to MgCl_2 . Distillation to remove isopropyl alcohol was continued; two 300-ml. portions of toluene were distilled. (Some reaction of MgCl_2 was occurring since HCl appeared in the distillate.) Analysis of the

slurry indicated it then contained 2.5 mole per cent isopropyl alcohol relative to the MgCl_2 present.

(2) Reaction of Activated MgCl_2 with *s*-butyllithium. To 175 ml. of the above slurry containing 6.5 grams (0.068 moles) of MgCl_2 was added 90 ml. of 1.24N *s*-butyllithium in hexane. The reaction mixture was stirred vigorously, first at 40°C for 1.5 hours, then at room temperature overnight. Color Test, IIa was negative. The supernatant solution on analysis showed a 0.32N total base, 0.29N active alkyl, and 0.28N Mg content.

1. From desolvated commercial $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$. A weight of 40.6 g. (0.2 mole) of $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$ was placed in a 3-necked 500-ml. flask equipped with Hershberg stirrer and attached to a Dean-Stark trap. Three hundred milliliters of isoamyl alcohol was added and the stirred mixture was heated to the boiling point. A total of 13.5 ml. of water, from a theoretical amount of 21.6 g., was collected in the trap during a period of 4-5 hours. No further removal of water occurred during several more hours of distillation. Isoamyl alcohol was then distilled to leave a residual volume of 50 ml. The MgCl_2 was soluble at the distillation temperature, but upon cooling to room temperature, the entire mixture solidified. One hundred milliliters of tetralin was added to the solidified mixture and the contents of the flask were heated to reflux. The mass again became a clear liquid. Tetralin and isoamyl alcohol were distilled. Another 100 ml. portion of tetralin was added and the distillation was continued. A crystalline precipitate formed during this stage of the distillation. The

distillate was acidic indicating some loss of HCl, presumably by forming an oxychloride (ClMgOR). After hydrolysis of a sample of the slurry, VPC of the upper layer (on carbowax 400 at 150°) showed only a trace of isoamyl alcohol to be present. Reaction of this slurry with 100 ml. of a 1.20N solution of s-butyllithium in hexane followed by analysis of the clear supernatant showed a negative Color Test IIa and an 0.62N total base 0.62N magnesium, and 0.44N active alkyl content. The analysis indicated complete exchange of Li and Mg took place, but that some of the Mg was present as alkoxide.

j. From commercial powdered anhydrous MgCl_2 . Using powdered anhydrous MgCl_2 as obtained from Alfa Inorganics in place of the above "activated" MgCl_2 , little or no observable exchange occurred with s-butyllithium in cyclohexane even with the high-speed stirring over night.

2. Preparation of Di-t-butylmagnesium

a. From dimethyl ether-solvated by-product MgCl_2 . Solid MgCl_2 (0.08 mole), in one of the tubes from the experiment described on page was washed with benzene, resuspended in 40 ml. of benzene, and transferred to a 200-ml. 3-necked flask equipped with a magnetic stirring bar. To the stirred slurry was added 83 ml. of a 1.44N t-butyllithium solution in pentane. The mixture was stirred for several hours and then allowed to settle. Analyses on the supernatant solution showed a negative Color Test IIa, 0.96N total base and 0.96N magnesium, indicating complete exchange of Li and Mg.

b. From ether-desolvated MgCl_2 by-product from reaction of a Grignard reagent with benzyl chloride. To a slurry of 13.3 g. (0.14 moles) of MgCl_2 (see next paragraph) in 50 ml. of benzene was added, with stirring, 50 ml. of 1.8N t-butyllithium solution in benzene. After the mixture was stirred for 45 minutes, Color Test IIa was negative. Another 50 ml. of t-butyllithium solution was added and again Color Test IIa was negative after 45 minutes of stirring. The flask was then stoppered and placed in the refrigerator overnight. NMR analysis of the supernatant solution showed only one t-butyl peak, no ethyl ether, and traces of pentane. For storage, about 150 ml. of clear solution was withdrawn into an amber bottle fitted with a serum cap. Analysis showed 0.83N total base, 0.84N active alkyl and 0.82N magnesium content.

The MgCl_2 used above was prepared in the following manner. To a Grignard reagent, prepared from 0.4 mole of s-butyl chloride and 0.4 g. atom of magnesium (turnings) in 150 ml. of anhydrous ethyl ether, was added, at reflux and with vigorous stirring, 50.6 g. (0.5 moles) of benzyl chloride (Baker analyzed reagent - 99.8%). A precipitate began to form immediately and copious gas evolution was noted. (VPC of the gas indicated that it was 1- and 2-butenes and n-butane.) After addition was complete, the mixture was stirred thoroughly and then allowed to settle overnight. Gilman Color Test I on the supernatant solution was negative; this solution was found by VPC to contain 12.5 mole per cent toluene, 70 per cent 1,2-diphenylethane, and 17.5 per cent 2-methylbutylbenzene. The MgCl_2 residue in the reaction flask

was washed five times with 100 ml. portions of benzene, allowing the solids to settle each time before removing the wash. The fifth wash was found to contain about 5 weight per cent ethyl ether. The slurry after the fifth wash on analysis showed a 5.4N Mg, 6.0N Cl, and 0.00N total base content. Continued washing of the solids did not remove all of the ethyl ether. The ether was removed by continuous codistillation with benzene. The final ether content (VPC) of the supernatant solution was found to be less than 0.02 weight per cent and the slurry was used as such for reaction with organolithium compounds in hydrocarbon media.

3. Preparation of Di-n-butylmagnesium

A weight of 25.5 g, (0.267 mole) of powdered anhydrous MgCl_2 and 100 ml. of anhydrous ethyl ether were placed in a 200-ml. round-bottom, 3-necked flask equipped with a magnetic stirrer and reflux condenser. To the stirred, cooled (ice bath) mixture was added all at once 30 ml. of 3.7N n-butyllithium in benzene. After two hours, Color Test IIA was negative. The mixture was stirred and allowed to come to room temperature overnight. Aliquots of the clear supernatant solution were withdrawn for analysis and found to contain 0.76N total base, 0.76N active alkyl and 0.88N chloride. Thus, the product appeared to be in the form of n-butylmagnesium chloride, not di-n-butylmagnesium. Approximately 80 ml. of the clear supernatant solution and 50 ml. of cyclohexane were transferred to a dry 200 ml., 3-necked, round-bottom flask flushed with nitrogen and fitted with a rubber septum and a vacuum-jacketed 12

inch Vigreux column with variable take-off fractionation head and receiver. After distillation of 50 ml. of solvent and addition of another 50 ml. portion of cyclohexane, the head temperature reached 78°C. This process of distillation and replenishment of solvent to the residual solution was continued until a total of 250 ml. of solvent had been distilled. The residual solution was allowed to cool to room temperature. A total of 71 ml. of a quite mobile supernatant solution was withdrawn (some white solid residue was left) and found to contain 0.44N total base, 0.42N active alkyl and 0.01N Cl. V C analysis of a hydrolyzed sample of the solution showed that it contained less than 2 mole per cent ethyl ether relative to the di-n-butylmagnesium. Thus, about 50 per cent of the original active alkyl content remained in solution after removal of the ethyl ether.

4. Preparation of Di-neopentylmagnesium

To 147 ml. of a solution of 0.47N neopentyllithium (0.069 moles) in a pentane-dimethyl ether mixture (ca. 10:1) contained in a 3-necked, 200-ml. round-bottom flask equipped with magnetic stirring bar and reflux condenser, and cooled in an ice bath, there was added 13 g. (0.137 moles) of powdered anhydrous $MgCl_2$. After the mixture had been stirred for several hours, Color Test IIa was negative. Some evaporation of solvent occurred during reaction. Analysis of the supernatant solution showed an 0.55N active alkyl, 0.56N total base and 0.54N Mg content.

D. DIRECT PREPARATION OF DIALKYL MAGNESIUM REAGENTS
FROM MAGNESIUM METAL AND ALKYL CHLORIDES

1. Preparation of Di-*s*-butylmagnesium

a. In dimethyl ether-cyclohexane solution. A weight of 2.43 g. (0.1 g. atom) of magnesium turnings and a few crystals of iodine were placed in a 500-ml., 3-necked flask fitted with a thermometer (-100 to +50°), mechanical stirrer, Dry Ice condenser and graduated dropping funnel. Enough DME (dried by passage over silica gel) was condensed into the flask to cover the turnings and 1-2 ml. of *s*-butyl chloride, from a total of 9.3 g. (0.1 mole) was added. After addition of a few drops of ethylene dibromide, the reaction appeared to begin as indicated by the disappearance of the iodine color and the development of a cloudy solution. The remainder of 100 ml. of DME was condensed into the flask at -25°C and the remainder of the *s*-butyl chloride was added. Reaction was slow and 100 ml. of cyclohexane was added gradually to the flask. The mixture was allowed to warm slowly to room temperature and allowed to stir at room temperature for two days. A white slurry formed during this time. The reaction mixture was heated to 45°C for 2 hours, resulting in almost complete disappearance of the magnesium turnings. The reaction mixture was allowed to cool and settle overnight. Analysis of the clear supernatant solution showed a 0.77N total base and 0.085N chloride content. Thus, the yield of di-*s*-butylmagnesium appeared to be quantitative; the NMR spectrum of the solution was identical with a similar solution prepared with the authentic magnesium alkyl.

b. By vacuum-stripping of solvent from the Grignard reagent, followed by re-solution in benzene. A solution of Grignard reagent, prepared from 9.7 g. (0.4 g. atom) of magnesium turnings and 37 g. (0.4 moles) of s-butyl chloride in 150 ml. of anhydrous ethyl ether, showed upon analysis a total base concentration of 2.20N and an active alkyl concentration of 2.13N. Eighty-five milliliters of this solution was transferred to a 200-ml., 3-necked round-bottom flask equipped with a capillary tube for admitting nitrogen below the liquid level and a distillation head leading to a receiver and vacuum line. The flask was heated with an oil bath. Solvent was removed under vacuum to about 3-4 mm pressure with a bath temperature of 75°C. The mixture eventually became quite viscous and slowly evolved ether. The residue was evacuated for 12 hours at this temperature. After returning to room temperature and atmospheric pressure, the flask contents, a viscous mass, were stirred with about 50 ml. of benzene. The mixture thinned out, with a granular white precipitate being evident in the mixture. On analysis, an ethyl ether to di-s-butylmagnesium molar ratio of 0.7 was found. The solution had a total base and active alkyl concentration of 1.7N and negligible Cl content. It was desolvated by continuous codistillation with a hydrocarbon solvent as previously described.

c. In diethyl ether-benzene solution. A weight of 10 g. (0.415 g. atom) of magnesium turnings were activated with iodine and mixed with 200 ml. of benzene and 50 ml. of anhydrous ethyl ether. The mixture was heated to reflux and 42 ml. (0.39 moles) of s-butyl chloride added portionwise to the vigorously stirred mixture. After 16 ml. of the halide

had been added, reaction was initiated by addition of a small portion of s-butyl magnesium chloride in ether. The reaction proceeded vigorously and intermittent cooling with an ice-bath was necessary. When the initial reaction had subsided, slow halide addition was continued. The reaction mixture was heated at reflux (77°C) for 1 hour and then allowed to cool to room temperature. No $MgCl_2$ precipitate was in evidence at this time. Total base concentration was found to be 1.33N indicating the yield of s-butylmagnesium chloride to be essentially quantitative. The solution was allowed to stand overnight, still no precipitation was evident.

Thirty milliliters of this solution was placed in a distillation apparatus as described above and desolvated as previously described. Slow precipitation of $MgCl_2$ began as soon as solvent started distilling. When between 10 and 15 ml. of solvent had been removed, the mixture was allowed to cool and settle. Analysis of the supernatant showed a 2.48N total base and 1.85N chloride content. The molar ratio of ether to carbon bound magnesium was 2:1. Thus, removal of 40-50 per cent of the solvent resulted in precipitation of 25 per cent of the $MgCl_2$, leaving an equivalent amount of di-sec-butylmagnesium in solution.

2. Preparation of Di-n-butylmagnesium

A weight of 2.43 g. (0.1 g. atom) of magnesium metal powder (40 mesh) was heated with a crystal of iodine in a few ml. of cyclohexane. A few ml. of a solution of 9.25 g. (0.1 mole) of n-butyl chloride in 80 ml. of cyclohexane was added to the mixture. The

iodine color disappeared and a cloudiness formed in the solution. The mixture was heated to reflux and the remainder of the halide solution was added over a period of 2 hours with vigorous stirring with high speed stirrer. Stirring and refluxing were continued for several hours after addition of the halide solution was complete. A white crystalline precipitate formed on the walls of the flask during this time. After the reaction mixture was cooled, the white precipitate was found to contain active alkyl, but none was found dissolved in the supernatant solution. DME was slowly bubbled into the mixture until all the white solid had dissolved. The mixture was allowed to settle and the clear yellow supernatant solution found to contain negligible Cl and to be 0.58N total base and in active alkyl. The yield of di-n-butylmagnesium was thus ca. 60 per cent.

3. Preparation of Di-n-amylmagnesium

Into a 200-ml., 3-necked, round-bottom flask equipped with Hershberg stirrer, reflux condenser, and 100-ml. graduated dropping funnel was placed 2.68 g. (1.1 g. atom) of magnesium turnings (under nitrogen) and a crystal of iodine. The flask was heated to 85° by means of an oil bath and 1-2 ml. from a total of 10.6 g. (0.1 mole) of 1-chloropentane was added. The reaction began readily with disappearance of iodine color and the appearance of fuming. The remainder of the halide was added over a 1 hour period while vigorous stirring and heating at reflux was maintained. About 1 hour after addition was complete, everything in the flask became dry and lumpy. Fifty milliliters of benzene was added with vigorous

stirring and heating at reflux. After one hour another 50 ml. of benzene was added and stirring and heating continued for an additional 3-4 hours. The mixture had become viscous during this time and was allowed to cool and settle overnight. The mixture was centrifuged. On analysis, the clear, colorless, viscous supernatant solution showed an 0.27N total base and 0.25N active alkyl content, but no residual 1-chloropentane. n-Pentane was the only new organic product found after hydrolysis.

4. Preparation of Diisopropylmagnesium

A weight of 9.7 g. (0.4 g. atom) of magnesium turnings were activated with iodine and covered with 100 ml. of dry benzene. Ten grams (0.2 mole) of dimethyl ether was condensed into the mixture and 2.3 ml. of isopropyl chloride was added. No reaction occurred. After one-third of a solution of the remainder of 31.4 g. (0.4 mole) of isopropyl chloride in 125 ml. of benzene had been added, reaction began as evidenced by a rise in temperature. Intermittent cooling with an ice bath kept the temperature between 35 and 45°C while addition of the halide solution was continued over a one hour period. During this time an additional 34 g. (0.74 moles) of dimethyl ether was also added. The reaction mixture was stirred and heated to 50° for two hours. The mixture was then allowed to cool and settle overnight. One hundred fifty milliliters of the clear colorless supernatant solution was removed and the remainder of the slurry of MgCl_2 and unreacted magnesium turnings was transferred to two 50 ml. centrifuge tubes and centrifuged. Sixty milliliters of the supernatant

solution was removed and combined with the 150 ml. of product solution. This solution showed 1.45N total base and 1.35N active alkyl, for an apparent yield of 80 per cent of diisopropylmagnesium.

E. . PREPARATION OF MIXED SOLUBLE DI-n-BUTYLMAGNESIUM
COMPLEXES WITH s-BUTYLLITHIUM AND n-BUTYLLITHIUM

1. Preparation of Di-n-butylmagnesium.

A weight of 16.7 g. (0.176 mole) of powdered anhydrous $MgCl_2$ was mixed with 75 ml. of anhydrous benzene in a nitrogen-flushed 200-ml., 3-necked, round-bottom flask equipped with reflux condenser, serum cap, and magnetic stirring bar. Thirty milliliters of anhydrous ethyl ether (0.3 moles) was added followed by 30 ml. of 3.7N n-butyllithium in benzene. The mixture became warm and was cooled and stirred in an ice bath for 1-2 hours. After allowing the mixture to come to room temperature, it was stirred overnight; analysis of the clear supernatant showed a negative Color Test IIa and 0.8N total base and 0.3N Cl content. One hundred ten milliliters of the clear supernatant solution was transferred to a 200-ml. flask fitted for distillation as described above and 9.2 ml. of 3.7N n-butyllithium in benzene added to react with the chloride ion present in solution. After it was stirred 30 minutes, the solution was analyzed for chloride ion. None was found. The ether was distilled using benzene as codistillate; solid di-n-butylmagnesium precipitated during the distillation. After 200 ml. of benzene had been distilled, ether was still found (VPC) to be present in the slurry. The slurry was then heated to 120° , almost to dryness, while

another 70-80 ml. of distillate was collected. Benzene was added to bring the total volume to 100 ml. while the mixture was allowed to stir and cool to room temperature.

2. Preparation of Butyllithium-Butylmagnesium Complexes

Three 5 ml. aliquots of the stirred slurry were placed in nitrogen-flushed centrifuge tubes fitted with serum caps. The following reagents were added to each tube: 0.81 ml. of 1.24N s-butyllithium in cyclohexane (tube No. 1); 0.625 ml. of 1.6N n-butyllithium in hexane plus 0.2 ml. of cyclohexane (tube No. 2); 0.81 ml. of cyclohexane (tube No. 3). The tubes were shaken well, centrifuged and the supernatant analyzed for total base by titration and for ethyl ether content by NMR. The total base contents in each of the three tubes were as follows: 4.70 meq. in tube 1; 4.47 meq. in tube 2; 0.70 meq. in tube 3. The residue in tube 3 was dissolved in THF and found to contain 3.88 meq. total base. Thus the total base content present in 5 ml. of original slurry was 4.58 meq. The percentage solubilizations of the di-n-butylmagnesium by n- and s-butyllithium reagents calculated from these data were 76 and 81 per cent respectively. Subtracting the amount of di-n-butylmagnesium itself soluble in this medium (determined with tube 3 above), the mole ratios of di-n-butylmagnesium to n- and s-butyllithium reagents in the solutions were found to be 1.9 and 2.0 respectively.

F. PREPARATION OF SOLUBLE, MIXED DIALKYL MAGNESIUM COMPLEXES
FROM INSOLUBLE DIALKYL MAGNESIUM COMPOUNDS

1. Preparation of a Soluble Diisobutyl-Di-*s*-butylmagnesium Complex

To 0.35 g. (5.0 meq.) of solid diisobutylmagnesium (prepared by reaction of isobutylmagnesium chloride with isobutyllithium in ethyl ether followed by desolvation with cyclohexane) was added 5 ml. of a 1.35N di-*s*-butylmagnesium solution in *n*-hexane and 2.5 ml. of cyclohexane. Complete dissolution of the diisobutylmagnesium (which was previously found to be soluble to the extent of only 0.09 moles/liter in cyclohexane) occurred yielding a solution having a total base concentration of 1.56N, which may be compared to a calculated value of 1.57N.

2. Preparation of a Soluble Diisobutyl-Di-*t*-butylmagnesium Complex

To 0.8167 g. (10.86 meq.) of solid diisobutylmagnesium suspended in a few ml. of benzene was added 7.54 ml. of 1.57N di-*t*-butylmagnesium in benzene (desolvated). After thorough mixing and centrifugation, the clear supernatant solution was analyzed for the ratio of *t*-butyl to isobutyl groups by NMR. An approximate 1:1 ratio was found, based on the ratio of *t*-butyl protons to methyl protons of the isobutyl group.

3. Preparation of a Soluble Di-*n*-butyl-Di-*t*-butylmagnesium Complex

To a slurry of 13.3 g. (0.14 moles) of activated MgCl_2 (ether-free) in 50 ml. of benzene was added with stirring 40 ml. of 1.75N *t*-butyllithium in benzene. After stirring the mixture for 15-20 minutes,

19 ml. of 3.7N n-butyllithium in benzene was added. The mixture immediately became quite warm. After stirring until cool, analysis of the supernatant solution showed a negative Color Test IIa and 1.03N total base, 1.02 active alkyl and 1.04 Mg contents. NMR analysis showed a t-butyl to n-butyl group ratio of 1:0.8.

G. INSOLUBLE COMPLEXES OF DIALKYL MAGNESIUM REAGENTS WITH
TRIETHYLENEDIAMINE AND METHYLTRIETHYLENEDIAMINE

1. Complexes with Triethylenediamine

a. Di-s-butylmagnesium-triethylenediamine complex. To 5.0 ml. of a 0.85N solution of di-sec-butylmagnesium (2.13 mmoles) in benzene-cyclohexane (desolvated) in a nitrogen-flushed dry centrifuge tube fitted with a serum cap was added 3.0 ml. of an 0.69M solution of triethylenediamine (TED) in cyclohexane (2.07 mmoles). A crystalline precipitate formed immediately. After shaking the mixture thoroughly, it was centrifuged and the solids washed twice with cyclohexane. NMR analysis of a solution of the solid in THF showed a triethylenediamine (all protons equivalent) to di-s-butylmagnesium (methine proton) ratio of 0.9 ± 0.1 .

In another experiment, 3.2 ml. of 0.69M TED (2.2 mmoles) in cyclohexane was added to 9.10 ml. of 0.98N di-s-butylmagnesium (4.4 mmoles) in benzene. A fine-grained white crystalline precipitate was formed which was centrifuged and the solids were washed three times with n-pentane. The centrifuge tube was heated in an oil bath at

80-90° and the solids blown dry with nitrogen. The tube was transferred to a glove bag and some of the dry solid transferred to a dry nitrogen-flushed melting point capillary. The melting point capillary was quickly sealed in a flame. The solid melted with decomposition (gas evolution) at 201-203°C. The remaining solid in the centrifuge tube was weighed on an analytical balance (0.5159 grams) and dissolved in 5 ml. of anhydrous THF. Active alkyl analysis of this solution showed the presence of 2.09 mmoles of di-s-butylmagnesium. The equivalent weight of the solid thus obtained was 248 (theory for $(C_4H_9)_2Mg \cdot C_6H_{12}N_2$, 250).

b. Other dialkylmagnesium-triethylenediamine complexes. In a similar manner there were prepared 1:1 complexes of triethylenediamine and di-n-butylmagnesium and di-t-butylmagnesium. No crystalline precipitate was formed when di-n-amylmagnesium solution in benzene was treated with an excess of 0.69M TED solution, regardless of cooling or concentration of the solution. Diisobutylmagnesium and diisopropylmagnesium were too insoluble in hydrocarbon solvents to permit the formation of crystalline precipitates with TED. On the other hand, in the presence of enough dimethyl ether to permit their solubilization in hydrocarbon solvents, they formed non-stoichiometric crystalline complexes with TED containing dimethyl ether. Attempts to obtain TED complexes of a mixed magnesium alkyl from a ~~benzene-cyclohexane~~ solution of t-butyl-n-butylmagnesium resulted in preferred complexation of di-t-butylmagnesium accompanied by a co-precipitation of insoluble di-n-butylmagnesium.

2. Complexes with Methyltriethylenediamine

a. Di-*s*-butylmagnesium-methyltriethylenediamine complex. A volume of 5.5 ml. of 0.85N di-*s*-butylmagnesium solution in benzene-cyclohexane (desolvated) was added to a centrifuge tube containing 0.3 ml. of methyltriethylenediamine (MTED) dissolved in 3 ml. of benzene (7.92 μ moles/ml.). The fine crystalline precipitate which formed slowly was centrifuged and the supernatant solution drawn off. The solid (0.54 g.) was recrystallized from 8-10 ml. of benzene to give monoclinic prisms, which on washing and drying, (as described for TED complexes) melted at 160°C (dec.) in a sealed tube. NMR analysis of a solution of these crystals in THF showed the presence of a 1:1 (*s*-Bu)₂Mg·MTED complex based on integration of the methylene protons of the MTED and the methine proton of the di-*s*-butylmagnesium.

b. Other dialkylmagnesium-methyltriethylenediamine complexes. Similarly there was prepared the 1:1 di-*tert*-butylmagnesium-MTED complex. Recrystallization from benzene gave star-shaped prisms, m.p. 163° (dec.). No crystalline precipitate was formed between MTED and di-*n*-butylmagnesium in benzene-cyclohexane regardless of cooling or concentration of the solution. MTED complexes of mixed magnesium alkyls such as *t*-butyl-isobutylmagnesium and methyl-isobutylmagnesium yielded non-stoichiometric complexes which melted over a wide range; NMR analysis showed a molar ratio of *t*-butyl to isobutyl groups in the former complex to be 1.62, while the molar ratio of methyl to isobutyl groups in the latter complex was found to be 1.48. In the

case of the methyl-isobutylmagnesium TED complex, the average ratio of dialkylmagnesium reagent to MTED was 4:1, indicating a breakup of the mixed alkylmagnesium with preferred complexation of dimethylmagnesium and coprecipitation of uncomplexed diisobutylmagnesium.

H.. METALLATIONS EFFECTED WITH DIALKYL MAGNESIUM REAGENTS

1. Metallation of Resorcinol Dimethyl Ether

a. In the absence of base. Thirty-four milliliters of 0.77N di-s-butylmagnesium (13.5 mmoles) in hexane-cyclohexane was placed in a 50-ml., 3-necked, conical-shaped flask which had been flushed with nitrogen and equipped with a reflux condenser, magnetic stirring bar and rubber septum on one neck. A volume of 3.8 ml. (27 mmoles) of resorcinol dimethyl ether (DMR) was added to the flask, stirring begun and the contents heated to reflux for 16 hours. Large lacy crystals formed in the mixture. After allowing the mixture to cool, the wet crystals were transferred under nitrogen to a centrifuge tube (using a Glove Bag to effect the transfer) and dissolved in 1 ml. of THF. The clear THF solution formed was analyzed by NMR, the aromatic region showed two signals, a 2:1 ratio of protons ortho and meta to methoxy groups in metallated resorcinol dimethyl ether; the aliphatic region showed a methine proton (like that in di-s-butylmagnesium) in a 1:1 ratio to the meta proton. NMR analysis of the supernatant solution from these crystals showed only unreacted resorcinol dimethyl ether (DMR) to be present, no di-s-butylmagnesium. (The remainder of the

reaction mixture was carbonated by pouring it into a Dry Ice-ether slurry, but evaporation of the carbonated slurry on a steam bath was inadvertently carried to dryness, which caused thermal decomposition of the salt to DMR and MgCO_3 .)

b. In the presence of base.

(1) THF and TMEDA. Employing the same procedure as described above, on a comparable scale, separate runs were carried out in which 2 mole equivalents of THF and in which 2 mole equivalents of TMEDA per mole of magnesium reagent were each added to the reaction solutions. No metallation occurred. NMR analysis showed only unreacted starting materials to be present after 16 hours reflux of the reaction solutions.

(2) THF plus potassium-*t*-butoxide. To the above run containing THF, after the 16 hours of reflux, there was added an amount of solid potassium *t*-butoxide equal, in moles, to twice the moles of di-*s*-butylmagnesium present. The mixture immediately turned red and then, after a few minutes almost black. A sticky precipitate formed. The reaction mixture was carbonated by pouring it into a stirred Dry Ice-ether slurry. The ether was carefully evaporated on a steam bath and the residual dry solid was washed three times with ether in a centrifuge tube fitted with a rubber septum. Some of the slurry was removed and the solid remaining in the tube was washed twice more with ether, and then blown dry under nitrogen. The solid was dissolved in D_2O and after centrifugation, the clear supernatant solution was examined by NMR. The salt of 2,6-dimethoxybenzoic acid was found to be present as well as the salt of 2-methylbutyric acid, presumably as their

potassium salts; integration of the aromatic protons in the 2,6-dimethoxybenzoic acid salt and the methine proton in the 2-methylbutyric acid salt gave a ratio of the two salts (aromatic:aliphatic) of 57:43.

(3) TMEDA plus lithium t-butoxide. To the run in (1) above containing TMEDA, after the initial 16 hours of reflux, there was added a molar excess of lithium t-butoxide (relative to the moles of R_2Mg present) as a hexane slurry. Only a slight deepening in color was noted. The solution was heated to reflux for 16 hours. During this time gases were evolved and a white precipitate formed. On cooling, a sample of the slurry was centrifuged. NMR analysis of the clear supernatant showed the presence of metallated product (cf. 1.a. above) as well as unreacted DMR. The solid residue, although sparingly soluble in THF, also showed the presence of metallated DMR by NMR analysis. The reaction mixture was carbonated by pouring it into a stirred Dry Ice-ether slurry and then the carbonated mixture was allowed to evaporate to dryness at room temperature. A portion of the residue was washed twice with ether and mixed with 3 ml. of D_2O . After centrifugation, an NMR examination of the supernatant solution showed the presence of the salt (presumably the lithium salt) of 2,6-dimethoxybenzoic acid, but no 2-methylbutyric acid salt. The yield thus appeared essentially quantitative.

2. Metallation of Thiophene

a. Metallation without Lewis base. A solution of 25 ml. of 0.77N di-s-butylmagnesium and 1.5 ml. (1.6 g., 19.3 μ moles) of thiophene in

hexane-cyclohexane was stirred overnight. NMR analysis of the solution showed no metallated thiophene and no loss of the magnesium alkyl. Heating the solution overnight at reflux resulted in the formation of a sticky precipitate on the walls. NMR analysis of both the supernatant solution and a solution of the precipitate in THF showed the absence of di-s-butylmagnesium. The THF solution contained metallated thiophene. Carbonation and work-up of the solution in the usual manner produced 2-thiophenecarboxylic acid in at least 34 per cent yield; a portion was inadvertantly lost during work up.

b. Attempted metallation with Lewis base. Addition of a molar excess of tetrahydrofuran (relative to the di-s-butylmagnesium) to another reaction mixture of the reagents used above did not effect the metallation of the thiophene after stirring for 16 hours at room temperature nor after 12 hours at reflux. THF solutions of the 1:1 complexes of di-s-butylmagnesium and of di-t-butylmagnesium with triethylene-diamine were also ineffectual in metallating thiophene even with heating at reflux for 24 hours.

c. Metallation with THF plus potassium t-butoxide. To the unreacted mixture in b. above containing thiophene, di-s-butylmagnesium and an excess of THF, there was added in solid form, 2 moles of potassium t-butoxide per mole of di-s-butylmagnesium. The mixture immediately turned red, then almost black, and generated heat. A considerable amount of black material precipitated. The mixture was carbonated and worked up to obtain a D₂O solution of carboxylic acid salts in the usual manner.

NMR examination of the D₂O solution of salts showed the presence of 2-thiophene carboxylic acid (presumably as the potassium salt) and t-butyl alcohol. Only a very small amount of 2-methylbutyric acid salt was found. The ratio of aromatic to aliphatic acid was about 10:1.

d.. Metallation in the presence of s-butyllithium plus TMEDA.

To 2 ml. of a solution containing 0.8 mmoles of di-n-butylmagnesium and 0.4 mmoles of s-butyllithium in a mixed hydrocarbon solvent there was added 0.17 ml. (2 mmoles) of thiophene and 0.2 ml. (1.3 mmoles) of TMEDA. After standing at room temperature for 5 days, the supernatant solution was examined by NMR. Metallatedthiophene was present as well as di-n-butylmagnesium. NMR signals of the latter could be seen clearly as an upfield triplet in the "organometallic region" around TMS. No sextet of lines indicating a s-butyl group could be found in that region.

3. Metallation of γ -Picoline

In an experiment comparable to 1.a. above, 1.80 g. (1.90 ml., 19.3 mmoles) of γ -picoline was added to 25 ml. of a 0.77N di-s-butylmagnesium in hexane-cyclohexane solution at room temperature. An immediate red color developed and deepened over a 16 hour period. A glossy dark solid had formed during this time. The supernatant solution was examined by NMR and found to contain a 3:1 mixture of metallated to unmetallated γ -picoline, as determined by integration of the methylene and methyl protons respectively. (The methylene protons were shielded

with respect to methyl protons by 25 cps). The methine proton sextet of the s-butyl group in the original magnesium reagent was absent from the spectrum. The glossy solid was dissolved in THF but a sticky material formed and coating the walls of the NMR tube, precluding taking a spectrum.

Both the original supernatant solution and the THF solution were added to a pre-cooled (0°C) solution of 3.0 ml. (3.6 g., 26 μ moles) of benzoyl chloride in 15 ml. of ether. A precipitate formed and the mixture became quite thick. More THF (20 ml.) and benzoyl chloride (5 ml.) were added and the mixture became less viscous. After stirring for 0.5 hr., water was added to hydrolyze the mixture. The layers were separated and to the water solution there was carefully added saturated aqueous Na₂CO₃ solution until gas evolution seemed to cease. The water layer was then extracted with ether. This ether solution still contained some unreacted benzoyl chloride; it was evaporated on a steam bath leaving a dark brown oily residue which did not crystallize on cooling. This residue was extracted with hot n-hexane and on cooling, white crystals formed along with some dark viscous oil. The crystals were dried and found to melt at 113-117° (lit. m.p. of γ -phenacylpyridine, 115°C). The remainder of the crystallized residue was dissolved in THF. NMR examination of this solution showed that the dissolved material was γ -phenacylpyridine.

4. Metallation of Toluene

a.: Attempted metallation. A volume of 100 ml. of 0.77 N di-s-butylmagnesium in hexane-cyclohexane was distilled under vacuum to 0.02

mm. and 40°C to give a light yellow oily liquid. After returning the system to atmospheric pressure with dry nitrogen, 50 ml. of toluene was added and the mixture stirred thoroughly. Analysis for total base showed that the toluene solution was 1.33N. This di-s-butylmagnesium had never been in contact with base, i.e., it was not produced by desolvation.

Twenty milliliters of the toluene solution and 4 ml. (26.6 mmoles) of TMEDA were mixed together and heated to 75°C for 16 hours. No change in appearance of the solution was noted. The solution was then heated to reflux for 16 hours. NMR examination showed no loss of di-s-butylmagnesium relative to TMEDA. The solution was carbonated and the salts were evaporated to a dark red viscous residue on a steam bath. The residue was then heated in an oil bath at 150° for a short time; on cooling it solidified to a red glass. To a portion of this glass was added D₂O and Na₂CO₃, but very little solution appeared to occur. Benzene and hexane were added; the mixture was stirred well and then heated in an oil bath to remove the organic solvents. The resulting aqueous (D₂O) suspension was centrifuged and an NMR spectrum taken on the supernatant solution. Only the salt of 2-methylbutyric acid was found; there were no NMR signals in the aromatic region.

b. Metallation with partially pyrolyzed di-s-butylmagnesium.

Volumes of 27 ml. of toluene and 15 ml. of a 1.68 M solution of di-s-butylmagnesium (25 mmoles) in n-hexane which had been partially desolvated of DME, were added to a 50-ml. nitrogen-filled flask equipped for distillation with a Vigreux column. Ten milliliters of hexane was

distilled slowly, during which cracking of di-s-butylmagnesium was apparent; a white precipitate formed and fumes were evolved. The mixture was allowed to cool and the residual solution was analyzed by VPC for the presence of hexane. About 5 wt. per cent hexane was still present in the solution. A volume of 7.5 ml. (50.1 μ moles) of TMEDA was added to the flask and the mixture was heated to reflux. After 2 hrs. the mixture was allowed to cool and settle. Analysis of the supernatant solution which was a pinkish-red in color, indicated that about 75 per cent of the di-s-butylmagnesium had reacted; no TMEDA could be found in the supernatant. The reaction mixture was carbonated in 200 ml. of a slurry of ether and Dry Ice. The ether slurry was treated with excess 6N HCl and the organic layer separated. The aqueous layer was washed twice with ether and the washings combined with the main layer. The ethereal layer was extracted with 30 ml. of 10 per cent aqueous NaOH and washed twice with water. The combined extracts were filtered, acidified with 6N HCl and extracted three times with ether. The ethereal extracts were dried over Drierite and evaporated on a steam bath. The residue, which partially solidified on standing, weighed 2.45 grams and was analyzed by NMR. The ratio of phenylacetic to α -methylbutyric acids in the residue was 1.6 and represented a yield of phenylacetic acid of 22 per cent, based on the original s-butylmagnesium content.

5. Metaliation of Benzene with Partially Pyrolyzed di-s-Butylmagnesium

To 13 ml. of a 0.73N di-s-butylmagnesium (4.8 μ moles) solution in benzene was added 1.4 ml. (9.5 μ moles) of TMEDA. During the original desolvation of the benzene solution, pyrolysis had been noted. The

mixture was refluxed. Gas evolution, as well as the formation of a yellow, sticky precipitate, was noted. After 4 hrs., the mixture was cooled; analysis showed that about one-half of the di-s-butylmagnesium had reacted. The reaction mixture was carbonated in a Dry Ice-ether slurry and worked up as in 1 above. NMR analysis of the residue showed the presence of about 14 per cent benzoic acid and 86 per cent α -methylbutyric acid; the yield of benzoic acid, based on initial s-butylmagnesium present, was about 10 per cent.

6. Metallation of Alkynes

a. Acetylene. The acetylene generated from the hydrolysis of 4 grams of lump CaC_2 (one gram at a time) was passed, with the aid of a nitrogen gas purge, through a tube of barium oxide and into 20 ml. of benzene contained in a 50 ml. 3-necked flask equipped with magnetic stirring bar, reflux condenser, gas inlet tube, and rubber septum. To the flask there was added 26 ml. of 0.77N di-s-butylmagnesium solution in hexane-cyclohexane. A light green, milky mixture resulted. Three more 1 g. lumps of CaC_2 were hydrolyzed and the gas so generated swept into the above mixture. The precipitate became more particulate and the mixture turned a deep lavender or purple. After it had been stirred for 30 min., the mixture was heated to boiling for 30 min. and allowed to cool and settle. The solid retained the purple color. D_2O was added to the contents of the flask and the gases evolved collected in a vacuum system and chromatographed on a special triethylamine column at -78° . No n-butane was found, and the acetylenes obtained were:

acetylene, 7 per cent, monodeuteroacetylene, 28 per cent, and dideuteroacetylene, 65 per cent.

b. 3-Methyl-1-butyne. To 35 ml. of 0.77N di-g-butylmagnesium (13.5 μ moles) in hexane-cyclohexane was added 1.3 ml. (0.92 g., 13.5 μ moles) of 3-methyl-1-butyne. Heat was generated, but no precipitate formed nor was any gas evolved. After it cooled the solution was analyzed by NMR. A shift of about 10 cps of the methine sextet (of the g-butyl group) was noted, but the rest of the spectrum was masked by solvent. The solvent was removed under vacuum (0.02 mm and 40°C), and the residual viscous yellow oil was dissolved by addition of 10 ml. of benzene. An NMR spectrum of the benzene solution showed loss of the g-butyl methine sextet in the expected region (9-9.5 τ) and gave a complicated pattern consisting mainly of eighteen lines between 6.2 and 8.66 τ .

c. 4-Methyl-1-pentyne. To 3 ml. of 0.63N di-t-butylmagnesium (0.95 μ moles) in benzene contained in a centrifuge tube fitted with a rubber septum was added a solution of 80 mg. (0.98 μ moles) of 4-methyl-1-pentyne in 2 ml. of benzene. After a few minutes the solution had become warm, but no gas evolution occurred; there was a slight haziness in the solution. After centrifugation the clear solution was examined by NMR. Two main sets of doublets appeared between 7.9 τ and 8.6 τ , and three much smaller broader peaks appeared at 7.2, 7.5 and 7.8 τ . The smaller lower field doublet had an area of about 1/2 that of the upper field doublet. The solution was carbonated in a Dry Ice-ether

slurry and on workup, the solution of salts in D_2O was examined by NMR. A low field doublet at 7.55τ indicated the presence of 5-methyl-2-hexynoic acid, and a single peak at 8.70τ corresponded exactly to that in an authentic sample of lithium pivalate dissolved in D_2O .

7. Metallation of Dimethyl Sulfoxide

A volume of 1.5 ml. of a hexane solution containing 3.34 meq. (1.67 μ moles) of di-s-butylmagnesium (and a trace of DME) was added with shaking and cooling (ice-bath) to a solution of 0.25 ml. (3.4 μ moles) of dimethyl sulfoxide (DMSO) in 3 ml. of benzene contained in a nitrogen-flushed centrifuge tube fitted with a rubber serum cap. Reaction was vigorous (gas evolution, formation of a precipitate) throughout the addition. After shaking the tube vigorously for a few minutes, 0.5 ml. (5 μ moles) of trimethylchlorosilane was added to the centrifuge tube. After vigorous shaking a fine white precipitate slowly formed and the mixture was centrifuged. Analysis of the clear supernatant solution by VPC and NMR indicated that there was present in the gas being evolved considerable dissolved n-butane, but only traces of DMS and DMSO were present, and that the trimethylsilylated derivative of DMSO was present. VPC and NMR characteristics of the latter were identical to those of this derivative produced on reaction of trimethylchlorosilane with authentic "Dimesyllithium," $LiCH_2SOCH_3$, supplied by Lithium Corporation of America.

I. ATTEMPTED HYDROGENOLYSIS OF DIALKYL MAGNESIUM REAGENTS

1. With and Without Added TMEDA

Following the procedure and apparatus for hydrogenolysis of alkyllithium reagents developed by Screttas,^{100b} 13 ml. of 0.77N di-s-butylmagnesium (5 mmoles) in hexane-cyclohexane and 37 ml. of n-hexane were mixed together and cooled to 0°C in the apparatus under vacuum. After filling the system to slightly above atmospheric pressure with hydrogen gas, stirring was begun and any pressure changes noted. No hydrogen absorption occurred after 6 min., and 0.1 mole of TMEDA per mole of di-s-butylmagnesium was injected into the system. No hydrogen uptake occurred after another 6 minutes and another 0.1 mole of TMEDA per mole of (s-C₄H₉)₂Mg was added. Still no hydrogen uptake was observed and none was taken up as more TMEDA was added. Periodically additional quantities of TMEDA (up to a total of 11.3 mmoles) were added.

2. In the Presence of Potassium t-Butoxide Alone and With Added THF and TMEDA

A weight of 0.112 grams (1.0 mmole) of potassium t-butoxide was placed in the hydrogenolysis unit and, after it was purged with hydrogen and evacuated, 37 ml. of n-hexane was added with stirring followed by 13 ml. of 0.77N di-s-butylmagnesium in hexane-cyclohexane. A brown sticky solid formed on addition of the (s-C₄H₉)₂Mg. The pressure was raised to slightly above atmospheric with hydrogen gas. When no hydrogen uptake occurred after 9 minutes, 0.4 ml. (5 mmoles)

of THF was added. No uptake occurred after 15 minutes, and another 0.4 ml. of THF was added. After 23 minutes 0.75 ml. (5 μ moles) of TMEDA was added, and after 30 minutes another 0.75 ml. TMEDA. No hydrogen uptake occurred at any time during and after these additions. After 36 minutes 1.1 ml. (10 μ moles) of anisole was added. No color change was observed as occurred in the metallation of resorcinol dimethyl ether under comparable conditions.

In another similar run, 0.56 g. (5 μ moles) of potassium t-butoxide was reacted with 13 ml. of 0.77N di-s-butylmagnesium (5 μ moles) in the presence of 37 ml. of hexane containing 1.5 ml. (10 μ moles) of TMEDA. The mixture turned a deep yellow and then after a few minutes a deep orange-brown with brown particles sticking to the walls of the flask. Hydrogen was admitted to atmospheric pressure. A total of 0.6 ml. of hydrogen was absorbed in 10 minutes (0.3 per cent of theory), but no further absorption occurred thereafter.

3. In the Presence of s-Butyllithium and a Limited Amount of TMEDA

Five μ moles of di-s-butylmagnesium and 5 μ moles of s-butyllithium contained in a total of 3 ml. of hexane were mixed with 0.37 ml. (2.5 μ moles) of TMEDA in 37 ml. of hexane in the hydrogenolysis unit under vacuum. Hydrogen was passed in to slightly greater than 1 atm. After 30 minutes, the total hydrogen absorption was 0.3 ml.

J. ATTEMPTED ADDITION OF DIALKYL MAGNESIUM REAGENTS TO ETHYLENE

Runs exactly comparable in size (and procedure) to those described in (I) above were carried out using ethylene instead of

hydrogen. No uptake of ethylene occurred in the presence of TMEDA alone or in the presence of potassium t-butoxide, alone or in combination with THF or TMEDA. In the presence of s-butyllithium and a limited amount of TMEDA, a total of 1.7 ml. of ethylene was absorbed (less than 1 per cent of theory) in 50 minutes.

K. REACTIONS OF DIALKYL MAGNESIUM REAGENTS WITH KETONES (BENZOPHENONE)

1. Di-t-Butylmagnesium and Benzophenone

To 1 ml. of an approximately 1.5N di-t-butylmagnesium solution in benzene was added 2 ml. of a 15 wt. per cent solution of benzophenone (ca. 1.5 mmoles) in benzene. Slow addition of the first few drops of benzophenone solution caused a transient color formation (brown) in the solution. Adding the remainder of the solution rapidly (giving a molar excess of ketone \gg organometallic) caused the brown color to persist indefinitely, i.e., several days. NMR examination of this solution showed the presence of benzophenone. In addition, aliphatic proton signals appeared at 8.32 τ and 8.52 τ in a ratio of 1:4; these were presumably singlets from t-butylmethyl groups, but the smaller lower field peak could be a narrow multiplet. A relatively broad unresolved region of signals between 8.6 τ and 9.2 τ were also present in the original di-t-butylmagnesium in benzene solution, due to n-pentane impurity. A small rather broadened peak also appeared at 5.15 τ possibly due to the methine hydrogen of a benzhydrol salt. The t-butyl signal at 8.52 τ appeared downfield by about 18.5 cps from its normal position with di-t-butylmagnesium in a hydrocarbon solvent. After hydrolysis of a small

portion of the reaction mixture, VPC analysis of the organic layer showed the presence of isobutane.

Addition of more di-t-butylmagnesium solution (ca- 1.0 ml., so that the organometallic reagent was now in excess) to the above stable brown-colored mixture caused the color to disappear instantaneously. NMR examination of the decolorized solution showed a change in the ratio of the peaks at 8.32 τ and 8.52 τ (from 1:4 to 1:20), a loss of the benzophenone spectrum, an increase in the size of the peak at 5.15 τ and a profile change in the broad upfield region. Hydrolysis of this solution and NMR examination of the upper layer showed the two peaks at 8.3 τ and 8.5 τ (now at a ratio of 1:6.5), a noticeable shoulder on the benzene peak, and a considerably increased and clearer region between 8.7 τ and 9.2 τ . This region now shows three distinct peaks with the upfield two most probably representing the isobutane doublet normally found at ca. 9.1 τ . The lower of these three peaks at ca. 8.8 τ could be due to the presence of t-butanol, 8.78 τ .

An ESR spectrum was obtained from another colored product solution from the reaction of equal volumes of 15 per cent benzophenone in benzene and the 1.5N di-t-butylmagnesium solution. A 44 line spectrum was obtained. Both the color and the ESR spectrum deteriorated after about one hour.

2. Di-s-Butylmagnesium and Benzophenone

a. NMR studies on the colored complexes. To 0.25 ml. of a 30 wt. per cent solution (supersaturated) of benzophenone (ca. 0.39 mmoles) in

cyclohexane in an NMR sample tube there was added in one portion 0.5 ml. of 0.77N di-s-butylmagnesium (ca. 0.2 mmoles) in hexane-cyclohexane. A green, sticky, curdy precipitate formed immediately after the formation of an initial transient pink color. It was impossible to centrifuge this mixture in order to obtain a spectrum. Another 0.5 ml. of the di-s-butylmagnesium solution was added to the tube and the green color disappeared; the precipitate became fine and particulate and remained suspended in the solution. One half of this mixture was transferred by syringe to another NMR tube and both tubes centrifuged.

NMR examination of the clear supernatant solution in one tube showed little or no di-s-butylmagnesium, but did show signals in the aromatic region just upfield (10-20cps) from the benzene peak; possibly that signal originated from the Mg salt of benzhydrol. Addition of 0.5 ml. of dry benzene to this NMR tube caused solution of most of the solid. The NMR spectrum of this solution was not significantly different from that prior to addition of benzene. Another 0.3-ml. portion of di-s-butylmagnesium solution was added to the tube, but the s-butyl methine sextet of lines normally seen with (s-C₄H₉)₂Mg in the 9-9.5 τ region did not appear, even at a spectrum amplitude of 120.

To the other NMR tube was added 0.5 ml. of ethyl ether; little or no dissolution of solids occurred. A spectrum of the supernatant solution now showed a triplet of lines in the 8.9-9.1 τ region. (This spectrum has not yet been fully rationalized.)

Solutions with different molar ratios of benzophenone (as a 15 per cent solution in benzene) to di-s-butylmagnesium were examined by

NMR. A green solution was obtained at a 1:1 ratio and higher, while at ratios from 1:1 to 1:2 (ketone:organometallic), a light violet-pink color was obtained. With less ketone, the color was no longer observable. No NMR signal for the methine sextet (9.0-9.5 τ) of di-s-butylmagnesium could be obtained until the 1:2 ratio (excess organometallic) was attained. ESR spectra of both the green and violet solutions were obtained.

b. Study of the products of reaction. To 2 ml. of the 15 wt. per cent benzophenone solution in benzene (ca. 1.5 μ moles) in a centrifuge tube fitted with a rubber septum was slowly added 4 ml. of 0.77N di-s-butylmagnesium in hexane-cyclohexane (1.5 μ moles). An intense green color was formed on mixing and heat was generated. (In another experiment it was observed that if small increments of di-s-butylmagnesium solution were allowed to layer on top of the benzophenone solution, a deep violet color resulted in the upper layer; mixing of the layers caused this color to immediately change over to green.) A small additional portion of di-s-butylmagnesium solution was added, ca. 0.5 ml., bringing the organometallic a molar excess over the ketone. With the addition of this portion, the green color disappeared; no heat was generated; no violet color formed; precipitation of solids occurred. The product mixture in the centrifuge tube was poured into a mixture of ice and 3N aqueous HCl to effect hydrolysis. The mixture was shaken well, the layers separated and the aqueous layer was washed with ether. The combined organic layers were treated with anhydrous

Na_2CO_3 and evaporated to dryness on a steam bath. The residue was heated for a few minutes on a hot plate and dissolved in CCl_4 . NMR examination indicated the presence of benzhydrol (CH at 4.53τ) and the expected addition product (peaks in aliphatic region - 8.3 - 9.4τ) in a ratio of $2.8:1$ (74 per cent benzhydrol and 26 per cent addition product). Some small additional unidentified single peaks appeared at 7.20τ and 7.55τ .

L. ATTEMPTED REACTION OF DIALKYL MAGNESIUM REAGENT WITH
PHENYLDIMETHYLCHLOROSILANE

To 1.0 ml. of a 1.3N solution of di-s-butylmagnesium in ether there was added 2.5 ml. of phenyldimethylchlorosilane (a large molar excess). No apparent reaction resulted, as indicated by a lack of precipitate formation and no heat of reaction. The reaction mixture was distilled until its b.p. reached 90° . No change in appearance was noted; no salt precipitated. The mixture was discarded.

M. EFFECT OF DIALKYL MAGNESIUM REAGENTS ON THE HALOGEN-METAL
INTERCONVERSION REACTION WITH ALKYL LITHIUM REAGENTS

It was noted that only a slight ~~pos~~ positive test (light orange color) was obtained with Gilman Color Test IIa on the supernatant solution from reaction of 100 ml. of a 1.3N s-butyllithium in cyclohexane solution with 50 ml. of a MgCl_2 slurry in cyclohexane. (The MgCl_2 had been prepared by reaction of chlorine gas with s-butylmagnesium chloride in ether.) A Mg analysis of this supernatant solution showed that only about 50 per

cent exchange of Mg for Li had occurred. The solution was found to be 0.4N in s-butyllithium, which concentration alone gives a strong Gilman Color Test IIa, intense red color.

To 3.5 ml. of the above supernatant solution, containing 0.4N lithium reagent and 0.4N magnesium reagent, in a centrifuge tube fitted with a rubber septum was added 5 ml. of a 15 wt. per cent p-bromodimethylaniline solution in benzene. To 3.5 ml. of 0.4N s-butyllithium (4.5 mmoles) in cyclohexane contained in another capped centrifuge tube was added 5 ml. of the p-bromodimethylaniline solution. After mixing the reagents in each tube for about one minute, the solution was withdrawn with a syringe and carbonated by addition to a stirred Dry Ice-ether slurry. After the mixtures from each tube had come to room temperature, the ether was evaporated on a steam bath and the residual salts were transferred to centrifuge tubes and washed once with ether. The salts were blown dry under a nitrogen stream at 50-60°C (oil bath). On cooling, the salts were dissolved in D₂O and the tubes centrifuged. NMR examination yielded the following results. From the s-butyllithium solution: no salt of 2-methylbutyric acid was present; two doublets of equal intensity were found in the aromatic region as well as a singlet above in the aliphatic region due to the six protons of the dimethylamino group; integration of the aromatic protons and the dimethylamino protons gave the correct ratio (4:6) for lithium p-dimethylaminobenzoate. From the 2:1 s-butyllithium-di-s-butylmagnesium solution: 2-methylbutyric acid salt was found to be the main product, at least 95 per cent of the total; only a trace of the salt of p-dimethylaminobenzoic acid was present.

N. HOMOLOGIZATION OF ALKYL LITHIUM REAGENTS AND DIMETHYL ETHER

1. s-Butyllithium

a. Determination of products of reaction. Into 50 ml. of a 1.24N s-butyllithium solution in n-hexane (0.062 mole), was passed (with ice bath cooling) approximately 5 grams of dimethyl ether (0.10 mole) and the mixture was allowed to warm to room temperature with stirring. After two hours VPC analysis of a hydrolyzed sample of the solution indicated that there was in the solution a DME:2-methylbutyllithium:s-butyllithium ratio of 8:4:1. The 2-methylbutane, which identified the 2-methylbutyllithium, was obtained by hydrolysis of an authentic sample of the lithium reagent prepared from lithium metal and 2-methyl-n-butyl bromide in pentane. Two columns were used to insure positive identification (SE-30 at 33°C, and DEG-AgNO₃ at 25°C). The NMR spectrum of the homologization product was found to be identical with that of the authentic 2-methylbutyl reagent. A trimethylsilyl derivative from a similar run, one which contained MgCl₂, was prepared by reaction of a sample with excess trimethylchlorosilane; the derivative was found to have the same VPC retention time (SE-30 column at 51°C) as an authentic sample prepared from 2-methylbutyllithium and excess trimethylchlorosilane.

b. Study of the kinetics of the reaction.

(1) Uncatalyzed. Into a 200 ml., 3-necked, round-bottom flask equipped with a magnetic stirring bar, reflux condenser, and thermometer was placed 100 ml. of 1.35N s-butyllithium in cyclohexane. The contents of the flask were cooled to 0-2°C.

A lecture bottle of dimethyl ether was weighed on a balance and then attached by a length of rubber tubing to a gas inlet tube inserted in one neck of the flask. The lecture bottle was weighed again and the needle valve barely opened and DME passed into the stirred solution until the lecture bottle had decreased in weight by about 9 to 9.5 g. (about 10 minutes). The temperature during the addition was maintained between 2 and 8°C (ice bath). The rubber tubing was then removed, the inlet tube replaced with a rubber septum, and the lecture bottle weighed again; 9.5 g. of DME were used (100 per cent in excess of stoichiometry). A sample of the solution was removed for NMR analysis at this point, NMR analysis of the solution 2 minutes after sample removal showed the methylene doublet of 2-methylbutyllithium emerging from the methine sextet of s-butyllithium. Within 5 minutes after sample removal, it was already difficult to pick out the methine sextet. The ice bath was removed and the temperature of the solution brought as quickly as possible to 40°C by means of a pre-heated oil bath and kept between 38-42°C throughout the study. One milliliter samples of the mixture were removed periodically (at 15 min., 45 min., 1 hr., 1.5 hr., 7.0 hr., and 23 hr.) with a syringe and added to 15 ml. centrifuge tubes fitted with rubber septa and containing 1-ml. quantities of trimethylchlorosilane. After reaction was complete (no further precipitation of LiCl), the tubes were centrifuged and the clear supernatant solutions analyzed for trimethylsilyl derivatives of s-butyl- and 2-methylbutyllithium by VPC on an 8 ft., 1/8 inch SE-30 column at 75°C (helium carrier gas, flow 7). Area counts were obtained by

multiplying peak heights of the two derivatives by their distances from the air peak (33 and 55.7 units respectively). The reaction was at least 95 per cent complete after 7 hours. After 23 hours, the clear supernatant solution had a total base concentration of 0.39N. VPC showed that the solid residue contained lithium methoxide.

The above run was repeated at a lower temperature (5°C). Similar runs were also made at 0° and at 40°C using just a stoichiometric amount of dimethyl ether, i.e., such that the molar ratio of s-butyllithium to DME was 2:1.5.

(2) Catalyzed. After obtaining a series of kinetic results as described above, incremental amounts of TMEDA were added to runs with stoichiometric DME and new series of kinetic data generated. At 0° the concentrations of TMEDA used were 0.010 and 0.033 moles per liter. At 40° the concentration of TMEDA was 0.024 M. A run with 100 per cent excess DME (as described above) and containing 0.013 moles TMEDA per liter of solution was carried out at 2.5°.

2. t-Butyllithium

A volume of 82 ml. of a 1.75N solution of t-butyllithium in n-pentane (0.192 moles) was cooled to -12°C in a Dry Ice-acetone bath and 9.1 g. (0.198 moles) of DME (37 per cent excess DME over stoichiometry) was added as previously described. The temperature was kept between -6 and -7°C throughout the run. On completion of the addition, the mixture was bright yellow. (An ESR spectrum was obtained from this yellow solution and a weak but definite signal was obtained from a paramagnetic species present.) The syringe had

to be pre-cooled with Dry Ice to take samples for reaction with trimethylchlorosilane, because of the high volatility of the solution, otherwise analyses were done as with n-butyl runs. After 2 hours reaction was 95 per cent complete and the yellow color was fading out; reaction was continued to over 99 per cent completion (almost 6 hours) and the yellow color was gone.

In addition to VPC characterization of the trimethylsilylation product from the homologization reaction, a carbonation product was prepared. The reaction mixture was poured into a stirred Dry Ice-ether slurry and the resulting salt slurry evaporated to dryness on a steam bath. The salts were washed 3 times with ether on a Buchner funnel, dried on a steam bath and a portion of them (0.5300 g.) dissolved in 1 ml. of D₂O. Methanol (100 μ l) was added as an internal standard. NMR examination showed the two peaks besides those for methanol and hydroxyl, characteristic of 3,3-dimethylbutyric acid.

0. GENERAL VPC ANALYSIS TECHNIQUE

For the preparation of organometallic solutions for VPC analysis, 0.5 to 1.0 ml. of the solution was syringed slowly into a cooled 15 ml. conical test tube fitted with a rubber septum and containing ca. 1 ml. of isopropyl or isoamyl alcohol. The tube was shaken thoroughly and several drops of 6N HCl added to clarify the solution. The tube was centrifuged and 3-5 μ l of the clear solution were syringed into the chromatograph for analysis. A similar technique was employed to determine the amount of ether or alcohol remaining in a desolvated

slurry of anhydrous MgCl_2 in hydrocarbon media. In this case 1 ml. of the slurry was syringed into a conical test tube containing an equal volume of an alcohol. After thorough shaking, the tube was centrifuged and the clear supernatant drawn off for VPC analysis.

CHAPTER IV

SUMMARY

Dialkylmagnesium reagents have been prepared by techniques involving (1) direct reaction of magnesium metal with alkyl halides in hydrocarbon media containing a limited amount of a Lewis base such as dimethyl ether, (2) reaction of Grignard reagents with stoichiometric amounts of lithium alkyls, and (3) reaction of "activated" magnesium chloride with lithium alkyls in hydrocarbon media. Those dialkylmagnesium reagents prepared in media containing ethers could be desolvated of the Lewis base by continuous codistillation with hydrocarbon solvents. It has also been found that alkylmagnesium chlorides in ethereal media can be desolvated in a similar manner and thereby converted to a mixture of insoluble magnesium chloride and soluble dialkylmagnesium reagents.

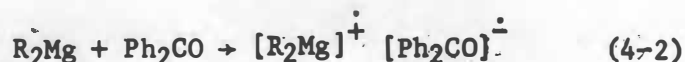
Reagent (R_2Mg), with long chain n-alkyl groups or with α - and β -branched groups (e.g., s-butyl or neopentyl) are soluble in hydrocarbon solvents. Other reagents (R'_2Mg) are relatively insoluble in hydrocarbons, but dissolve if the hydrocarbon contains one mole of Lewis base per gram-atom of magnesium. Admixture of a soluble reagent, R_2Mg , with an insoluble one, R'_2Mg , solubilizes the latter in hydrocarbons. Admixture of R'_2Mg with a hydrocarbon solution of a lithium alkyl also causes dissolution. These solubility properties indicate the formation of mixed reagents, e.g., $RMgR'$ and R_3MgLi , with specific structural features.

Solid complexes of dialkylmagnesium compounds were formed with triethylenediamine and with methyltriethylenediamine, R'_2Mg forming 1:1 and 2:1 complexes and the branched R_2Mg forming only 1:1 complexes. NMR analyses of the dialkylmagnesium compounds and of their complexes confirmed the existence of mixed reagents with specific structural features. In the presence of dialkylmagnesium reagents the normally facile halogen-metal interconversion reaction between *p*-bromodimethylaniline and a lithium alkyl was suppressed almost completely, also indicating the formation of intermetallic reagents between lithium and magnesium alkyls.

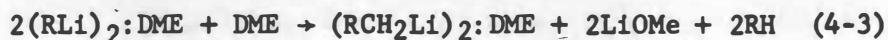
Successful metallations of several different aromatic substrates, ArH , were carried out with R_2Mg reagents in the absence of Lewis bases; in some cases a mixed reagent, $ArMgR$, could be isolated. These metallations and certain other reactions did not occur with Lewis bases present. Such results are not consistent with interpretation of magnesium reagent reactivity in the simple terms of carbanionic character.

NMR and ESR studies of the addition of dialkylmagnesium reagents to benzophenone in hydrocarbon solvents showed that under certain conditions and at certain preferred reagent ratios, stable paramagnetic, colored complexes could be formed. Tentatively, these complexes are represented as containing radical anions which arise both by the addition of one mole of R_2Mg to benzophenone, followed by transfer of an electron to excess benzophenone to form a charge-transfer complex (4-1), and by the direct formation of a charge transfer species from

benzophenone in the presence of excess R_2Mg (4-2).



It was found in the course of these investigations that s- and t-alkyllithium reagents were homologized to the primary reagent by reaction with dimethyl ether. The kinetics of the reaction was studied and appeared to follow the stoichiometry of the reaction represented below (4-3) i.e., the reaction was found to



be third order overall in the presence of the indicated stoichiometric amount of DME and pseudo-second order overall in the presence of sufficient excess of DME. In the presence of catalytic amounts of tetramethylenediamine (TMEDA) the homologization was found to be first order in lithium reagent and to vary with TMEDA concentration. These results are consistent with the concept of a kinetic role for base, DME, or TMEDA, being the catalysis of charge transfer from reagent to substrate; in (4-3) one solvated dimer acts as reagent, the other as substrate and DME is a catalyst. TMEDA acts as such a good charge-transfer catalyst that it washes out the order with respect to the reagent. During reaction, the yellow t-butyllithium-DME mixture was found to be paramagnetic.

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In 1965, through the generosity and foresight of the President of Lithium Corporation of America, Mr. Harry D. Feltenstein, he was permitted to pursue his studies fulltime at the University of Tennessee toward a Ph.D. degree under the direction of Professor Jerome F. Eastham. In December 1967 he was granted the Doctor of Philosophy degree from the University of Tennessee.

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