Nuclear Magnetic Resonance Spectroscopy. The Configurational Stability of Primary Grignard Reagents. Structure and Medium Effects

George M. Whitesides and John D. Roberts
Qualitative and semiquantitative examination of the temperature dependence of the $RCH_2-Mg$ proton n.m.r. spectra of several Grignard reagents indicates that the rate of inversion at this center is relatively insensitive to the structure of the group $R$. Secondary Grignard reagents invert much more slowly, if at all. The dependence of the inversion rate of the primary organometallic compounds on solvent character and on added salts suggests that inversion proceeds by means of a mechanism having kinetic order greater than one.

Introduction

The preceding paper$^2$ presented n.m.r. spectral evidence demonstrating that $3,3$-dimethylbutylmagnesium chloride$^3$ in diethyl ether solution undergoes rapid inversion of configuration at the $CH_2-Mg$ center.

$$
\begin{array}{c}
\text{H} \\
\text{R} \quad \text{MgX} \\
\text{H} \\
\text{H}
\end{array}
$$

(1) Supported in part by the Office of Naval Research and the National Science Foundation.


(3) For convenience, the organometallic compound formed by reaction of an alkyl halide with magnesium in an ethereal solvent will again be called an alkylmagnesium halide.

This observation suggests that careful examination of the spectrum of this and related compounds in different solvents and at different concentrations might provide data pertinent to the mechanism of this inversion and to the nature of Grignard reagents in solution.

Much of the modern work concerned with the structure of Grignard reagents has centered around attempts to evaluate the importance of the so-called Schlenk equilibrium in describing the Grignard reagent.

$$
2RMgX \rightleftharpoons R_rMg \cdot MgX_r \rightleftharpoons R_rMg + MgX_r
$$
magnesium,$^3$ and concluded from these experiments that the equilibrium

$$
2RMgBr \rightleftharpoons R_rMg + MgBr_r
$$
was not important in the Grignard reagents studied. In addition, conductometric measurements were reported to give identical$^3$ values for the dielectric constant of a 1:1 mixture of diethylmagnesium and magnesium bromide and of an equivalent concentration of "ethylnmagnesium bromide." It was therefore con-
cluded that the Grignard reagents studied were best represented by the equilibrium and that no species represented by the formula "RMgX" is present in solution. Recent however, Stucky and Rundle and Ashby and Beckere have presented data suggesting that Dessy's conclusion may have been premature. Stucky and Rundle demonstrated by the X-ray crystal structure determination of phenylmagnesium bromide dietherate that the magnesium atom was tetrahedrally coordinated to one phenyl group, one bromide atom, and two oxygen atoms; that is, that this Grignard reagent was in fact "RMgBr\cdot2EtO" in the solid state.

Ashby and Becker were able to obtain a crystalline solid from a tetrahydrofuran solution of ethylmagnesium chloride whose empirical formula corresponded to EtMgCl\cdotTHF. This fact, and their observation that ethyl Grignard reagent was monomeric in tetrahydrofuran, led them to conclude that the most important species in solution was actually EtMgCl.

Both of these studies depended on compounds existing in the solid state, and in consequence neither is necessarily pertinent to the structure of the Grignard reagent in solution. However, the X-ray study in particular provides evidence that "RMgX" may exist under suitable conditions, and suggests that further work on the structure of Grignard reagents in solution must take into consideration the possibility of its existence.

Results

Organomagnesium compounds derived from halides similar in structure to 3,3-dimethylbutyl chloride show an analogous temperature dependence in their spectra. Thus, the spectra of the CH\(_2\)-Mg protons of 3-methylbutylmagnesium chloride and \(n\)-butylmagnesium chloride are triplets at room temperature; at -50\(^\circ\)C, the spectra become more complicated (Figure 1). The degree of complexity is unfortunately sufficiently great to discourage attempts to analyze the spectra explicitly. The 3,3-dimethylbutyl group provides a particularly simple system for analysis, because the four protons of the ethylene fragment are not coupled to the protons of the \(n\)-butyl group. In the 3-methylbutyl and \(n\)-butyl derivatives however, the chemical shift between the methyl protons and the adjacent methylene protons is of the same order of magnitude as the coupling constant between them, and the \(\alpha\)-proton spectrum is consequently complicated.

Although little quantitative information can be obtained from the spectra of these Grignard reagents, or from the spectra of the corresponding dialkylmagnesium compound (Figure 2), qualitative comparison with the 3,3-dimethylbutylmagnesium compounds makes clear two similarities in their temperature dependence. The first of these is that the low-temperature spectra of the Grignard reagents are very similar to the room-temperature spectra of the corresponding dialkylmagnesium compounds. The second is that the

Grignard reagent spectra do not seem to change at
temperatures below approximately -70°, and the
dialkylmagnesium spectra change little below +30°.

Both of these observations are compatible with the
explanation previously proposed for the temperature
dependence of the spectrum of 3,3-dimethylbutyl
Grignard reagent based on the rate of inversion. More-
over, the second of these observations would be dif-
cult to reconcile with important changes in popula-
tions of rotatioal conformations with temperature.
If changes in the populations of the \( \text{trans} \) and \( \text{gauche} \)
conformations were important in determining the
temperature dependence of these spectra, the broadening
observed in the central line for di-\( \text{n-butylmagnesium} \)
compared with \( \text{n-butylmagnesium chloride} \) would be
the consequence of an increase in the energy dif-
ference between \( \text{trans} \) and \( \text{gauche} \) conformations of
these compounds. Decreasing the temperature of the
Grignard reagent produces a broadening of the central
line of its spectrum. If this change were a reflection of
changes in conformer populations, lowering the tem-
perature of the dialkylmagnesium compound should
result in an analogous change in its spectrum. In
fact, little change in the spectrum of the latter compound
is observed on decreasing the temperature. There-
fore, changes in conformer populations are probably not
important in determining the temperature dependence
of the spectra.

An analogous argument can of course be applied to the
3-methylbutylmagnesium and 3,3-dimethylbutyl-
magnesium compounds studied.

The high-temperature spectral behavior of bis(3-
methylbutyl)magnesium and di-\( \text{n-butylmagnesium} \) appears comparable with that observed for bis(3,3-di-
methylbutyl)magnesium. Each changes from its "low-
temperature" form to a triplet over the temperature
range +50 to +110°.

The similarity in the spectral behavior of these three
structurally similar Grignard reagents suggests that the
rates and thermodynamic parameters for the processes
which result in the simplification of their spectra are approximately the same. This qualitative
observation that all the primary Grignard reagents ex-
amined exhibit the same spectral behavior is further
supported by analysis of the temperature dependence
of the spectrum of 2-phenyl-3-methylbutylmagnesium
chloride as will be described below.

The most plausible interpretation of the temperature
dependence of the spectrum of 2-phenyl-3-methyl-
butylmagnesium chloride is the same as that proposed
for 3,3-dimethylbutylmagnesium chloride. The mag-
netic nonequivalence of the methylene hydrogens at
+33° demonstrates clearly that inversion of configura-
tion at the \( \text{CH}_2-\text{Mg} \) center is slow on the n.m.r.
time scale. The loss of the magnetic nonequivalence as the
temperature is increased is taken as evidence that a
rapid inversion of configuration, analogous to that
proposed previously, averages the magnetic environ-
ments of the methylene hydrogens.

Quantitative discussion of these spectra is more dif-
cult than that of the spectra of the 3,3-dimethylbutyl-
magnesium derivatives because the chemical shifts
and coupling constants obtained on analysis of the
former compound are less precise. The AB part of an
ABX spectrum theoretically consists of eight lines, of
which four may be of low intensity. The positions
of these low-intensity lines are unfortunately difficult to
determine exactly in the room temperature spectra of
either 2-phenyl-3-methylbutylmagnesium chloride or
bis(2-phenyl-3-methylbutyl)magnesium. These lines
are necessary for accurate determination of the gem-
inal methylene coupling constant. The spectrum in
ether solution is further confused by the accidental
near degeneracy of two of the intense lines and by the
high-field \( ^13\text{C} \)-ether satellites. Moreover, no informa-
tion can be obtained from the X part of the spectrum,
due both to its low intensity and to its complexity.

Therefore, although agreement can be obtained be-
tween the observed and calculated spectra, the values
obtained from analysis cannot be regarded as highly
precise. Coupling constants and chemical shifts for a
solution of this Grignard reagent in diethyl ether solu-
tion at -14°, and in tetrahydrofuran solution at
+33°, and for the corresponding dialkylmagnesium
compound in ether at +33° are reported in Table I.
The starting halide has an \( \text{A}_2\text{X} \) type spectrum in car-
bon tetrachloride solution.

The protons of a methylene group near a center of
molecular asymmetry may be magnetically non-
equivalent and display AB-type n.m.r. spectra. 11
Recent investigations indicate that conformational
preference is responsible for the major part of the
magnetic nonequivalence of the methylene protons. 11-12
A primary Grignard reagent which might be expected
to have magnetically nonequivalent methylene protons
would thus be one in which one rotational confor-
maion around the \( \alpha \)-carbon-carbon bond would be
significantly lower in energy than the other two. The
\( \text{CH}_2\text{Mg} \) protons of two Grignard reagents, 2-phenyl-
propylmagnesium bromide and 2-phenyl-3-methylbu-
tylmagnesium chloride, were examined for evidence of
magnetic nonequivalence. The \( \alpha \)-methylene hydrogens
of the former in diethyl ether solution had an \( \text{A}_2\text{X} \) type
spectrum from +33 to -80° (viscous broadening pre-
vented measurement below this temperature). The
methylene protons of the latter had a spectrum char-
nacteristic of the AB part of an ABX spectrum at room
temperature: at +110°, the spectrum collapsed to an
\( \text{A}_2\text{X} \) type (Figures 3 and 4).

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Chem. Soc., 86, 2628 (1964), and references therein.
The temperature dependence of the $\alpha$-proton spectrum of 2-phenyl-3-methylbutylmagnesium chloride depends on the response of the ABX spectrum to the exchange rate of a process interchanging the A and B protons. The AB part of the observed ABX spectrum consists of two overlapping quartets, arising from transitions within two separate sets of energy levels. 

### Table I. Spectral Parameters (c.p.s.) for the Methylene Protons of 2-Phenyl-3-methylmagnesium X Treated as an ABX System

<table>
<thead>
<tr>
<th>X = Cl</th>
<th>X = Cl</th>
<th>X = R</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\nu_A$</td>
<td>12.9</td>
<td>9.2</td>
</tr>
<tr>
<td>$\nu_B$</td>
<td>150°</td>
<td>150°</td>
</tr>
<tr>
<td>$\nu_X$</td>
<td>±12.1</td>
<td>±12.5</td>
</tr>
<tr>
<td>$J_{AX}$</td>
<td>±10.3</td>
<td>±9.7</td>
</tr>
<tr>
<td>$J_{BX}$</td>
<td>±4.3</td>
<td>±5.6</td>
</tr>
</tbody>
</table>

* Accuracy in the chemical shift and coupling constant values is estimated to be ±0.5 c.p.s. * Diethyl ether solution at -14°. * Tetrahydrofuran solution at +33°. * This value was assumed.

(i.e., the two sets of transitions have no energy levels in common). Figure 5 indicates the transitions which are expected to collapse under the influence of an exchange process averaging states 3' and 4', and 5' and 6'. It can be shown that each of these quartets behaves approximately as an AB quartet with "effective chemical shifts" $\nu_B - \nu_A + J_{BX} - J_{AX}$ or $\nu_B - \nu_A - J_{BX} + J_{AX}$, respectively, and coupling constant $J_{AB}$, under the influence of the exchange process.

Analysis of the temperature dependence of the $\alpha$-proton spectrum of 2-phenyl-3-methylbutylmagnesium chloride is complicated by the fact that only the four
Figure 6. Calculated line shapes for the CH2–Mg part of the spectrum of 2-phenyl-3-methylbutylmagnesium chloride in diethyl ether solution, at different values of the pre-exchange lifetime τ. The parameters used and the method of calculation are described in the text.

Figure 7. Calculated line shapes for the CH2–Mg part of the spectrum of 2-phenyl-3-methylbutylmagnesium chloride in tetrahydrofuran solution, at different values of the pre-exchange lifetime τ.

intense central lines of the AB part of the ABX spectrum can be observed, in the region of intermediate exchange rates. In order to obtain values for the rate of exchange of the A and B protons at each observed temperature, a series of theoretical spectra were calculated at values of the pre-exchange lifetime which spanned the region in which the spectrum changed from its ABX form to an AX form. Each of the theoretical spectra was obtained by summing two AB type spectra using “effective chemical shifts” and an “effective coupling constant” obtained using the parameters of Table I and the relations given above (Figures 6 and 7). Comparison of the observed and calculated spectra permitted the assignment of a value for the pre-exchange lifetime τ to each observed spectrum. Following the well-known relation between τ and the Arrhenius parameters for the exchange process, a plot of log (1/τ) vs. 1/T yielded Ea and A (Figure 8). For 2-phenyl-3-methylbutylmagnesium chloride in diethyl ether the values obtained for the activation energy and pre-exponential factor were Ea ≈ 12 kcal./mole and A ≈ 10^{10} sec.−1; for 2-phenyl-3-methylbutylmagnesium chloride in tetrahydrofuran, the corresponding values were Ea ≈ 18 kcal./mole and A ≈ 10^{14} sec.−1. The spectrum of bis(2-phenyl-3-methylbutyl)magnesium does not collapse in the accessible temperature range (see Table II).

Table II. Temperatures and Pre-exchange Lifetimes Used to Obtain the Dependence of 1/τ on 1/T for 2-Phenyl-3-methylbutylmagnesium Chloride

<table>
<thead>
<tr>
<th>Temp., °K.</th>
<th>τ, sec.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diethyl ether solution</td>
<td></td>
</tr>
<tr>
<td>305</td>
<td>0.070</td>
</tr>
<tr>
<td>323</td>
<td>0.020</td>
</tr>
<tr>
<td>330</td>
<td>0.010</td>
</tr>
<tr>
<td>346</td>
<td>0.007</td>
</tr>
<tr>
<td>372</td>
<td>0.001</td>
</tr>
<tr>
<td>Tetrahydrofuran solution</td>
<td></td>
</tr>
<tr>
<td>339</td>
<td>0.300</td>
</tr>
<tr>
<td>360</td>
<td>0.070</td>
</tr>
<tr>
<td>365</td>
<td>0.050</td>
</tr>
<tr>
<td>373</td>
<td>0.022</td>
</tr>
<tr>
<td>379</td>
<td>0.015</td>
</tr>
<tr>
<td>387</td>
<td>0.010</td>
</tr>
<tr>
<td>401</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Two further points related to the spectral behavior of this compound deserve brief comment. First, the line broadening observed in the region of intermediate exchange rate for 2-phenyl-3-methylbutylmagnesium chloride again confirms that exchange and not changes in the populations of the rotational conformations open to the molecule is responsible for the temperature dependence of the spectrum. Second, the absence of a temperature dependence on the spectrum of the related compound 2-phenylpropylmagnesium bromide does not necessarily imply that inversion of configura-
Figure 9. Spectra of 3,3-dimethylbutylmagnesium chloride in diethyl ether as a function of concentration. The sharp triplet at lower field is the ether methyl $^{13}$C satellite.

Figure 10. Room temperature spectra of the CH$_3$Mg protons of 3,3-dimethylbutylmagnesium chloride as a function of solvent: (a) diethyl ether, (b) tetrahydrofuran, (c) diglyme.
The spectrum observed for such a solution is not a superposition of the spectra of the Grignard reagent and chloride present in solution is only partially removed. The dialkylmagnesium compound separately, but an ether, for example, a solution of 3,3-dimethylbutylmagnesium chloride is treated with less than a stoichiometric quantity of magnesium bromide is the result of rapid migration of halide ion from magnesium to magnesium, of rapid migration of magnesium chloride as a separate species, or of some other process occurring in solution. The absence of a chemical shift between the two methyl groups would not have allowed an unambiguous interpretation. Because either rapid inversion of configuration at the CH-Mg center or an accidental degeneracy may be expected to be useful, in light of the probable pertinence of such data to considerations of the mechanism of inversion. Unfortunately application of the techniques used in examination of the primary Grignard reagents to several secondary Grignard reagents has been less successful. It is not proved possible to measure the rate of inversion of a secondary Grignard reagent; however, it is possible to establish a lower limit on this rate from the experiments described below.

The spectrum of the Grignard reagent prepared from 3,3-dimethylocyclobutyl bromide in tetrahydrofuran solution at room temperature shows a doublet for the methyl protons (Figure 12). The magnetic non-equivalence of the methyl groups can reasonably be explained only as the consequence of slow inversion of configuration at the CH-Mg center. If the Grignard reagent is inverting slowly, two types of methyl groups are present: one cis to the magnesium atom, one trans. The absence of a chemical shift between the two methyl groups would not have allowed an unambiguous interpretation, because either rapid inversion of configuration at the CH-Mg center or an accidental degeneracy of the chemical shifts of a slowly inverting Grignard would give the same result. However, the observation of two kinds of methyl protons indicates clearly that inversion is slow with this molecule.

Similarly, the two isopropyl methyl groups of 2,3-dimethylocyclobutyl Grignard reagent are magnetically non-equivalent at room temperature in both tetrahydro-
The carbon atom bearing the magnesium atom in this compound is a center of molecular asymmetry. The observation that the adjacent isopropyl methyl groups are magnetically nonequivalent indicates that inversion of configuration at the CHCH$_2$-Mg center is slow on the n.m.r. time scale.$^{13}$

Neither of these compounds shows significant temperature dependence in its spectrum. The chemical shift between the methyl protons of 3,3-dimethylcyclobutylmagnesium bromide does not change over the temperature range +33 to +120$^\circ$. The chemical shift between the methyl protons in the isopropyl group of 2,3-dimethylbutylmagnesium chloride does decrease by approximately 0.7 c.p.s. between +33 and +120$^\circ$; however, this decrease occurs gradually over the indicated temperature range, and is probably due to changes in the rotational conformation populations of the isopropyl group rather than to a change in the rate of inversion.

The absence of a significant temperature dependence in the spectra of these two compounds suggests that the barrier to inversion of configuration is higher in the secondary than in the primary Grignard reagents. It might be argued that 3,3-dimethylcyclobutyl Grignard reagent is not a representative secondary Grignard reagent since the ring strain of the molecule and hybridization of the carbon atoms are atypical. However, 2,3-dimethylbutyl Grignard reagent seems a reasonable model for a secondary Grignard reagent.

It should be noted in connection with these observations that the reaction of a dialkylmercurial with mercuric bromide proceeds at the same rate for di-isopropyl- and di-n-propylmercury compounds and faster for dicyclopentymercury and diphenylmercury.$^{14}$ This dissimilarity between the influence of the alkyl group on the rate of this reaction and on that of the Grignard inversion suggests that the well-established Se2 mechanism for the mercurials and the mechanism of inversion in the Grignard reagents are probably not closely related.

Discussion

The experimental observations presented in this and previous$^{13}$ papers indicate that inversion of configuration of several primary Grignard reagents occurs with similar activation parameters. An important question to be asked concerning the mechanism of the inversion reaction concerns its kinetic order. If inversion proceeds by an uncomplicated ionization-recombination pathway, the inversion rate should be approximately

\[
\text{MgX} + \text{R}-\text{C}-\text{H}_3 \rightarrow \text{MgX} + \text{R}-\text{C}-\text{H}_3
\]

independent of the concentration of organometallic compound or magnesium salts in solution, if salt effects and the effect of concentration on the dielectric constant of the medium are neglected. If inversion is a process of higher kinetic order, its rate should vary with the concentration of the reactants. It is observed experimentally that the inversion rate does depend on a very striking manner on the concentration of the Grignard reagent in solution, being slower in dilute than in concentrated solution. The actual decrease accompanying a decrease in concentration can be estimated for 3,3-dimethylbutylmagnesium chloride from Figure 9, which indicates that a change in the concentration of the organometallic compound from approximately 15$^\circ$ to approximately 1$^\circ$ at $-6^\circ$ is sufficient to change the spectrum from its fast exchange form to its slow exchange form. The fast exchange and slow exchange forms of the Grignard reagent spectra correspond to inversion rates differing by approximately a factor of 100.$^{15}$

This observed dependence of inversion rate on the concentration of the Grignard reagent is in reasonable qualitative agreement with that which might be expected using a bimolecular mechanism as a model. The observed change in inversion rate might also be within the range which would be predicted on the basis of unimolecular mechanism, provided the transition state for the inversion in the mechanism has very much more charge separation than the ground state. In this case, the change in rate would be a consequence of the change in the bulk dielectric constant of the solvent accompanying the change in concentration.

The effect of the concentration and kind of halogen anion present in solution is best discussed by considering the influence the anion might have on the transition state for unimolecular and bimolecular reactions.

In a unimolecular ionization-recombination reaction, the anion would probably exert its influence by its effect on the carbon-metal bond strength and the effect would, of course, be largest for halide ion bonded directly to the magnesium atom. An increase in the electronegativity of a substituent X bonded to magnesium should increase the p-character of the magnesium bonding orbital directed toward X.$^{19}$ An increase in the p-character of the Mg-X bond will be accompanied by a decrease in the p-character of the magnesium bonding orbital directed toward carbon and an increase in the ionic character of the C-Mg bond. The ease of ionic dissociation of the R-Mg bond of organomagnesium compounds is thus predicted to be R-MgCl > R-MgBr > R-MgI > R-MgR, in agreement with the observed order.

If the mechanism of inversion is bimolecular, it probably involves electrophilic attack on the Grignard reagent by some species containing the fragment MgX$_2$: either R'MgX, MgX$_2$, R'Mg, or some more complicated magnesium-containing species. The rate of inversion would then be expected to increase with increasing electrophilicity of the attacking species.


The more electronegative the halogen atom attached to the magnesium, the more electrophilic the MgX fragment should be. Hence, using a bimolecular model for the reaction and assuming that the rate depends primarily on the electrophilicity of the fragment MgX, one would predict that the rate of inversion should also increase in the observed order R-MgCl > R-MgBr > R-Mgl > R-MgR.

It is likely that the anion present in solution influences the inversion reaction in some manner other than through its effect on electrophilicity or on the bulk dielectric constant of the solution. Magnesium bromide added to a solution of 3,3-dimethylbutylmagnesium chloride in ether slows the rate of inversion. It would be inconsistent to assume that electrophilicity of the MgX fragment were the sole important factor in determining the rate of inversion, and then to say that adding a weak electrophile to a strong electrophile should decrease the overall electrophilicity of the MgX fragments in solution.

The spectrum observed for the mixture of Grignard reagent and magnesium bromide does not consist of two superimposed spectra corresponding to "RMgCl" and "RMgBr" but rather of an averaged spectrum intermediate between the two. This observation suggests that migration of halide ion (or magnesium halide) between organometallic centers occurs rapidly in solution. In consequence, the solution of "RMgCl" with added magnesium bromide probably contains an equilibrium concentration of "RMgBr." It seems possible that the anion present in solution might influence the inversion rate both through its effect on electrophilicity of the MgX fragment in solution and through its effect on the carbon-magnesium bond strength.

This same approach may be used to rationalize the dependence of the inversion rate on solvent. Ethers are electron-donor solvents, by virtue of their non-bonding oxygen electrons: as such, they are known to be capable of forming strong dative bonds to positively charged magnesium species. In an ionization-recombination mechanism, solvation in the transition state should be more important than solvation to the ground state because charge separation in the transition state will be greater. Inversion should therefore proceed more rapidly in a basic ether such as tetrahydrofuran than in a relatively nonbasic ether such as diethyl ether because of the greater capability of the former to solvate the positively charged magnesium fragment in the transition state.

If, on the other hand, the rate of inversion is primarily dependent upon the electrophilicity on the MgX fragment, inversion should be slowest in the most basic ether: the ability of the basic ether to donate electrons to the magnesium atom should considerably reduce the electrophilicity of this atom.

The spectra of Figure 10 indicate that inversion is fast in diethyl ether, slower in tetrahydrofuran, and slowest in diglyme. Consequently, the dependence of inversion rate on solvent character also provides

qualitative support for the suggestion that the inversion mechanism is characterized by a molecularity higher than one.

The effect of structure on the rate of inversion has not been investigated carefully. The activation parameters obtained for inversion of 3,3-dimethylbutylmagnesium chloride and 2-phenyl-3-methylbutylmagnesium chloride in ether suggest that inversion occurs at approximately the same rate in both compounds: the secondary Grignard reagents examined definitely invert more slowly. This difference in rate may reflect the differences in the relative stabilities usually ascribed to primary and secondary carbonium, or major differences in the geometry of the molecules near the C=Mg bonds.

The possibility of inversion involving rapid elimination and addition of magnesium hydride is ruled out by the fact that this would be expected to give intermolecular hydrogen exchanges which would affect the spin-spin splitting patterns: however, there is no definite evidence which excludes some sort of homolytic cleavage recombination mechanism for the inversion process.

If the mechanism of the inversion reactions bears any resemblance to the electrophilic substitution reactions of organomercury compounds, it is interesting to speculate on the possible rate of alkyl-group migration with retention of configuration. The organomercury compounds commonly exchange through a four-center transition state and the rate of exchange with retention of configuration is much greater than that with inversion. If this type of transition state is also favorable with organomagnesium compounds, the rate of metal-metal exchange with retention of configuration may be very much faster than the rate of inversion.

Experimental Section

Nuclear magnetic resonance spectra were obtained with the spectrometers described previously. Analyses of the ABX spectra of the 2-phenyl-3-methylbutylmagnesium derivatives were considerably more uncertain than those for the AA'XX' systems because the low-intensity outer lines of the AB part of the spectrum frequently could not be distinguished from noise in the spectrum and because the X part of the spectrum could not be analyzed at all.

To obtain the activation energies for the 2-phenyl-3-methylbutylmagnesium derivatives, the observed spectra were compared with those calculated as described previously. The comparison in the region of intermediate exchange rate is a fairly subjective procedure and consists of visual comparison of the "shape" of the observed and calculated spectra. This estimation procedure, coupled with the dependence of the calculated line shape on the value chosen for 1/\tau_2, combine to introduce a certain arbitrary character to the analysis of these spectra. The values chosen for 1/\tau_2 were 0.20 and 0.25 sec. for 2-phenyl-3-methyl-

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Experimental Section

Nuclear magnetic resonance spectra were obtained with the spectrometers described previously. Analyses of the ABX spectra of the 2-phenyl-3-methylbutylmagnesium derivatives were considerably more uncertain than those for the AA'XX' systems because the low-intensity outer lines of the AB part of the spectrum frequently could not be distinguished from noise in the spectrum and because the X part of the spectrum could not be analyzed at all.

To obtain the activation energies for the 2-phenyl-3-methylbutylmagnesium derivatives, the observed spectra were compared with those calculated as described previously. The comparison in the region of intermediate exchange rate is a fairly subjective procedure and consists of visual comparison of the "shape" of the observed and calculated spectra. This estimation procedure, coupled with the dependence of the calculated line shape on the value chosen for 1/\tau_2, combine to introduce a certain arbitrary character to the analysis of these spectra. The values chosen for 1/\tau_2 were 0.20 and 0.25 sec. for 2-phenyl-3-methyl-

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butylmagnesium chloride in ether and tetrahydrofuran, respectively.

The samples of the Grignard reagents were prepared as described previously. Grignard reagents and dialkylmagnesium compounds containing $\text{C}_2\text{H}_5\text{Mg}$ groups were identified by the characteristic chemical shift and spin-coupling patterns of their $\alpha$-protons. The resonances of protons adjacent to a strongly electropositive metal occur at significantly higher field than those of any of the other compounds likely to occur in the solution; these protons could consequently be recognized and examined without difficulty. The $\alpha$-proton resonances of the secondary Grignard reagents were usually complicated by spin coupling and of lower intensity than those of the primary Grignard reagents, and were frequently difficult to locate. These Grignard reagents were characterized by addition of a slight excess of water to the sample tube followed by centrifugation to remove the precipitated magnesium salts. Comparison of the spectrum of the organometallic solution and that of the hydrolyzed solution with the spectra of solutions in the same solvent of the starting halide and of the hydrocarbon expected from hydrolysis (when available) usually allowed the resonances due to Grignard reagent to be identified without difficulty.

The quantity of solids produced during the preparation depended primarily on the type of halide used: bromides frequently produced no solids at all; chlorides often gave small quantities of a white flocculent precipitate.

Grignard reagents prepared in tetrahydrofuran were occasionally pale yellow after heating, and showed a tendency to precipitate larger amounts of solids than the corresponding ether solutions. Occasionally, a tetrahydrofuran solution of an alkylmagnesium chloride would give such heavy deposits of crystals as to fill the liquid phase; however, sufficient sample for n.m.r. examination could usually be recovered by centrifugation. The signal intensity in such samples was usually slightly less than that of the same solutions before crystallization.

Tetrahydrofuran solutions occasionally gave broad spectra immediately after their preparation: resolution always improved after the sample had aged for several days.

Solutions prepared in diglyme had approximately the same characteristics as those prepared in tetrahydrofuran, except that the viscosity of the final diglyme solution was significantly greater.

The yields of Grignard reagent prepared in diethyl ether solution were estimated to be 70–95% by comparison with the $^{13}$C satellites of solvent, based on starting halide.

2-Phenyl-3-methyl-1-butanol. Diisopropylmagnesium was prepared by addition of 66 g. (0.75 mole) of dry dioxane to a Grignard solution prepared from 92 g. (0.75 mole) of 2-bromopropane and 18 g. (0.75 mole) of magnesium in 300 ml. of ether in a 1-l. three-necked, round-bottomed flask equipped with mechanical stirrer, condenser, and pressure-equalized dropping funnel. The precipitated magnesium bromide dioxanate was not separated from the dialkylmagnesium solution to which was then added 60 g. (0.50 mole) of styrene oxide at such a rate as to maintain gentle refluxing. The reaction mixture was stirred for 4 hr. at room temperature, heated under reflux for 1 hr., and hydrolyzed with saturated aqueous ammonium chloride solution to the point at which the solids conglomerated on the sides of the flask. The ether layer was decanted from the salts and dried over calcium sulfate. Removal of the ether on a rotary evaporator and distillation of the residue through a 20-cm., wire-spiral-packed column yielded 53 g. of product, b.p. 84–88°C at 2 mm. (lit.33 b.p. 90° at 4 mm.); the purity of the product was estimated to be 90–95% from the n.m.r. spectrum.

2-Phenyl-3-methylbutyl chloride was prepared by addition of 50 ml. of thionyl chloride to a solution of 25 ml. of 2-phenyl-3-methyl-1-butanol and 50 ml. of dimethylformamide in a 200-ml. erlenmeyer flask immersed in an ice bath. The temperature of the solution was maintained at 15 ± 5°C during the addition. The solution was allowed to stand at room temperature for 6 hr. after addition of the thionyl chloride, then hydrolyzed by pouring into 200 ml. of cold water. The organic layer was separated and the aqueous layer was extracted twice with 50-ml. portions of ether. The combined extracts were dried over calcium chloride, then distilled twice through a 20-cm., wire-packed column at reduced pressure to yield 12 g. (approximately 45%) of product, b.p. 67–74°C (0.8 mm.).


2-Phenyl-3-methylbutylmagnesium chloride could be prepared from the chloride only with difficulty. The most successful procedure involved mixing 0.1 ml. of the chloride and 0.1 ml. of ether with magnesium turnings in an n.m.r. tube. The magnesium turnings were then broken up with a Nichrome wire. Onto this mixture was poured 0.4 ml. of ether without mixing the layers. The tube was sealed and heated in the usual manner: after approximately 1 hr. at 100°C reaction between magnesium and the halide occurred. The remainder of the preparation was unexceptional.

1,3-Dibromo-2,2-dimethylpropane. The procedure used was a modification of that of Schurink. In a 500-ml. round-bottomed, three-necked flask equipped with a pressure-equalized dropping funnel and air-cooled condenser was placed 183 g. (0.92 mole) of 2,2-dimethyl-1,3-propanediol. The flask was heated on the steam bath and 500 g. of freshly opened phosphorus tribromide was added over the course of 2 hr. The steam bath was exchanged for an oil bath and the temperature was increased to 160°C. The temperature was maintained at this level for 24 hr. The heterogeneous mixture resulting was then cooled and poured into 1 l. of water. The lower layer was separated and dried over calcium sulfate. The n.m.r. spectrum indicated that this material was approximately 70% of the desired bromide. The yield was 200 g., and the product was used without further purification.

3,3-Dimethylcyclobutane-1,2,4-tricarbonylic acid was prepared following the procedure of Campbell and Rydon, substituting the crude 1,3-dibromo-2,2-dimethylpro-

pane prepared above for the 1,3-diiodo-2,2-dimethyl-propane used by these workers. The yield of acid was 22 g., b.p. 75–103° at 12 mm. (lit. b.p. 105–106° at 15 mm.).

Silver 3,3-dimethylcyclobutanecarboxylate was prepared from 3,3-dimethylcyclobutanecarboxylic acid following the procedure of Cason and Way. The silver salt was air dried at room temperature, and then dried at 0.5 mm. for 4 days prior to its use in the brominative decarboxylation.

3,3-Dimethylcyclobutyl Bromide from Silver 3,3-Dimethylcyclobutanecarboxylate. The procedure was modeled after that described for the preparation of cyclobutyl bromide. The reaction flask was dried by distilling 50 ml. of carbon tetrachloride from it immediately before use. Bromine and carbon tetrachloride were dried by distillation from phosphorus pentoxide.

The silver salt (38.9 g., 0.17 mole) was added over the course of 1 hr. to 250 ml. of carbon tetrachloride and 28.9 g. (0.18 mole) of bromine in a 500-ml., three-necked, round-bottomed flask equipped with mechanical stirrer and thermometer and immersed in a Dry Ice-acetone bath. The salt was added through a piece of Gooch tubing connecting one inlet of the reaction flask directly to the erlenmeyer flask in which the salt had been dried. No carbon dioxide evolution was observed until the solution had been warmed briefly to +20°; after the reaction had started, the solution was cooled to 0° and the remainder of the silver salt was added. When gas evolution had ceased, the reaction mixture was allowed to stand overnight and then filtered, washed once with aqueous sodium bisulfite, once with 2 N potassium hydroxide solution, and once with water. The organic layer was dried over calcium sulfate, and the carbon tetrachloride was removed through a 10-cm. glass-helix packed column. The bromide was distilled under slightly reduced pressure through a 30-cm. Vigreux column. The product (12 g., 45%) had b.p. 132° by the capillary boiling point method. The purity of the product was approximately 95% as estimated by v.p.c. (column K, 110°). The n.m.r. and infrared spectra were consistent with the desired structure.

Anal. Calcd. for C_9H_4Br: C, 44.19; H, 6.80; Br, 49.01. Found: C, 44.13; H, 5.94; Br, 48.80.