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Rearrangements in Organomagnesium Chemistry

E. ALEXANDER HILL

Department of Chemistry, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53201 (U.S.A.)

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CONTENTS

I. INTRODUCTION

The term "rearrangement" most generally brings to mind the picture of 1,2- "Wagner-Meerwein" shifts, common in carbonium ion chemistry. By contrast, the 1,2-shift of alkyl or hydrogen appears to be rare or absent in organometallic or carbanion

chemistry. Here, typical rearrangements, when they occur, are dominated by β-cleavage processes and their reverse, intramolecular addition to an unsaturated function. This review will be concerned most extensively with these reactions--a survey of cases in which they have been observed and a critical summary of mechanistic information. The discussion will involve primarily organomagnesium compounds, though examples involving other metals will be mentioned when useful for illustration, comparison, or contrast. A survey will be made first of 1,2-shifts and allylic rearrangements, and to complete the review, some radical processes which have led to rearrangement in organomagnesium formation and reactions will be discussed.

II. 1,2-SHIFTS

Some years ago, the mechanism chemist's repertoire of 1,2-shifts in "carbanion chemistry" was fairly impressive. These included,* among others, the Wittig and Stevens rearrangements and some carbon-to-carbon rearrangements of organoalkali compounds [eqns 1-3]. However, time and more detailed study have taken

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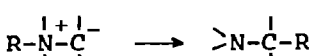

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their toll among those reactions formerly believed to be bona fide simple 1,2-migrations in anions.

First of all, there is good theoretical justification for believing that the anionic analog of Wagner-Meerwein rearrangement,

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*See, for instance, references 1-5.

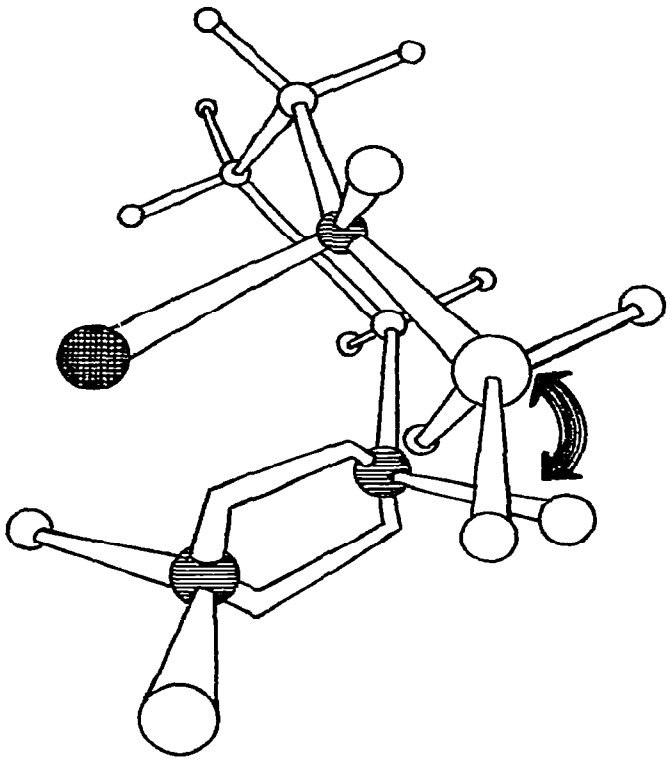


Figure 1. Cyclization of 1-hepten-6-yl organometallic to trans-2-methylcyclopentylmethyl organometallic. The three carbon atoms and the metal atom directly involved in the addition are shaded. Steric interaction of the methyl group with the double bond is indicated by the arrow. Solvation and other coordination to the metal is omitted.

a 1,2-alkyl shift with retention of configuration at the migrating carbon [see Fig. 1a], should be quite difficult. Molecular

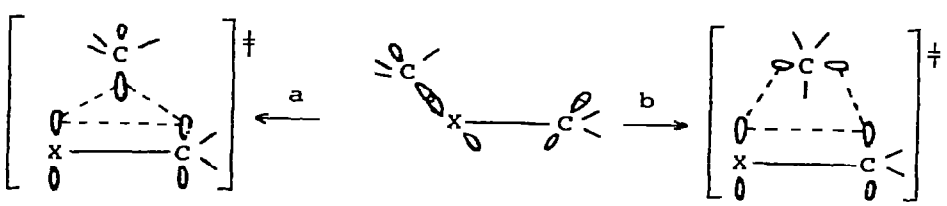
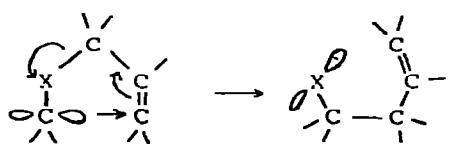


Figure 1. Transition states for anionic 1,2-alkyl rearrangement

orbital calculations for the rearrangement [6,7] suggest that the bridged intermediate or transition state should have quite a high energy. This is not unexpected, since the four electron - three orbital system is basically that of the antiaromatic cyclopropenyl anion. Viewed as a [1,2] sigmatropic rearrangement, both carbanion and radical rearrangements are forbidden processes if they occur suprafacially and with retention of configuration [8,9]. Rearrangement would be allowed if it occurred with inversion at the migrating carbon [Fig. 1b] or in antarafacial fashion, but these may be be energetically prohibitive for steric reasons.

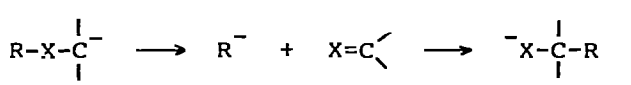
Rearrangement of an allyl group is an allowed [2,3] sigmatropic process if rearrangement is accompanied by "allylic inversion" of the migrating allyl [eqn 4]. Published experimental evidence



(4)

appears to support such a concerted rearrangement [10-13].

Experimentally, evidence against a simple 1,2-shift was first put forth in support of a heterolytic cleavage process for the Wittig rearrangement [eqn 5].* More recent work on Wittig



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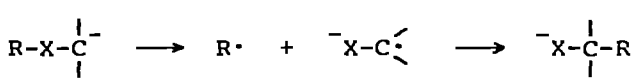
and Stevens-type ylid rearrangements has been more consistent with a homolytic radical pair mechanism for alkyl group migration [eqn 6]. A carbon-to-carbon migration of the benzyl group [15]



(6)

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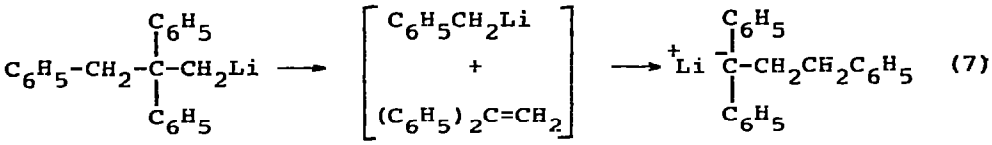
*For reviews of the evolution of mechanistic thought on Wittig and Stevens rearrangements, see references 10 and 14.

was observed by Grovenstein [eqn 7]. The reaction was considered

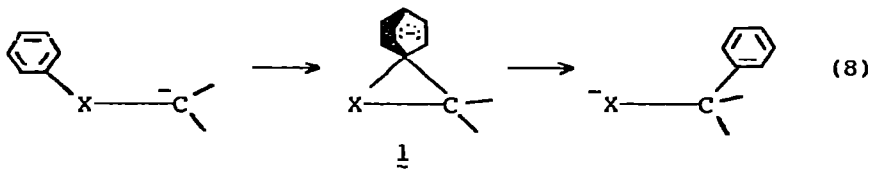


(7)

to occur via the heterolytic cleavage and recombination shown, since the alkyl group of external alkyllithium was incorporated [16].

The interesting suggestion has been made that 1,2-migrations might be symmetry-allowed if the carbanion is tightly associated with a metal ion; concurrent alkyl and metal migration in opposite directions would be involved [8]. Molecular orbital calculations have also suggested a favorable "metal catalysis of carbanion rearrangement" by a transition metal species [7].

Aryl migration may present a different picture. A concerted intramolecular migration of phenyl creates no problems relating to orbital symmetry, and is suggested by molecular orbital calculations to be reasonable in energy [6,7]. Formation of the transition state in such a migration (or intermediate, if one exists) corresponds to nucleophilic attack by the carbanion or organometallic function on the aromatic ring, with electron delocalization [eqn 8]. Experimental results in agreement with



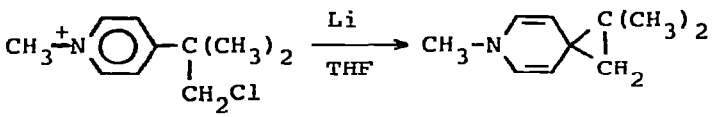
(8)

1

aryl bridging include an apparent requirement for the perpendicular geometry shown in 1 in a "nitrogen Wittig" rearrangement [17], and relative migratory aptitudes in some carbon-to-carbon aryl rearrangements [6,18-21]. However, observation of esr signals during a carbon-to-carbon

rearrangement, and an unexpected migratory preference suggest that the situation may be more complex [21]. A radical-pair mechanism for aryl migration in the Wittig rearrangement has been proposed [22].

Spiro structures analogous to 1 have been isolated or observed in the instances of eqns 9 [21] and 10 [23]. In eqn 10,



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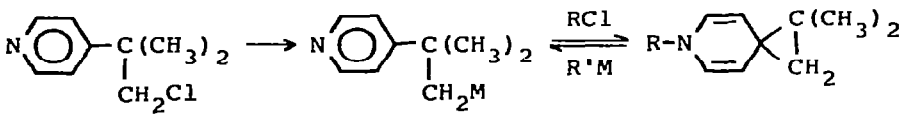
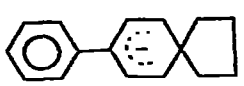


(10)

R = $COOC_2H_5$, $COOCH_3$, COC_6H_5, $COCH_3$, $(CH_3)_3Si$

M = Na, Li, Mg, Hg (forward only)

cyclization might either precede or follow electrophilic attack on the nitrogen. With higher homologs, spiro intermediates 2 and 3 have been observed or isolated [24,25]; ion 3 is quite stable to cleavage.



2

3

Since organomagnesium compounds are generally more covalent than their alkali-metal analogs, such carbanionic or organometallic 1,2-shifts are understandably less common. Only quite recently has the Wittig rearrangement of 4 been observed in HMPT* [26].

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*Abbreviations used for solvents in this review are as follows: ethyl ether - ether; tetrahydrofuran - THF; N,N,N',N'-tetramethylethylene diamine - TMEDA; hexamethylphosphoric triamide - HMPT.

$$C_6H_5O^-(C_6H_5)_2{}^+MgX \longrightarrow {}^-O\text{-}C(C_6H_5)_3 \; {}^+MgX \qquad (11)$$

4

It is significant that the rearranging solutions were deep red in color, whereas colorless solutions in the absence of HMPT do not rearrange. It appears probable that more rearrangements of organomagnesium compounds may be observed in the future by taking advantage of the ionizing power of this solvent. The cyclization in eqn 10 occurs with the Grignard reagent or even with the mercury derivative [23], and the magnesium derivative of ion 3 was stable to ring opening, in common with the alkali metal compounds [25].

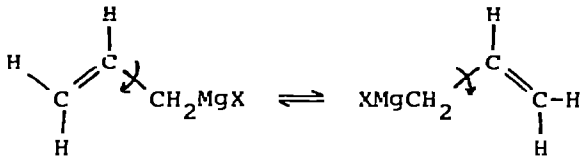
III. ALLYLIC REARRANGEMENTS

A second broad rearrangement category -- allylic rearrangement -- is better represented in organomagnesium chemistry. It was found at an early stage the Grignard reagents prepared from halides that are allylic isomers, such as crotyl and α-methylallyl, appear on the basis of chemical reactions to be identical [27]. From the behavior of "butenylmagnesium bromide" in a variety of reactions, it was concluded that its structure is primarily the crotyl structure, quite likely in equilibrium with much smaller concentrations of the α-methylallyl isomer [27-29].

A. Allylic Rearrangement and the Structure of Allylmagnesium Compounds

The structures of allyl and substituted allylic organometallic compounds have been investigated spectroscopically. The nmr spectra have been particularly important, but at the same time their interpretation has been somewhat ambiguous. A classical σ-bonded structure, such as 5a or 5b, with unhindered rotation

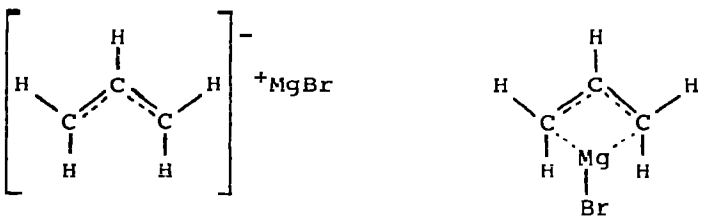
about the formal single bond, should have four different resonances,



(12)

5a 5b

in an $ABCX_2$ pattern (type I). With rapid allylic rearrangement of σ-bonded structures as in eqn 12, all four methylene protons would become equivalent on the nmr time scale, giving an AX_4 pattern (type II). A planar allylic anion (6) or a bridged or π-complex structure (7) would have equivalent methylene groups, but unless



6 7

rotation about the partial double bonds were fast, the two protons of each methylene group would be different. This would yield an ABB'CC' spectrum (type III). Rapid rotation in either of these structures would make all methylene protons again equivalent, giving a type II spectrum.* A spectrum of type III

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*A bridged structure similar to 7, but having the magnesium coplanar with the allyl system, and the methylene protons symmetrically disposed above and below this plane, would also give the type II spectrum. However, such a structure seems unlikely, since all π-electron overlap with the central carbon would be lost.

could also be observed with the equilibrium in eqn 12, provided some factor should hinder rotation about the formal single bonds in 5a and 5b. Such factors might be interaction of the metal atom with the double bond, or partial delocalization of the C-metal bond electrons. In the limit, these descriptions could merge with 6 or 7.

In 1959, Nordlander and Roberts [30] reported that the nmr spectrum of allylmagnesium bromide is of type II, and concluded that the most likely interpretation was the rapid equilibrium of eqn 12. The spectrum is reported to undergo no change at very low temperatures [31]. However, there is recent indication of some temperature dependence [32] which would be consistent with a slowing of eqn 12.

With methyl substitution, the spectra are most satisfactorily interpreted as arising from predominantly or exclusively the primary isomers 8a [33] and 9a [34]. Furthermore, the chemical

$$\underset{\underset{8a}{}}{CH_3CH{=}CH{-}CH_2MgBr} \rightleftharpoons \underset{\underset{8b}{}}{CH_3\overset{\overset{MgBr}{|}}{C}H{-}CH{=}CH_2} \qquad (13)$$

$$\underset{\underset{9a}{}}{(CH_3)_2C{=}CH{-}CH_2MgBr} \rightleftharpoons \underset{\underset{9b}{}}{(CH_3)_2\overset{\overset{MgBr}{|}}{C}{-}CH{=}CH_2} \qquad (14)$$

shifts of the unsubstituted allyl Grignard may be interpreted as an average of the two covalent structures 5a and 5b using 8a and 9a as models. With 9, the two methyl groups appear as separate peaks at low temperature, but coalesce below room temperature [34]. Equilibration of the two methyl groups via a low concentration of the tertiary isomer 9b provides an explanation. Only a single methyl resonance is observed for 8 at all

temperatures [33]. A recent study of the coupling constants in spectra of 8 and other substituted allylic Grignard reagents indicates that both cis- and trans-isomers are present, and in rapid equilibrium [35]. With bis(neopentylallyl)magnesium, 10, spectra of the cis- and trans-isomers are observed at low temperature [36].

$$[(CH_3)_3CCH_2\text{-}CH{=}CH\text{-}CH_2]_2Mg$$

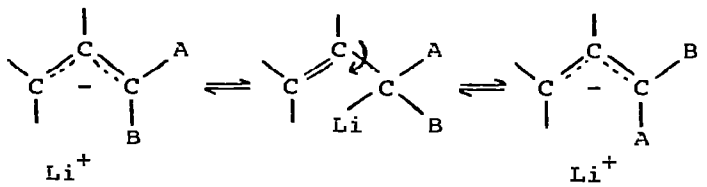
10

As indicated above, there are alternatives to the rapid allylic rearrangement in eqn 12 for interpretation of the AX_4 spectrum of allylic organomagnesium compounds. The ^{13}C shifts of allylmagnesium bromide may be more compatible with the ionic structure 6 [37]. In a recent review, the case was presented for "delocalized bonding" to the metal in allyl derivatives of lithium, magnesium, zinc, and cadmium [38]; that description appears to correspond to symmetrical π-allyl bonding, presumably with a fully anionic allyl anion 6 (in an ion pair) as the extreme case. The question is then whether allylmagnesium compounds are more correctly considered as rapidly equilibrating unsymmetrical structures (eqn 12) or as symmetrical structures which undergo rotation about partial double bonds (6 or 7).

The symmetrical picture receives some support from studies of allylic lithium compounds. Allyllithium gives a type III spectrum at low temperature in ether or THF, interpreted as an allyl anion--lithium ion pair (probably occurring in a higher aggregate)[39]. The ionic picture of allyllithium is in accord with its ir and uv spectra [39,40]. At higher temperatures, the spectrum is of type II, indicating rapid internal rotation about the partial double bonds. Though the chemical shifts of

protons in allylmagnesium bromide may be adequately explained on the basis of eqn 12, they are also quite similar to those of allyllithium. Furthermore, butenyllithium, which might also be expected to be ionic, has an nmr spectrum at room temperature not greatly different from butenylmagnesium bromide [41]. On cooling in dimethyl ether, changes occur in the butenyllithium spectrum which are in accord with freezing out first the rotation of the $CHCH_3$ group (which interconverts cis- and trans-isomers), and then at lower temperatures, the rotation of the CH_2 group [42]. Somewhat similar results, also implying an allylic anion which can undergo cis-trans isomerization by rotation about a partial double bond, have been found for pentadienyllithium [43] and phenylallyllithium [44]. With 3-neopentylallyllithium (the adduct of t-butyllithium and 1,3-butadiene), the evidence appears to favor covalent and slowly equilibrating structures in hydrocarbon solvent [45], but an ion pair structure in ethers [46].

There is not agreement on the nature of the process leading to cis-trans isomerization in the allylic lithium compounds. It may be either hindered rotation in an allylic anion, or be due to equilibrium with a low concentration of covalent isomer, in which a rotation could occur (eqn 15). It may be significant that the



(15)

presumably more ionic sodium and potassium phenylallyl derivatives undergo this rotation more slowly than the lithium compound [44]. Rotation in the lithium compound could be faster because it reverts more readily to a covalent isomer, or because stronger interaction in an ion-pair or π-complex weakens the π-bonds.

In contrast with the alkali metal derivatives, there is nmr evidence in other metal-allyl compounds for covalent σ-bonded structures, leading to type I spectra. For instance, these are observed for allyldiethylaluminum [47] in ether at -20°, for diallylzinc [48] in THF at -100°, and for triallylboron and tri(methallyl)boron at reduced temperatures [49-51].

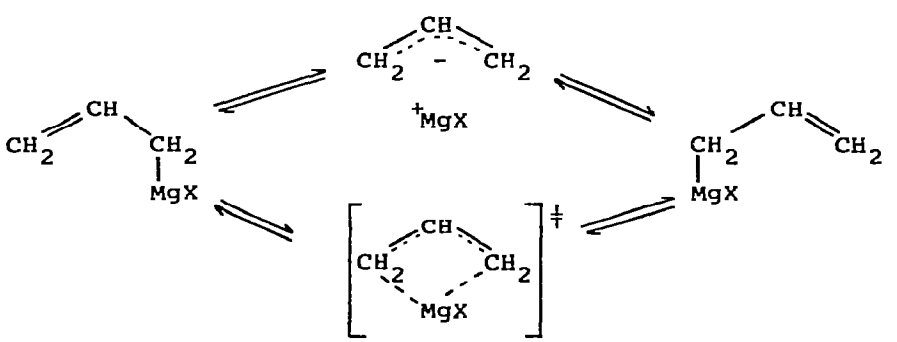
The low-temperature spectrum of diallylmagnesium coordinated with the diamine bispidine in THF shows spectral changes similar to those published for triallylboron [49], though at the lowest temperature used, the transition to an $ABCX_2$ spectrum was incomplete [32]. In addition to decreasing the accessibility of the magnesium, the amine might be expected to make the bond between allyl and magnesium more ionic. Hence, approach of the spectrum to type I, rather than to type III, argues for the unsymmetrical allylmagnesium structure, undergoing rapid allylic rearrangement at ordinary temperatures. Additional possibilities may remain for temperature-dependent equilibria between ionic and covalent structures.

A few further comments may be in order, since the interpretation of the reactions of allylmagnesium compounds (and possibly even the legitimacy of their inclusion in a review of rearrangements) depends upon the picture adopted for their structure. (a) In the ir spectrum, the double bond stretch [31] of allyl organomagnesium compounds (1565-1588 cm^{-1}) falls between those of clearly covalent allyl compounds (e.g., diallylmercury, 1620 cm^{-1}) and that of allyl sodium (1535 cm^{-1}). The band in the latter has been assigned as the antisymmetric stretching mode of the allyl anion [52]. The antisymmetric stretch of the allyl group in transition metal π-allyl complexes (where the carbon-to-carbon bonding is presumably weakened by interaction

with the metal) appears to occur at somewhat lower frequencies [53]. (b) Ultraviolet spectra of benzyl and cinamyl organomagnesium compounds have maxima at shorter wavelength than corresponding alkali metal derivatives, but longer wavelength than the hydrocarbons from which they are derived [54].

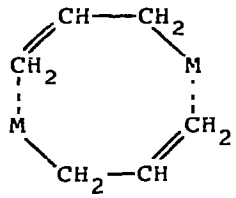
These facts, taken together with nmr data noted above, would appear to be best accomodated by the view that allylic (and benzylic) organomagnesium compounds have a polar covalent carbon-metal bond, with partial delocalization of the electron pair into the π-electron system. Hybridization at the allylic carbon, and the extent of delocalization of the C-Mg bond electrons might be expected to depend upon solvent, substitution of the carbon skeleton, and perhaps the temperature [32]. Based on a variety of nmr and electronic spectral data, such a picture has been considered for benzylic [40,55] and allylic [45] lithium compounds. Such delocalization of carbon-metal bonding electrons resembles the "carbon-metal hyperconjugation" utilized by Traylor to explain electron-releasing effects by CH_2M groups [56]. Interaction of the double bond with the metal atom (in the manner of a π-complex) might also contribute to the picture.

Assuming for the moment the rapidly rearranging σ-structure for allylmagnesium compounds, there appear to be two limiting mechanisms for the rearrangement [eqn 16): (a) the covalent



(16)

carbon-magnesium bond may dissociate to an ion pair, which reassociates at the other end of the allylic anion; or (b) the magnesium may interact with the double bond, and shift synchronously from one end of the allylic system to the other, passing through a symmetrical transition state or intermediate possibly resembling a π-complex. The two mechanisms differ in the extent of covalent interaction between magnesium and allyl groups at the half-way point in the migration. Allylic rearrangement of allylboron derivatives is first order, and is inhibited by either donor solvents or electron-donor substituents (such as alkoxy groups) on the boron [49-51]. Both would tend to satisfy the Lewis acid site on the boron, decreasing its ability to interact with the double bond. Hence, alternative (b) seems most probable for the boron derivatives. In the magnesium case, the situation is not so clear, since observation of the "frozen" Grignard structure [32] is less certain. The equilibration rate of diallylmagnesium at low temperature in the presence of bispidine appears to be concentration independent [32]. Separate, discrete spectra are observed for the bispidine complex and the uncomplexed organomagnesium (presumably complexed to tetrahydrofuran), above the temperature at which slowing of the rearrangement is found. Since amine complexing apparently slows the exchange rate, arguments similar to those in the boron case would suggest again albernative (b). The lack of firm knowledge about the association of allyl organomagnesium compounds weakens the conclusion. However, it seems less likely that the rearrangement takes place during a bimolecular allyl exchange between metal atoms (11) as suggested by a concentration dependent broadening in the spectrum of diallylmercu··· [39,57].



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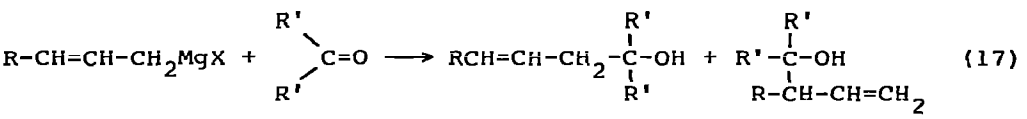
B. Rearrangement in the Reactions of Allylmagnesium Compounds

In addition to the mobile rearrangement equilibrium of allylic organomagnesium compounds, rearrangement during the process of reaction of the organomagnesium with an electrophile is quite common. Thus, even though the "butenyl Grignard" appears to have almost entirely the crotyl structure (12a, R = CH_3), adducts to all but the most hindered carbonyl groups have largely the α-methylallyl structure 13b.* Rearrangement must then occur either during or prior to reaction of the Grignard.



(17)

12a 13a 13b

Until quite recently, the favored explanation for the formation of rearranged products was the cyclic mechanism of

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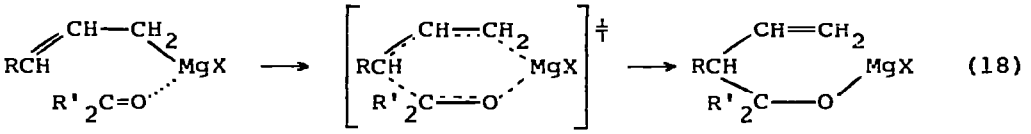
*Preparation and reactions of the allyl and "butenyl" Grignard reagents have been reviewed from the synthetic point of view [29], and more recently a review of the reactions of various allylic organometallic compounds has appeared [58]. Discussions of the reactions of allylic Grignard reagents are also found in reviews of reactions of allylic compounds [28,59,60] and Grignard reagents [61].

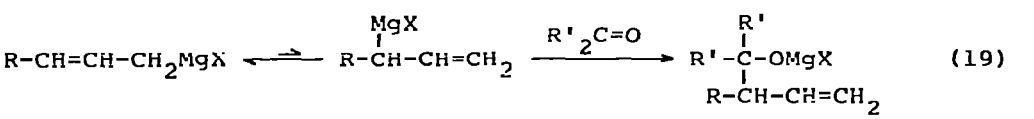
eqn 18, originally proposed by Young and Roberts [27]. This



(18)

mechanism is referred to as the S_Ei' mechanism. It can also explain the overall high reactivity of allylic Grignard reagents, the formation of adducts in preference to enolization products with hindered carbonyl groups, and the strong preference of 1,2- over 1,4-addition with conjugated carbonyl functions [29].

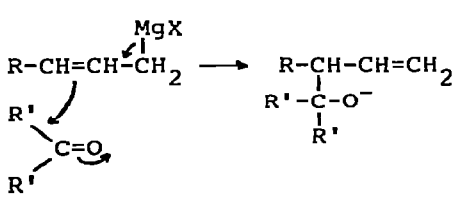
An alternative mechanism, suggested at an early date [27], and recently claimed to be more in accord with the stereochemistry of addition to carbonyl compounds [62], is the S_E2 mechanism. It has the allylic Grignard reacting without rearrangement. Formation of rearranged product requires that the small equilibrium concentration of secondary reagent 12b react much more rapidly than the primary (eqn 19).



(19)

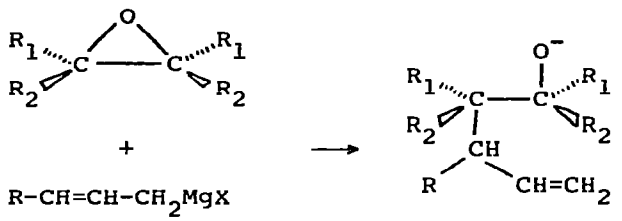
12a 12b

Recently, Felkin and coworkers have presented rather strong arguments that neither of the above mechanisms is correct, and that the dominant mechanism in most reactions of allylic organomagnesium compounds is the non-cyclic S_E2' mechanism (eqn 20), in which coordination of magnesium with the carbonyl



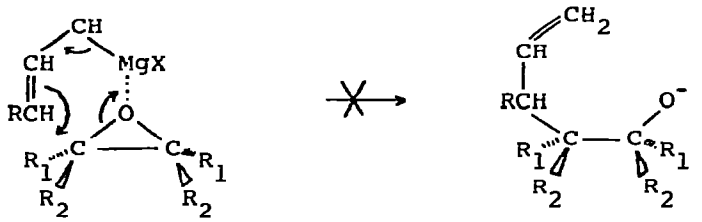
(20)

oxygen is not required. The following points are critical to the argument: (a) Reaction of allylic or saturated organomagnesium compounds with epoxides occurs with complete inversion of configuration at the epoxide carbon (eqn 21)[63,64]. The only



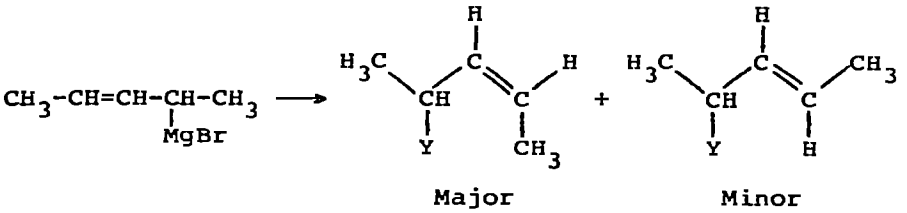
(21)

sterically reasonable result of a cyclic mechanism for reaction with epoxides would be retention of configuration (eqn 22), so epoxides must not react by a cyclic mechanism. (b) The reactions



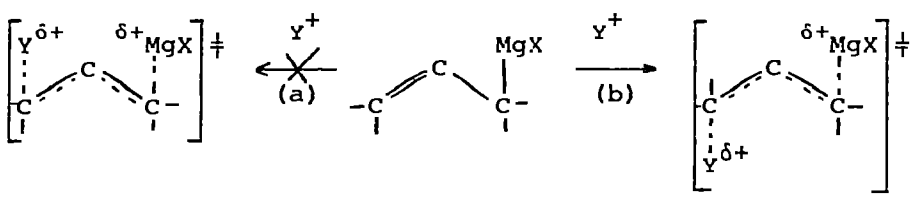
(22)

of Grignard reagents with epoxycyclohexane and with acetone have marked similarities [65,66]. In both reactions, allylmagnesium bromide is more reactive than propylmagnesium bromide by a substantial and similar margin (820 and 700, respectively); 3-substituted allylic Grignards react entirely at the secondary carbon; and α,γ-dimethylallyl Grignard forms product with a <u>cis</u> double bond preferentially (eqn 23)[67]. The conclusion was



(23)

drawn that the two reactions have similar mechanisms. Since the mechanism of the epoxide reaction cannot be cyclic, neither may the acetone reaction. (c) The allyl, "butenyl" and α,γ-dimethylallyl Grignard reagents all have very similar reactivities, in either reaction with epoxycyclohexane or with acetone. This contributes to the conclusions reached in (b). Furthermore, it is inconsistent with the S_E2 mechanism, which requires that the minor α-methylallyl isomer (12a, R = CH_3) of the "butenyl Grignard" must react much more rapidly than the more plentiful primary crotyl isomer. (d) A further argument against the cyclic mechanism comes from orbital symmetry principles [68,69]. It is predicted that a synchronous electrophilic displacement with allylic rearrangement should occur antarafacially (eqn 24b).



(24)

This is possible in the S_E2' mechanism, but sterically unlikely in the cyclic S_Ei' mechanism.

The S_E2' mechanism is also felt by Felkin and coworkers to be most consistent with the stereochemistry of some addition reactions of allylic Grignards to aldehydes [70], as well as the reactivity and tendency toward addition of allylic organomagnesium compounds. It is also interesting to note that allylic rearrangement has recently been observed in the unusual instance of conjugate addition of an allylic Grignard (eqn 25)[71].

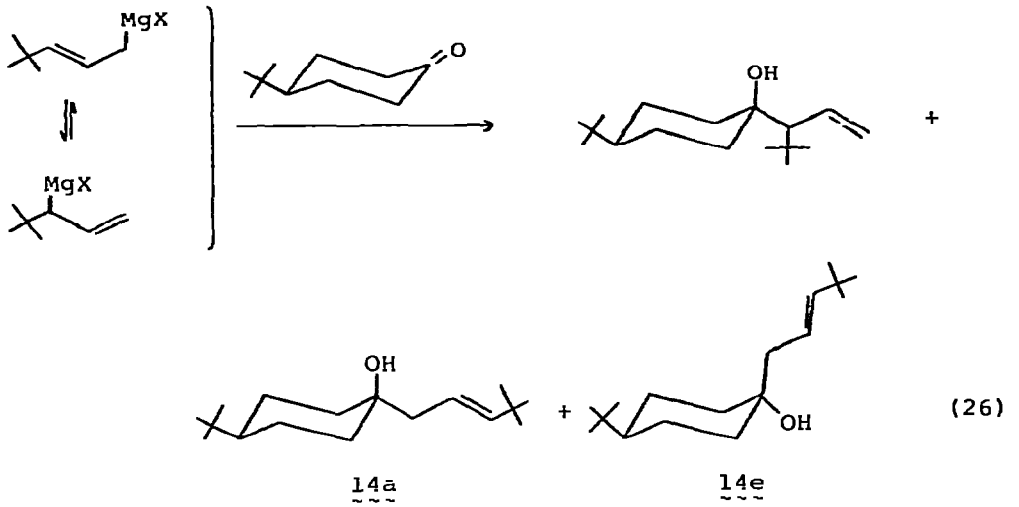
$$CH_3CH{=}CHCH_2MgBr + (CH_3)_2C{=}C(COOR)_2 \longrightarrow CH_2{=}CHCH(CH_3)C(CH_3)_2{-}CH(COOR)_2 \quad (25)$$

In reaction of allylic organomagnesium compounds with carbonyl groups where there is much steric hinderance, larger amounts of the "unrearranged" structure 13a may be formed. These also present a mechanistic dilemma. Are they the products of S_E2 addition of the major primary allylic isomer 12a, or do they result from the S_E2' mechanism with rearrangement from the minor secondary allylic isomer, 12b? In a study of the reaction of the crotyl Grignard with a variety of ketones, Benkeser and coworkers found increasing amounts of products having the crotyl structure 13a with increasing bulk of substituents on the carbonyl carbon [72]. In addition, these crotyl compounds had cis/trans ratios greater than unity. They concluded that the predominance of cis- product is inconsistent with the cyclic S_Ei' mechanism for steric reasons, and more consistent with an S_E2 mechanism. No serious consideration appears to have been given the S_E2' mechanism.

The preference for the cis- structure was felt to arise from the apparent stability of cis-allylic carbanions relative to their trans-isomers [73]. By analogy, a cis- geometry for the Grignard, and for a carbanion-like transition state might predominate. The preferential formation of cis- products was also noted by Felkin in a case where the primary-vs.-secondary Grignard structure question does not exist (eqn 23)[67], but results were interpreted with the S_E2' mechanism.

Substantial amounts of "abnormal" linear products are also obtained when ketones of modest steric requirement react with 3-t-butylallyl Grignard (studied by Felkin and coworkers)[74]. In the addition to 4-t-butylcyclohexanone, a mixture of products shown in eqn 26 is obtained.

The ratio (1.2:1) of 14e to 14a was similar to that from the allyl



(26)

14a 14e

Grignard itself (1.06:1) but quite different from that for the propyl Grignard (0.35:1). It was concluded that products 14a and 14e are formed by a mechanism quite similar to that of the allyl Grignard, hence S_E2'.

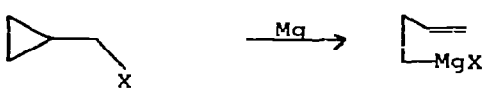
One word of caution in all of these interpretations might be noted. It was recently found by Benkeser [75] and by Miginiac [76] that some additions of allylic Grignard reagents to ketones may be reversible. Thus, by reversal of the addition, the more sterically congested product 13b may be isomerized to the more stable linear isomer 13a. In the absence of control experiments to test for this possibility, there is some uncertainty whether or not the product distributions represent kentically controlled preferences.

IV. REARRANGEMENT PATHWAYS INVOLVING RING CLEAVAGES AND INTRAMOLECULAR ADDITIONS

A. Survey of Rearrangements Studied

1. The cyclopropylmethyl Grignard reagent

In 1951, Roberts and Mazur [77] reported that attempts to prepare the cyclopropylmethyl Grignard reagent from either the chloride or the bromide gave unsaturated products derived from the ring-opened Grignard (eqn 27). Previously, Smith and McKenzie [78] had obtained similar products, but had not recognized that rearrangement of the Grignard reagent was involved. In later work, Roberts and coworkers [79] also found rearrangement products in a reaction involving the Grignard reagent prepared from 4-chloro-1-pentene (eqn 28). Similar rearrangement, followed by isotopic labelling, was found for the allylcarbinyl (or 1-buten-4-yl) Grignard (eq 29), and could be studied knetically by nmr ($t_{1/2}$ = 30 hr at 27°, 40 min at 55°; E_{act} = 26 kcal).



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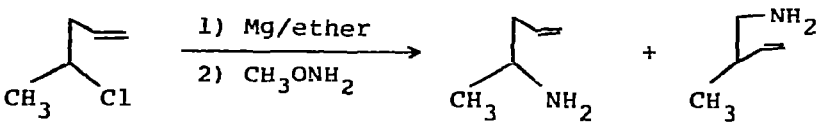

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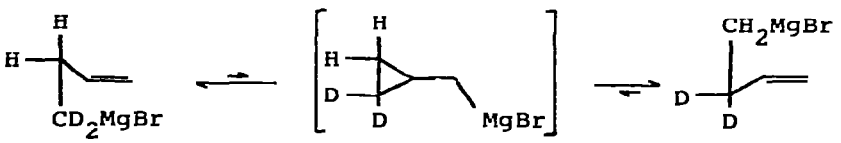
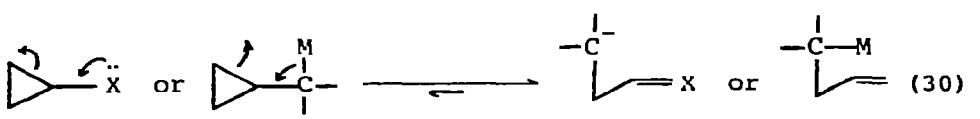


(29)

Although the cyclopropylmethyl Grignard could not be detected spectroscopically or by hydrolysis of solutions, it could be

prepared [80] from cyclopropylmethyl bromide in refluxing dimethyl ether. It underwent ring cleavage with a half-life of 121 min at -24°. When cyclopropylmethyl halides reacted with magnesium in the presence of a carboxylic acid, which could protolyze the Grignard as it was formed, methylcyclopropane was found to be present in the hydrocarbon products in amounts up to 50% and more. It thus appears reasonable that a cyclopropylmethyl Grignard is an intermediate in the rearrangement of eqns 28 and 29 as well as eqn 27.

By this time it had also been shown that cyclopropylmethyl lithium readily undergoes a similar ring cleavage [81,82], and that ring-cleaved product (1-butene) is formed in reaction of cyclopropyl methyl chloride with sodium under Wurtz-type conditions [83]. Cyclopropylmethyl and substituted cyclopropylmethyl anions, generated under various conditions, cleave in like manner [84-87]. Further, under basic conditions, cyclopropanols [88] and cyclopropylamines [89] rearrange by ring cleavage. All of these reactions appear to be examples of a rather general "anionic ring-chain tantomerism" (eqn 30).



(30)

Since the original experiments of Roberts and Mazur, numerous examples of such rearrangements have appeared in organometallic chemistry, including ring closures and cleavages, a range of ring sizes, and a variety of metals. In the following pages, cyclization and ring cleavage rearrangements in organomagnesium chemistry will be surveyed, along with some related examples involving other metals. These will be taken in order of increasing ring size. Most quantitative or semiquantitative data have been

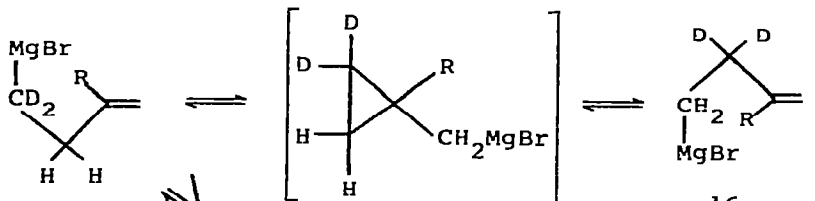
collected in section IVB, and a general discussion of mechanistic aspects is deferred to section IVC.

It has been found that rearranged Grignard reagent may be formed directly from the halide in some cases, apparently without intervention of the unrearranged organometallic (see section V). Hydrocarbons of rearranged structure may also be formed. For this reason, in the equations that follow, Grignard structures are drawn only when there appears to be evidence for their presence. They may well be involved in the other examples as well, but their existence as intermediates remains to be shown.

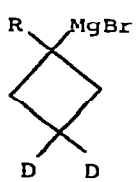
2. Other rearrangements involving three-membered rings

In addition to the [cyclopropylmethyl ⇌ 1-buten-4-yl] system originally studied by Roberts and coworkers [78-80], a wide variety of substituted cases involving the cyclopropane ring have been investigated. These appear in eqns 31-50.

Maercker and Weber [90] studied the kinetics of eqn 31, and determined in addition [91] that the 1-phenylcyclobutyl



15 16



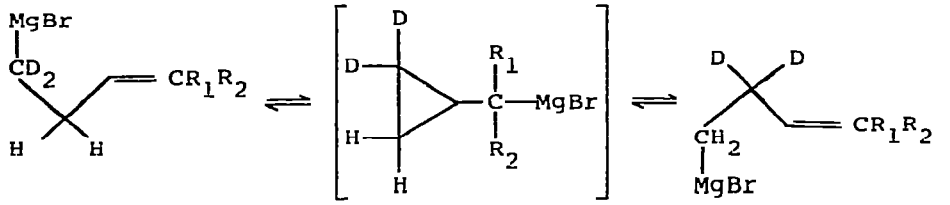
17

a, R = CH_3

b, R = C_6H_5

(31)

Grignard 17b is not equilibrated with 15 and 16. The distribution of deuterium shown in 16 was favored by an equilibrium isotope effect. A kinetic study has also been made in the isotopic scrambling 18a ⇌ 20a [92]. The distribution of deuterium shown in 20a was again favored. The phenyl and methyl groups slowed the equilibration in both cases. Successive substitution of terminal methyl groups on the double bond in 18b-18d (eqn 32) decreased the rate of isotopic scrambling [93]. Isotopic



(32)

18 19 20

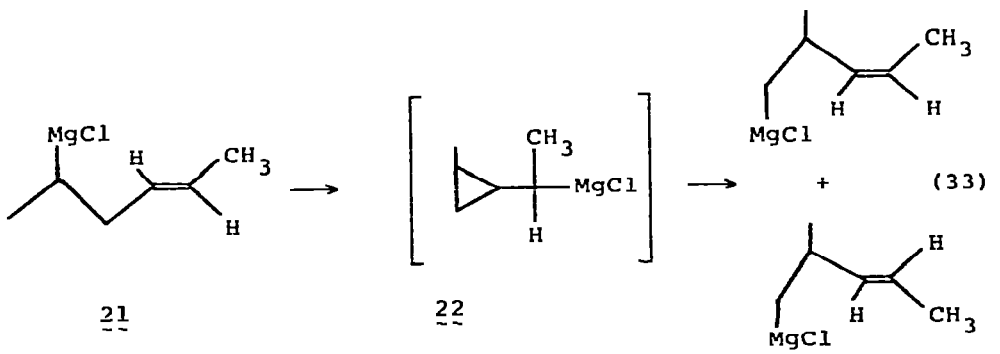
a, R_1 = H; R_2 = C_6H_5

b, R_1 = R_2 = H

c, R_1 = H; R_2 = CH_3

d, R_1 = R_2 = CH_3

equilibrium of labelled 18c occurred at the same rate as cis-trans equilibration at the double bond. Cis-trans equilibration was also observed in the products of eqn 33 [94]. In this case, the

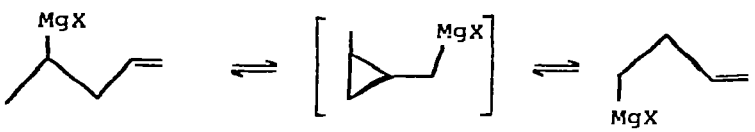


(33)

21 22 23

intermediate 22 cleaves almost exclusively in the direction to yield the primary Grignard product 23, so starting material does not undergo cis-trans isomerization.

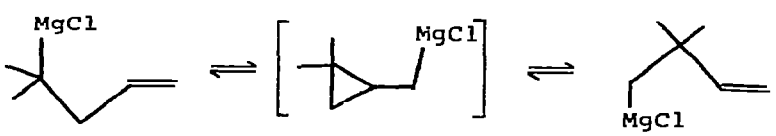
In eqn 34, the reaction was studied starting with bromides and chlorides of both primary and secondary structure [95]. The



(34)

24 25 26

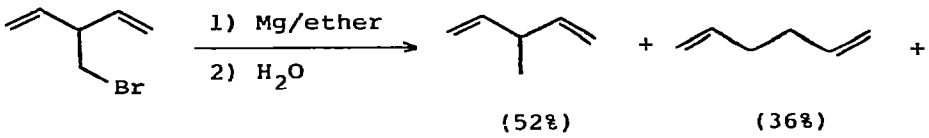
Grignard has been characterized by reaction with an aldehyde. Rearrangement was observed only in one direction: secondary Grignard ⟶ primary Grignard (24 → 26), though rearrangement products formally derived from 24 were found in oxygenation, where a free radical mechanism is likely (see section V). Grignard preparation from the bromide corresponding to 25 led to products derivable from only 26 in ether, but a 19:81 ratio of 24:26 in THF. It was not clear in this study how much rearrangement occurred during Grignard reagent formation. Tertiary ⟶ primary Grignard rearrangement was found in eqn 35 [96].



(35)

27 28

In eqn 36, the monomeric hydrocarbon products shown were isolated in low yield, accompanied by substantial amounts of alcohols (from air oxidation) and dimeric hydrocarbons of corresponding structures [97]. Product resulting from rearranged Grignard was also found in a synthesis of tetraallylmethane via a Grignard coupling reaction with allyl bromide (eqn 37)[98].

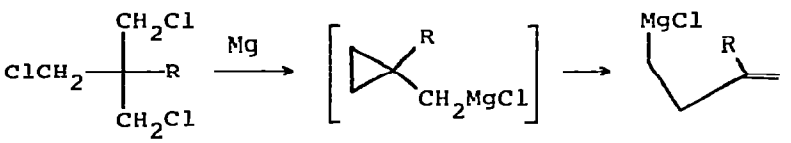


+ alcohols + dimeric hydrocarbons (36)

(12%)

$$(CH_2{=}CHCH_2)_3CCl \xrightarrow[THF]{Mg} (CH_2{=}CHCH_2)_3CMgCl + (CH_2{=}CHCH_2)_2C(CH_2MgCl)(CH{=}CH_2) \quad (37)$$

The reaction of trichlorides in eqn 38 with magnesium led to rearranged Grignard, as shown by hydrolysis and carbonation [99].



(38)

R = CH_3, C_2H_5, C_3H_7

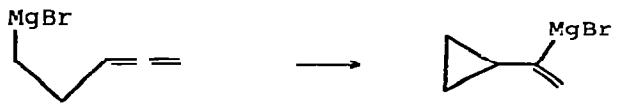
The first step was thought to be 1,3-elimination of chlorine to form the cyclopropane ring. In addition, small amounts of methylcyclobutane and 1,1-dimethylcyclopropane were isolated on hydrolysis. It is not clear whether Grignards corresponding to the latter two were present before hydrolysis. Reaction of 1-chloromethyl-1-methylcyclopropane with magnesium led, after hydrolysis, to a similar product.

In all cases discussed so far, ring strain renders the ring-closed Grignard unstable relative to its acyclic isomer. In eqn 35, the carbonation product from cyclic Grignard 27 was detected in less than 0.1% yield [96]. However, in eqn 39, where the acyclic Grignard must be tertiary, cyclization occurs

more than 99.9% [96]. Formation of a vinylic organomagnesium

(39)

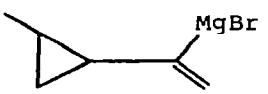
compound also appears to confer sufficient stability that the equilibrium in eqn 40 lies exclusively toward 29 [100]. Grignard



(40)

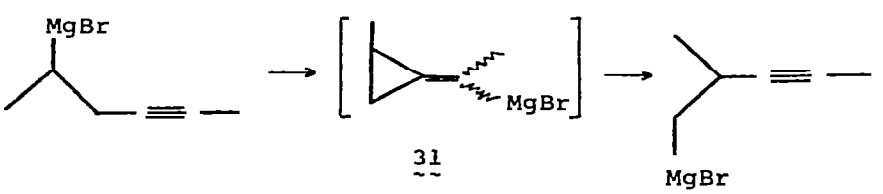
28 29

reagent 28 was formed in relatively low yield (accompanied by hydrocarbon products) and rearranged on heating. Stability of the α-cyclopropylvinyl Grignard structure is confirmed by the preparation of 30 from the corresponding bromide; the cyclic Grignard undergoes no ring cleavage during 12 hr reflux in



30

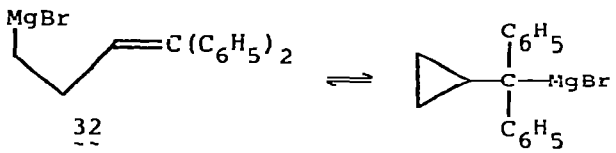
THF [101]. In contrast, the rearrangement of eqn 41 does not yield an isolable amount of cyclic Grignard [102]. Presumably the increased strain of a methylenecyclopropane structure (31) more than compensates for the stabilization of the vinylic organomagnesium grouping.



31

(41)

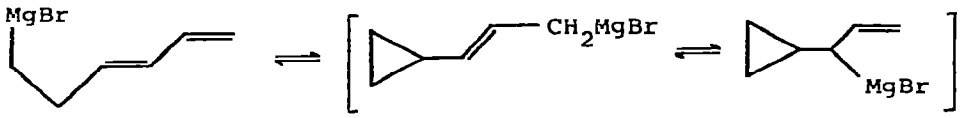
Another likely means of stabilizing the cyclopropylmethyl organomagnesium structure is by resonance. Maercker and Roberts [103] found that α,α-diphenylcyclopropylmethyl potassium is stable to ring cleavage, existing as ions or ion pairs. Addition of magnesium bromide to the red solution of the potassium derivative gave a colorless organomagnesium compound of exclusively



(42)

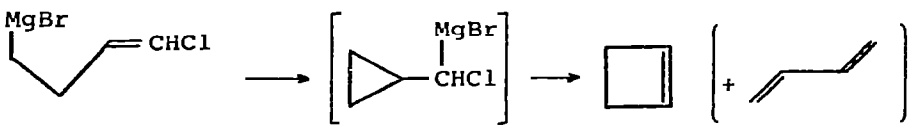
32

ring-opened structure 32. Sodium and lithium were intermediate: in THF, both gave red solutions, decomposing more rapidly than the potassium derivative to acyclic products, presumably via primary organometallics analogous to 32. The lithium derivative was colorless (and acyclic) in diethyl ether. Grignard reagent 32, prepared conventionally from the corresponding bromide and magnesium, was open-chain in structure, but isotopic labelling experiments showed complete equilibration of the two methylene groups, presumably through a cyclic intermediate [104]. That result was taken to imply a marked acceleration of the cyclization reaction by phenyl, but more recent results [92] suggest that the scrambling occurred during Grignard formation (see section V). Some cyclized hydrocarbon (3-5%) was present in the Grignard solutions, and a substantial amount of α,α-diphenylcyclopropylmethanol was formed on oxygenation of the Grignard, but these may probably be ascribed to free radical processes. Stabilization of the cyclized Grignard by vinyl conjugation in eqn 43 was also investigated [104]. Cyclized products were found in oxygenation, coupling with allyl bromide and protolysis with ethanol, but not in carbonation. It is not established that any of these resulted from cyclized Grignard.



(43)

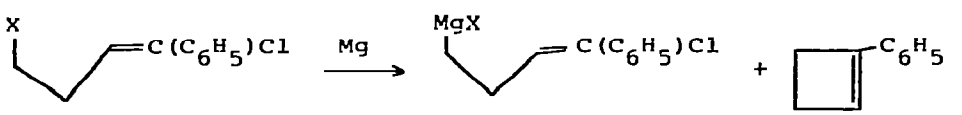
The Grignard reagent 33 from 4-bromo-1-chloro-1-butene (eqn 44) decomposes on heating to a mixture consisting largely of cyclobutene, accompanied by smaller amounts of 1,3-butadiene [105]



(44)

33 34

By isotopic labelling experiments, it was shown that the rate-determining step in this conversion is cyclization to a carbenoid intermediate (34). An apparently similar reaction was observed on treatment of 1,4-dichloro-1-phenyl-1-butene with magnesium [106], phenylcyclobutene being a major product (eqn 45, X = Cl). A Grignard cyclization analogous to eqn 44 was later proposed for

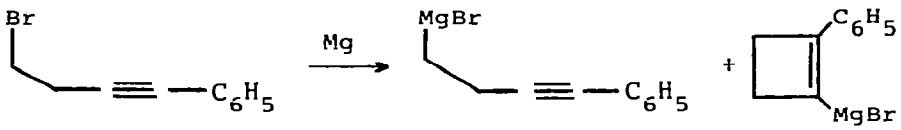


(45)

35

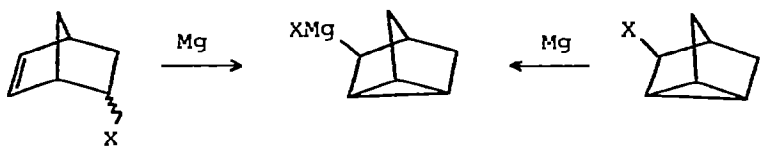
that case, also on the basis of labelling experiments [107]. However, it was subsequently found that the Grignard reagent from the bromide (35, X = Br), once formed, is converted to phenylcyclobutene very slowly, if at all [108]. Hence, the phenylcyclobutene product must arise during formation of the Grignard. Phenylcyclobutene was also formed from treatment of the chlorobromide with butyl- or methyllithium [108]. Another rearrangement, leading to phenylcyclobutene as a minor product,

is shown in eqn 46 [109]. The two Grignards formed do not equilibrate under the reaction conditions. Radical cyclization during Grignard formation was suggested.



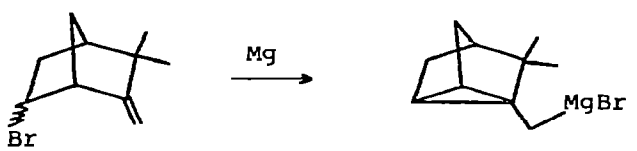
(46)

Several Grignard rearrangements have been reported involving bi- and polycyclic structures. Another instance in which the α-cyclopropylorganomagnesium structure is stable to cleavage is the 3-nortricyclyl Grignard in eqn 47 [110,111]. Grignard



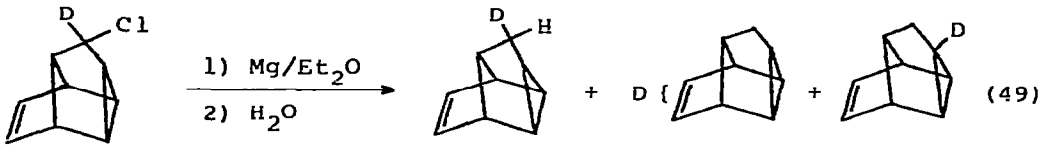
(47)

preparation from halides (Cl or Br) of either the 3-nortricyclyl or 5-norbornenyl structure led only to nortricyclyl products, and an nmr spectrum most consistent with that structure for the Grignard. No indication was obtained of any norbornenyl Grignard in equilibrium with the nortricyclyl. Another example involving a nortricyclyl structure (eqn 48) led to ring-closed products [112].



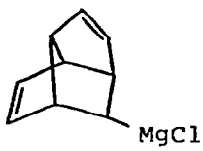
(48)

Products from the Grignard reagent from 36 (eqn 49) may have been formed in a series of degenerate rearrangements involving intermediate structures such as 37 [113].



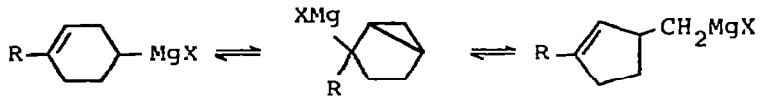
(49)

36



37

The equilibration between the 3-cyclohexen-1-yl (38a) and 2-cyclopenten-1-ylmethyl (40a) Grignard reagents has been studied by Maercker and Geuss [114]. They determined both rate and equilibrium constants for the reaction under a variety of conditions. The equilibrium constant (K = [40]/[38]) showed some variation with solvent and concentration, ranging from 5.71 in an ether-HMPT mixture to 9.26 in a dilute solution in ether; it was essentially independent of temperature between 80° and 120°. In ether at 100°, the thermodynamic parameters obtained were ΔG° = -1.44 kcal/mole; ΔH° = -0.11 kcal/mole; ΔS° = 3.57 eu. Using the difference in strain energy between cyclohexene and 3-methylcyclopentene (3.60 kcal/mole), an enthalpy difference of 3.7 kcal/mole favoring a primary Grignard function over a secondary one was derived. Equilibrium isotope effects favored protium α to the magnesium. A Grignard reagent prepared from the bromide corresponding to 39a gave a mixture of 38a and 40a in a ratio of about 1:5 to 1:7. The system in eqn 50 has also been used to study the electronic effect of substituents on the rate of cyclization. Rates for compounds 36b-d, with



(50)

38 39 40

a, R = H; X = Br

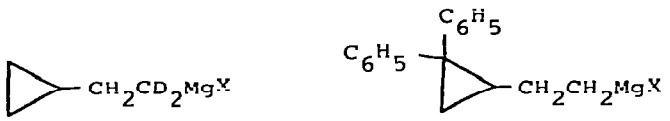
b, R = C_6H_5; X = Cl

c, R = p-$CH_3C_6H_4$; X = Cl

d, R = m-$CH_3C_6H_4$; X = Cl

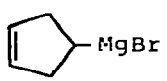
phenyl, p-methylphenyl, and m-trifluoromethylphenyl substituted on the double bond, were determined [115].

Also worthy of note are some rearrangements which did not occur. No rearrangement was noted with the homologs 41 and 42 of cyclopropylmethyl Grignard reagents, nor with the corresponding



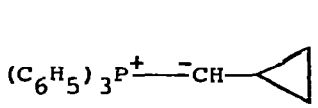
41 42

lithium compounds [116]. Nor was there rearrangement of 43, potentially possible via an intramolecular cyclization [114].



43

The absence of ring-cleavage reactions in phosphorus ylids 44 [117,118] and 45 [119] and the enolate ion 46 [120] has been noted, and base-catalyzed isotopic hydrogen exchange in the benzylic position of phenylcyclopropylmethane appears to occur without rearrangement [121].



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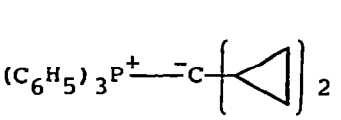

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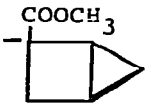
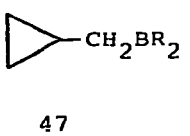


46

Ring cleavage rearrangements have been observed in the boranes 47 [122] and 48 [123], in the radical anion 49 [124], in the cleavage of 50 with lithium metal [125], and in organolithium compounds 51 [126] and 52 [127].



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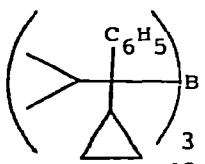

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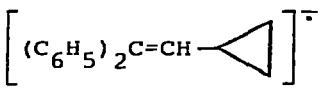

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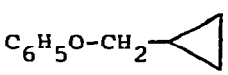

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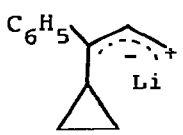

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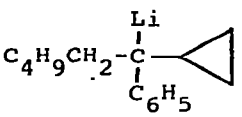
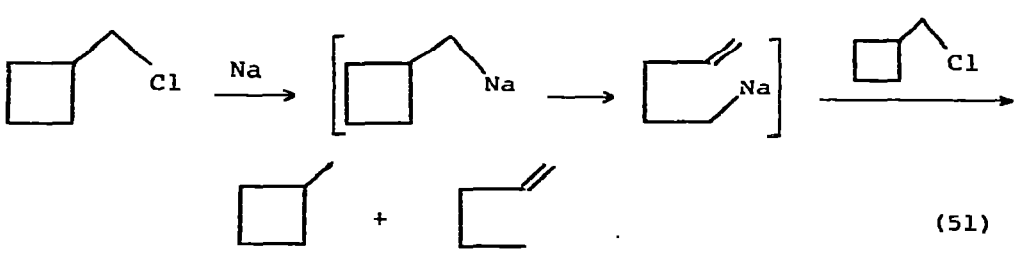


52

3. Rearrangements involving four-membered rings

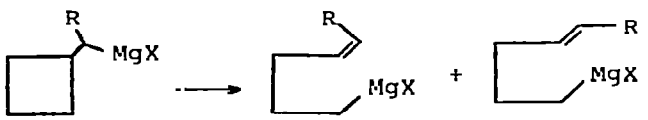
The first reported cleavage of a cyclobutylmethyl organometallic compound appears to be in the Wurtz-type reaction of cyclobutylmethyl chloride with sodium in eqn 51 [83,128].



(51)

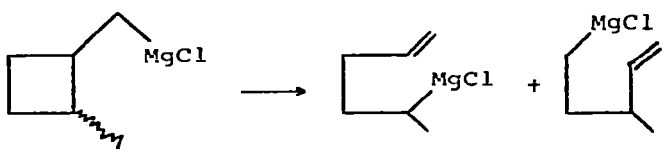
In subsequent work [128] it was found that the corresponding Grignard reagent undergoes a slow cleavage reaction ($t_{1/2}$ = 60 hr at 60° in THF); the cleavage is at least 99.8% complete at equilibrium. Detailed kinetics studies [129] reported for this system will be discussed in Sections IVB and IVC. The corresponding lithium reagent was prepared in benzene, but was found to be completely rearranged when analyzed shortly after formation [128].

Cleavages of the simple substituted homologs in eqns 52 [129] and 53 [130] were also investigated. In eqn 52, a 1:1



(52)

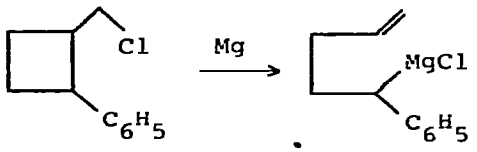
R = H, CH_3



(53)

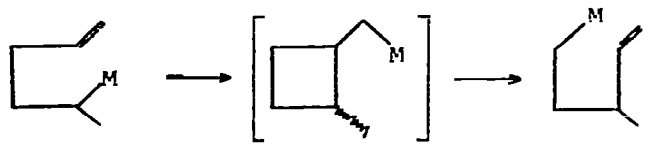
53 54 55

mixture of cis- and trans- isomers at the double bond is generated. The cleavage in eqn 53 lends preferentially to the primary organometallic 55, by a ratio of 100:1 or greater. Only ring-opened Grignard reagent was found in the Grignard preparation in eqn 54. This may have been the result of either ring cleavage during Grignard formation, or very rapid Grignard rearrangement due to formation of a benzylic compound [131].



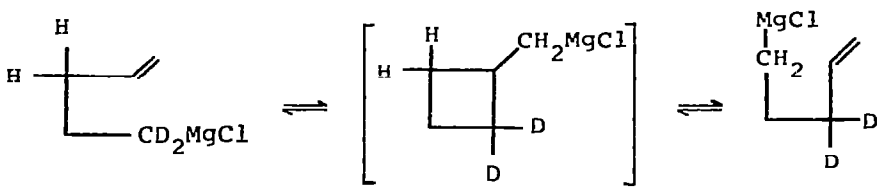
(54)

Cyclization to a cyclobutylmethyl organometallic was proposed to account for the rearrangement in eqn 55, studied with sodium, lithium, and Grignard reagents [128,132]. With the lithium



(55)

the rearrangement occurs to an extent of at least 99%. The reversibility of the ring cleavage of the cyclobutylmethyl Grignard was also demonstrated by the isotope position rearrangement in eqn 56 [133]. The rate of this rearrangement, combined with kinetics results for cleavage of the cyclobutylmethyl Grignard,

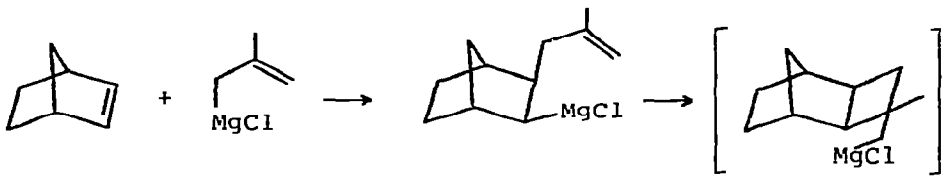


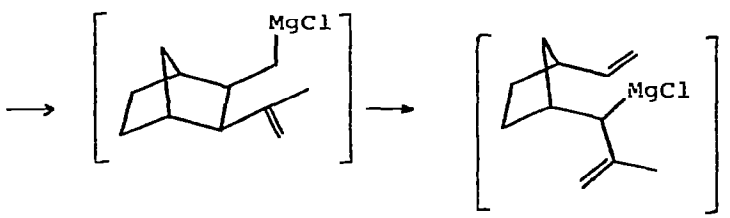
(56)

led to an estimate of the strain energy of a cyclobutane ring (24 kcal/mole) in reasonable agreement with the accepted thermochemical value of 26.2 kcal/mole [133]. This result lends support to the assumption that the rearrangements of eqns 55 and 56 do, indeed, pass through a cyclobutylmethyl Grignard as an intermediate.

Rearrangements involving ring closure to a four-membered ring were also noted in a study of the addition of allylic Grignard reagents to carbon-carbon double bonds. Adducts from

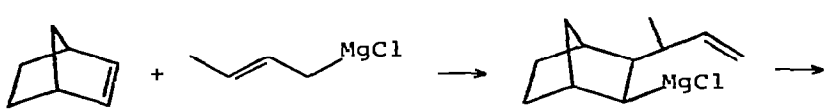
the addition of the methallyl (eqn 57) and crotyl (eqn 58) Grignard reagents to norbornene undergo further reaction on more

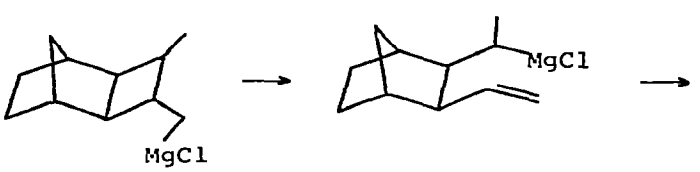




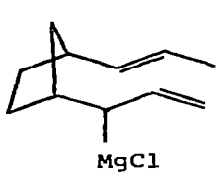
56

$$\xrightarrow{\text{norbornene}} \quad C_{18} \text{ and } C_{25} \text{ products} \qquad (57)$$





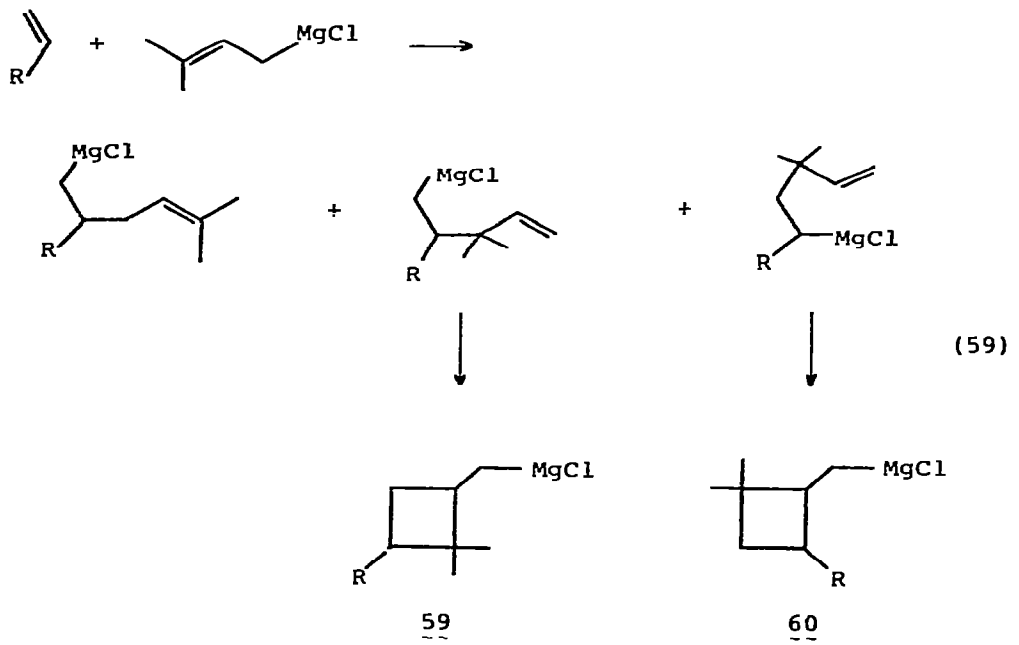
57



(58)

58

vigorous heating [135], which is best rationalized through the rearrangements shown. In the former case, products of further addition to one and two additional norbornene molecules were formed, which require rearrangement eventually to the allylic Grignard 56. In the latter case, products derived from hydrolysis of the cyclobutylmethyl and allylic Grignards 57 and 58 were identified. Cyclobutylmethyl Grignard reagents 59 and 60 are also formed on rearrangement of the initial adduct of the γ,γ-dimethylallyl Grignard to 1-octene [136].

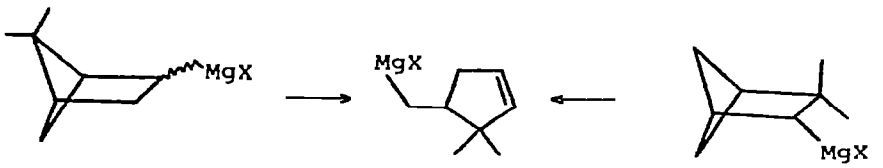


(59)

59 60

Grignard cleavages of a cyclobutane ring in bi- and polycyclic ring systems are shown in eqns 60-66. Reactions 60-62 were quite slow [137,138] when compared with the monocyclic analog in eqn 52 (2° starting Grignard → 1° product). In eqn 62, the bicyclic Grignard 62 yields the primary product 63 with a 10:1 preference over the secondary Grignard 61; 61 is then slowly converted to 63, as shown by its independent preparation and rearrangement [139].

(60)



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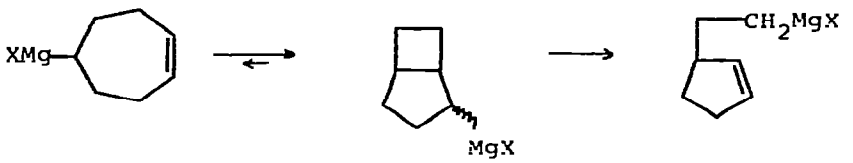
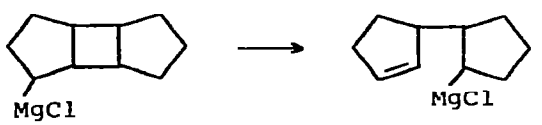


(62)

61 (10%) 62 63 (90%)

In eqn 63, no product of cleavage to a cycloheptene was found [138]. In the rearrangement of eqn 64, the starting Grignard is initially mostly exo in configuration. It undergoes exo-endo



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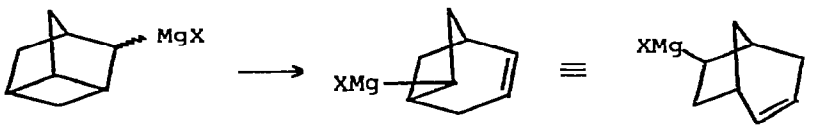
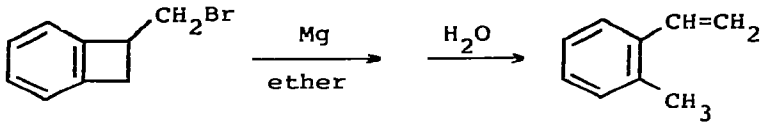


(64)

equilibrium more rapidly than cleavage [140]. The product is exo. The Grignard preparations of eqns 65 [141] and 66 [142] produced ring-opened products, but no evidence for formation of unrearranged Grignard was reported.



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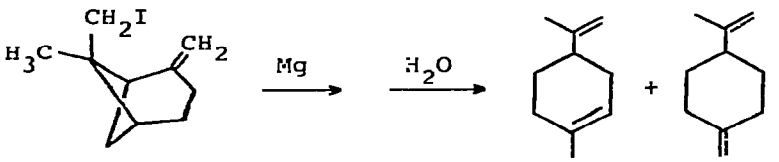
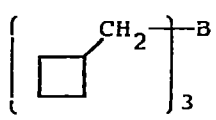


(66)

Cleavage of a four-membered ring has also been reported in some other organometallics. Unsaturated products possibly formed by cleavage of the borane 64 have been noted [143]. Cleavage products from the ylid 65 (R = H, C_6H_5) and anion 66 are formed, along with Stevens- and Wittig-type rearrangement products [144]. A cleavage reaction of the dianion of 67 has been observed, but the mechanism is not established [145]. An anionic ring-cleavage mechanism was considered for the base-catalyzed rearrangement of 6



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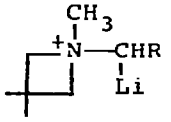

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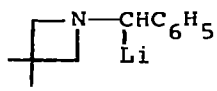

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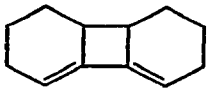

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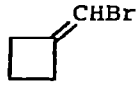


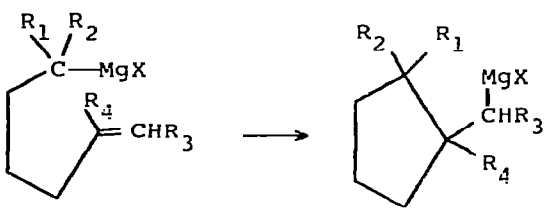
68

to 1-bromocyclopentene, but more recently a "Beckman-like" rearrangement of a carbenoid was favored [146].

4. Rearrangements involving five-membered rings

With a five-membered ring, the reduced ring strain leaves the cyclic product more stable than its open-chain isomer in most cases. Therefore, the commonly observed reaction is ring closure.

The system of eqn 67 has been most thoroughly studied by Richey and coworkers [92,147,148]. In comparison with the unsubstituted compound (69a), methyl substitution at R_1 increases the rate (69b), but a second α-methyl in the tertiary Grignard (69c) produces a decrease. Methyl groups at either end of the double bond (69d and 69e) slow the reaction. In cases where the product may have cis-trans isomerism of groups on the ring (70b, 70d and 70g, there is a sizable preference for the trans isomer. A



(67)

69 70

a, $R_1 = R_2 = R_3 = R_4 = H$

b, $R_1 = CH_3$; $R_2 = R_3 = R_4 = H$

c, $R_1 = R_2 = CH_3$; $R_3 = R_4 = H$

d, $R_1 = R_3 = CH_3$; $R_2 = R_4 = H$

e, $R_1 = R_4 = CH_3$; $R_2 = R_3 = H$

f, $R_1 = R_2 = R_4 = H$; $R_3 = CH_3$

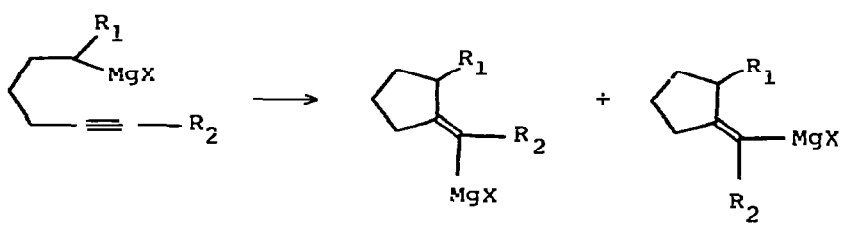
g, $R_2 = R_4 = H$; $R_1 = CH_3$; $R_3 = C_6H_5$

similar effect was noted on cyclization to a six-membered ring.

Several of the same and related cases have been reported by other workers. With 69a, initial cyclization on formation of Grignard is reported to an extent of 5 to 10% [149-151]. Subsequent cyclization was found not to occur with times of up to a day in

THF at 65° or six months at room temperature [150], but slow cyclization ($t_{1/2}$ ≈ 125 hr in refluxing THF) was reported elsewhere [151]. The neat dialkylmagnesium (prepared from the corresponding mercurial with magnesium metal) cyclizes completely in 24 hr at 110° [152]. The corresponding lithium reagent cyclizes completely in an hour or less at room temperature in ether, but requires several days in benzene or cyclopentane [150,152 The Grignard 69b and the corresponding lithium reagent were reported to cyclize readily [150]. In contrast, the Grignard 69f, which on cyclization to 70f involves conversion from a primary to a secondary Grignard, showed no sign of reaction over a period of 20 hr at 114° in THF (aside from 2.5% initial cyclization)[151]. At higher temperature, cyclization did occur slowly ($t_{1/2}$ ≈ 39 hr at 155°) in competition with attack on the solvent.

Cyclization by addition to a triple bond has also been observed (eqn 68).



(68)

71 72

a, R_1 = H; R_2 = CH_3; X = Cl, Br

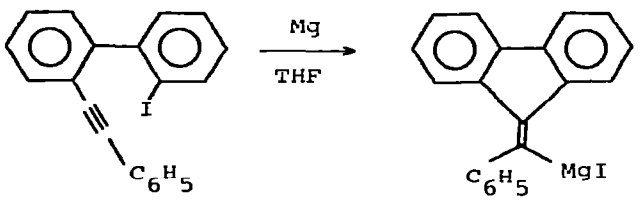
b, R_1 = R_2 = CH_3; X = Cl, Br

c, R_1 = H; R_2 = C_4H_9; X = Br

d, R_1 = H; R_2 = C_6H_5; X = Cl, Br, I

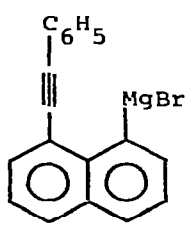
Rearrangements of 71a and 71b occurred substantially more rapidly than the corresponding double bond additions of 69d and 69f [153]. Major amounts of hydrocarbon product accompanied formation of Grignard from the chloride. It was undertain whether the mixture of cis and trans isomers of 72b was formed in the addition, or by isomerization of a single isomer after addition. Cyclizations of Grignard reagents 71c and 71d were studied in several solvents and under varying conditions [154]. Substantial amounts of rearranged Grignard originated during Grignard formation. Kinetic results will be discussed in section IVB.

Another intramolecular addition to a triple bond, forming a five-membered ring, is shown in eqn 69 [155]. However, there was no evidence for the presence of uncyclized Grignard. Preparation of the lithium derivative led similarly to cyclic



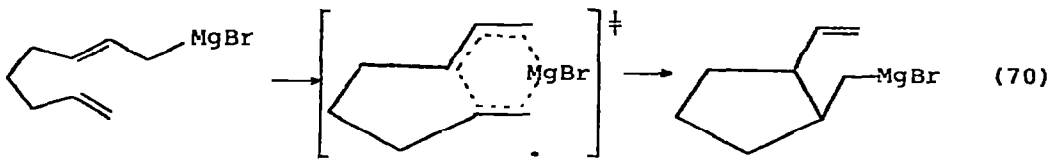
(69)

product. In a related system, 73 failed to cyclize, though the corresponding lithium derivative did, and treatment of the Grignard with cuprous chloride yielded a dimeric hydrocarbon with ring closure [155].



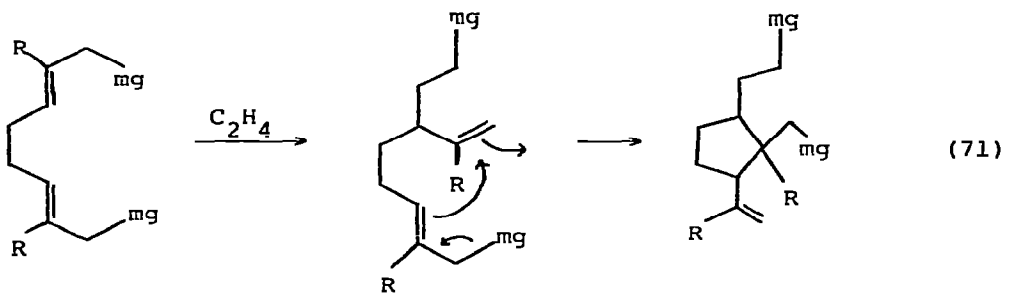
73

Felkin has studied the facile cyclization of an allylic Grignard reagent (eqn 70). The stereospecific cis- disposition



(70)

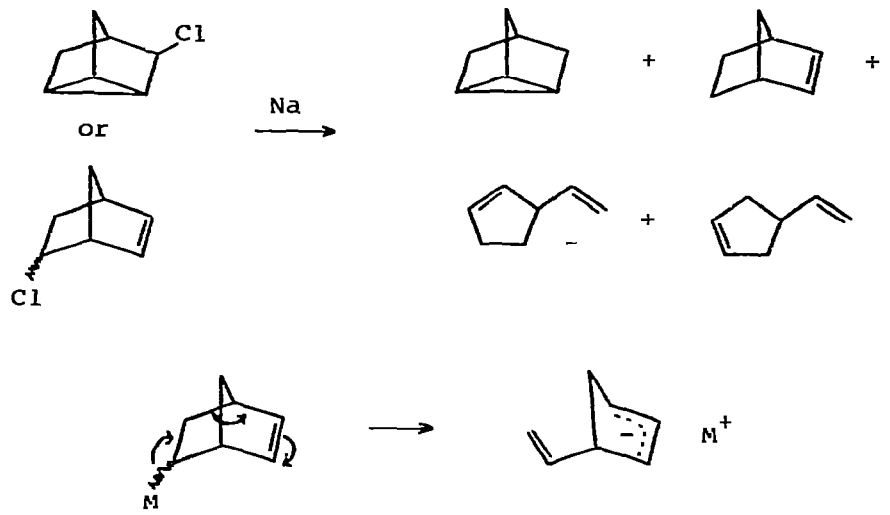
of groups on the five-membered ring was considered as definitive evidence for a cyclic, cis-addition mechanism [156]. Somewhat similar cyclizations have been found in the reaction of ethylene with "octadiendiylmagnesium" (from butadiene and magnesium) or its dimethyl analog (from isoprene), as illustrated in eqn 71 [157].



(71)

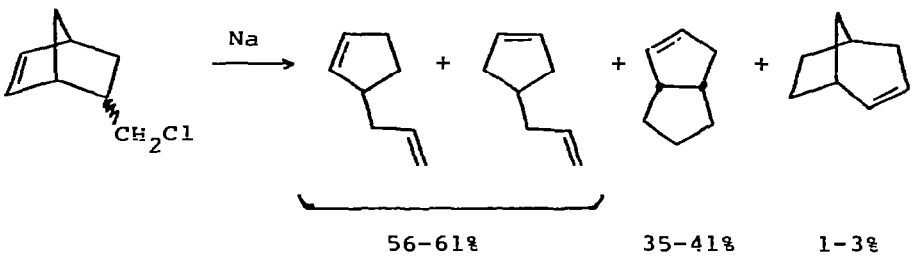
R = H, CH_3

When favored both by relief of additional strain and by formation of an allylic organometallic as product, cleavage of a five-membered ring may be observed. Several instances have been reported in which the five-membered ring is in a bicyclo[2.2.1]heptyl system. Two such cases have been previously illustrated in eqns 57 and 58 [135]. When either 5-chloro-norbornene or nortricyclyl chloride was allowed to react with sodium in n-decane or dibutyl ether, ring-cleaved products were found (eqn 72), which may be attributed to a cleavage reaction of dehydronorbornyl sodium [158]. Grignard reagents from the

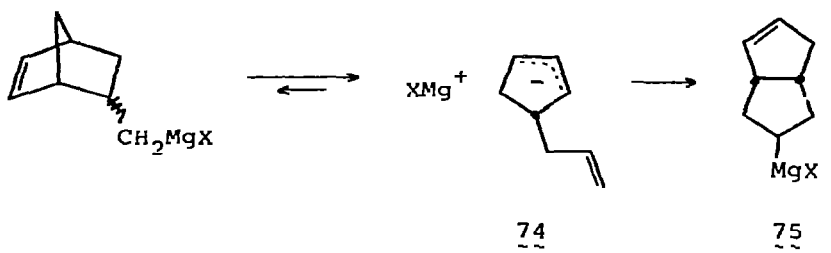


(72)

two halides, heated in dibutyl ether at 90 or 130°, gave traces (0-0.5%) of the vinylcyclopentene products, in a rather variable pattern. Treatment of either exo- or endo-5-chloromethylnorbornene with sodium led also to cleavage products (eqn 73) [159]. The



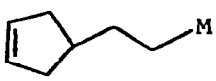
(73)



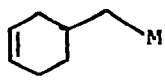
(74)

corresponding Grignard reagent, when hydrolyzed after extended periods of heating in THF at 110-120°, led to a similar mixture

of ring-cleaved hydrocarbons [140], with the exception of the last product shown. The results may be rationalized as resulting from cleavage to the allylic Grignard mixture (abbreviated as 74), which is either hydrolyzed or cyclizes to 75. The initial cleavage appears to be reversible, as remaining uncleaved Grignard was of altered exo:endo ratio. The bicyclo[3.2.1]hexene product was presumably formed in the sodium reaction via a route analogous to eqn 64. The necessity of unsaturation in these reactions is shown by the failure of either saturated analog, 2-chloronorbornane or 2-chloromethylnorbornane, to yield any ring-cleaved products on reaction with sodium [151,158,159]. In the norbornyl system, neither cleavage of the norbornyl lithium or Grignard reagents, nor cyclizations of the lithium and Grignard reagents 76 or 77 was observed [151]. It was concluded that both reactions are



76

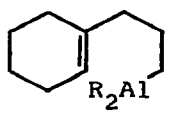


77

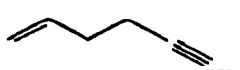
close to thermoneutral, and in the absence of a strong driving force in either direction, rearrangements are too slow to compete with attack on solvent or other decomposition paths.

With other metals, a number of cyclization and cleavage reactions involving five-membered rings have been observed. Analogs of 69a, involving aluminum, gallium, and indium, have been studied [152,160-162]. Cyclizations of aluminum alkyls have been particularly well studied (frequently involving initially the addition of an organoaluminum compound to one double bond of a diene, followed by cyclization involving the second double bond). Cyclizations in organoaluminum chemistry include those of 78 [163], cyclization of the hydrocarbons 79 [164], and 80

[165] by reaction with dialkylaluminum hydrides, and a



78



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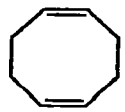
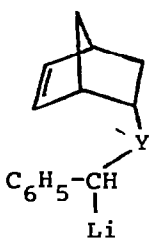


80

81

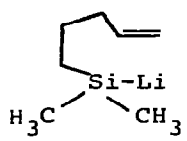
cyclodimerization of 1,3-butadiene with aluminum alkyls, leading to 81 [166]. Similar processes are probably involved in the cyclizations of 6-phenyl-1-hexene with sodium, potassium, or cesium [167], and 1,3-cyclooctadiene with potassium hydride [168]. Intramolecular additions are observed in the cyclization of lithium reagents 82a and 82b [169] and 83 [170].



82

a, Y = CH_2

b, Y = O



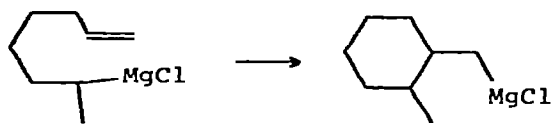
83

The cleavage of norbornadiene to acetylene and cyclopentadienyl sodium on treatment with amylsodium probably proceeds through an organometallic ring-cleavage rearrangement of norbornadienylsodium [171].

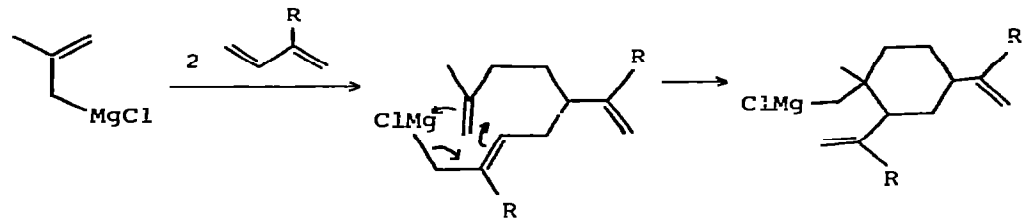
5. Rearrangements involving six-membered rings

Ring closure becomes much less facile when a six-membered ring is formed, and few examples are available. The Grignard

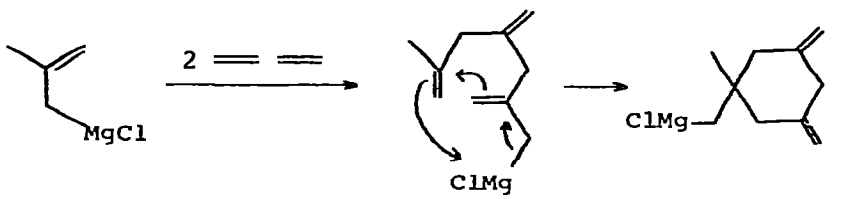
cyclization in eqn 75 is slower by a factor of 2800 than the cyclopentane analog 69b [148]. Again, the trans- isomer predominates.

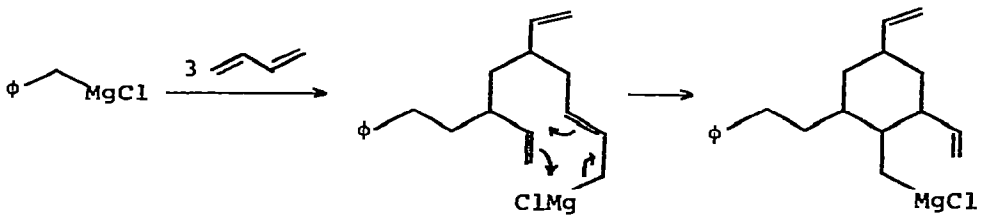


Cyclizations forming six-membered rings have also been observed subsequent to the addition of allylic Grignard reagents (eqns 76 and 77) and benzylmagnesium chloride (eqn 78) to dienes [157,172].

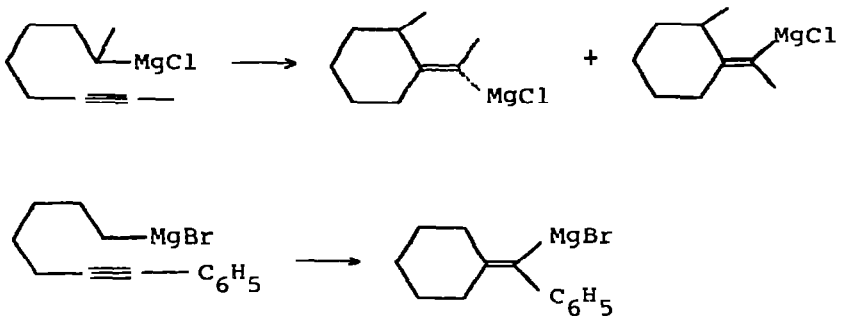


R = H, CH_3





Cyclization to a six-membered ring by addition to a triple bond has also been observed, as shown in eqn 79 [102,154].



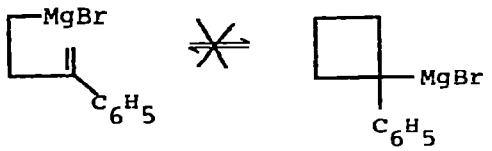
(79)

Cyclization of α,ω-dienes with diisobutylaluminum hydride occurs much less readily in six-membered rings than five; only about 1% of cyclic product is formed via 83 under conditions which lead to over 97% of cyclic product with a five-membered ring [160].

83

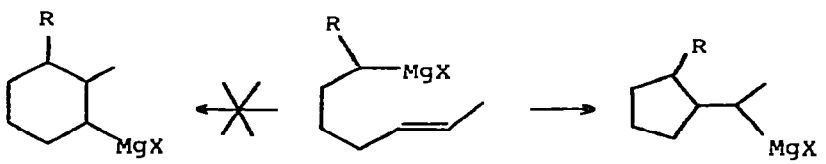
6. Ring-size in cyclization reactions

A noteworthy feature of essentially all cyclization reactions summarized here is that whenever there is a choice between forming rings of different sizes by addition in the opposite sense across the multiple bond, the smaller ring is formed preferentially. For example, careful examination has excluded the possibility that the cyclobutyl Grignard 17 is in equilibrium with 15, even though it should be stablized as a benzylic Grignard [90]. While it is true in a majority of instances cited that the addition to give the larger ring would also form a less stable secondary (vs.



15 17

primary) Grignard reagent, there are instances, such as eqn 80, where a secondary Grignard would be formed in either addition, but only the smaller ring is observed [148,151]. A similar



(80)

R = CH_3 (69d), H (69f)

preference has been noted in intramolecular additions of free radicals [173-175]. The preference for forming the smaller ring has been explained as resulting from approach of the partially carbanionic carbon along a direction close to the axis of the double bond p-orbital [147,151,153]. If the terminal carbon is attacked, it may be more difficult to maintain maximum π-overlap as the new σ-overlap develops. In cases where the choice is between three- and four-membered or four- and five-membered rings, this preference appears quite reasonable from examination of models, but it is somewhat less clear for larger ring sizes. The preference could also arise from constraints on a cyclic four-centered transition state for addition (see section IVC).

B. Quantitative Observations on Organomagnesium Cyclization and Cleavage Rearrangements

In a number of the Grignard rearrangement studies cited in the previous section, quantitative or semiquantitative observations of reaction rate have been included. Before considering possible reaction mechanisms for these rearrangements, we will collect and compare data which may bear upon the mechanism.

One general observation, which may be noted in connection with rate studies of these organomagnesium rearrangements, is a characteristic first order kinetic behavior with respect to unrearranged alkyl groups. In a solution in which rearrangement of "RMgX" to "R'MgX" is occurring, a number of rearranging species may be present, including RMgX, R_2Mg, RR'Mg, and various aggregates of these. As we will note later, RMgX and R_2Mg species rearrange at substantially different rates. Therefore, the linear first order behavior implies that the equilibrium among these species, which must be rapid at the usual reaction temperature, cannot be markedly affected by the change from R to R', and that R groups of R_2Mg and RR'Mg must rearrange at comparable rates [92].

1. Solvent effects on rearrangement rate

In a number of the rearrangements studied, the solvent has been varied--either by preparation of the Grignard reagent in different ethereal solvents, or by addition of another solvent to that in which the Grignard was prepared. Results are listed in Table I. It is consistently found that the more polar and more basic tetrahydrofuran leads to rates slower than those in diethyl ether by factors ranging from 2 to over 100. 1,2-Dimethoxyethane also leads to rates faster than those in THF.

TABLE I. SOLVENT EFFECTS AND ORGANOMAGNESIUM REARRANGEMENTS

Compound	Equation Number	Temp (°C)	Concentration (M)	k_{rel}				Reference
				THF	Ether	DME	Other	
RING CLEAVAGE REACTIONS								
c-$C_4H_7CH_2MgCl$	52, R=H	60-80	0.1-1.6	(1)	4-6	9	THF + Et_3N (1 equiv) 1.9	129
							Ether + Isooctane (50%) 7	177
							Ether + THF (15%) 10	
$(c\text{-}C_4H_7CH_2)_2Mg$	52, R=H	61.5	0.1-1.1	(1)	-	-	THF + Et_3N (37-60%) 1.25-1.7	129
							THF + C_6H_6 (55%) 2	
							THF + Isooctane (50%) 1.7	
							THF + DME (60%) 2.5-6	

TABLE I (continued)

Compound	Equation Number	Temp (°C)	Concentration (M)	k_{rel} THF	Ether	DME	Other	Reference
c-$C_4H_7CH(CH_3)MgCl$	52, R=CH_3	61.5	0.1-0.5	(1)	2	-		129,138
RING FORMATION REACTIONS								
CH_2=CH-$(CH_2)_3$-$CH(CH_3)MgCl$	67	100	ca. 0.3	(1)	24	8		148,179
$CH_3C{\equiv}C$-$(CH_2)_4$-MgBr	68	100	0.1-0.66	(1)	15	20		102
$CH_3C{\equiv}C$-$(CH_2)_4$-MgCl	68	100	0.2	(1)	-	-	THF + TMEDA (1 equiv) 0.5	102
$C_6H_5C{\equiv}C$-$(CH_2)_4$-MgBr	68	66-67	0.04	(1)	-	13		154
REARRANGEMENTS VIA CYCLIZATION-CLEAVAGE								
CH_2=CH-$(CH_2)_2$-$CH(CH_3)MgCl$	55	109.9	0.35-0.94	(1)	1.7	7	THF + Et_3N (25%) 0.7	132
							4-Methyltetrahydropyran 0.7	
							HMPT 31	

TABLE I (continued)

Compound	Equation Number	Temp (°C)	Concentration (M)	k_{rel} THF	Ether	DME	Other	Reference
$[CH_2=CH-(CH_2)_2-CH(CH_3)]_2Mg$	55	109.9	0.5-0.6	(1)	-	-	THF + cyclohexane (25-50%) 1.4-1.7	132
$CH_2=C(CH_3)CH_2CD_2MgBr$	31	80	ca. 0.7-1.5	(1)	22	-	$(C_2H_5)_2O$ + HMPT 68	90
$CH_2=C(C_6H_5)CH_2CD_2MgBr$	31	100	0.3-1.4	(1)	100-200			90
	50	80	0.6-3.5	(1)	10		$(C_2H_5)_2O$ + HMPT (ca. 30%) 20	114
							$(C_2H_5)_2O$ + c-C_5H_{10} (ca. 30%) 8	
							$(C_2H_5)_2O$ + C_6H_{10} (40-75%) 11-70	
$ClCH=CHCH_2CH_2MgBr$	44	107	1.4	(1)	3			105

Hydrocarbon diluents seem generally to increase the rate, and the dipolar aprotic solvent HMPT produces sizeable increases (relative to THF). The solvent effects are generally quite modest in magnitude, however, suggesting that the transition state is not markedly different in polarity from the original Grignard. A general pattern of increased rates in less polar solvents may simply imply that the transition state is less polar than starting state. However, greater complexity undoubtedly exists, since the solvent very likely affects the degree of association of the organometallic, and probably the position of the Schlenk equilibrium. Solvent polarity and solvent basicity may both affect the rate, possibly in opposite directions. The variable magnitude of the effects observed, and the effect of THF added to an ether solution [178] suggest the inadequancy of a single simple explanation. In contrast to organomagnesium rearrangements, the lithium reagent $CH_2=C(CH_3)CH_2CD_2Li$ rearranges faster in ether than in cyclopentane or in ether--benzene [90].

2. Concentration effects

The Grignard rearrangement shows a decided concentration dependence at high concentrations (above 0.5 or 1.0 M, depending upon the system). In this range, the increase in several systems appears to be roughly linear in total organometallic concentration [90,114,129] with rates in 2-4 M solutions rising to values as much as ten times as large as those in more dilute solutions. At lower concentrations (below ca. 0.5 or 1.0 M) the rate appears to change less rapidly, and may be nearly independent of concentration. The concentration dependence studies may be summarized as follows:

Rate increase at higher concentrations and slight dependence at lower concentrations observed

(THF, 0.1-4.4 M) [129]

(ether, 0.23-3.5 M) [114]

$[CH_2=C(C_6H_5)CH_2CD_2]_2Mg$ (ether, 0.2-2 M) [90]

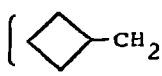
Rate increase at higher concentrations observed

(THF, 0.6-1.3 M) [114]

$CH_2=C(CH_3)CH_2CD_2MgBr$ (ether and THF, 0.7-1.7 M) [90]

$CH_2=C(C_6H_5)CH_2CD_2MgBr$ (ether and THF, 0.3-1.4 M) [90]

Little or no rate variation with concentration observed at low concentrations



(THF, 0.1-1.1 M) [129]

$CH_2=CHCH_2CH_2CH(CH_3)MgCl$ (THF, 0.3-0.9 M) [132]

$CH_3C\equiv C-(CH_2)_4-MgBr$ (THF, 0.1-0.66 M) [102]

$CH_2=CH-(CH_2)_4-MgBr$ (THF, 0.1-0.5 M) [92]

3. Effect of added alcohol, water, or air

In several instances [92,102,129], a portion of Grignard reagent was deliberately destroyed by addition of water, alcohol, phenol, or air. In all cases, an apparent small rate decrease (~25%) was observed. With the cyclobutylmethyl Grignard, the rates (in 0.6-0.8 M Grignard solution) were virtually identical after addition of amounts of water equivalent to 2.5% or 25% of the Grignard, or phenol equivalent to 12% of the Grignard [129].

4. Effect of magnesium purity

In several studies, different grades of magnesium have been used to prepare the Grignard reagent. In the reactions of compounds 69a [92] and 69b [178], no significant difference was noted between triply sublimed and single crystal magnesium, or between different sources of sublimed and "Grignard grade" magnesium. Small rate increases (10-30%) are found for eqns 52 [129] and 55 [132] on replacing sublimed magnesium by "Grignard grade" and with compound 71d (X = Br) [154], the rate increase was a factor of two for reagent grade and four for "Grignard grade." (It may be significant that the latter was the only case in which the excess magnesium was left in contact with the reagent during the reaction.)

The common interpretation of a rate-enhancement with a less-pure magnesium grade might be that transition metal impurities catalyze the reaction, perhaps via a sequence such as:

$$RMgX + m\text{-}X \rightleftharpoons R\text{-}m + MgX_2$$

$$R\text{-}m \longrightarrow R'\text{-}m$$

$$R'\text{-}m + MgX_2 \rightleftharpoons R'MgX + m\text{-}X$$

Details of the second step of this sequence, rearrangement of the alkyl group in the transition-metal alkyl, might be mechanistically the same as the rearrangement of the organomagnesium compound itself, though much faster. Alternatively, a completely different mechanism might apply to the organo-transition metal intermediate.

The significant question arises whether Grignard rearrangement itself takes place at all, or whether all rearrangement observed is mediated by transition metal impurities present in even the purest magnesium samples. The relatively small differences observed between magnesium samples of significantly different

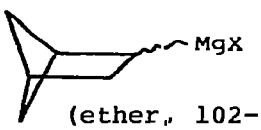
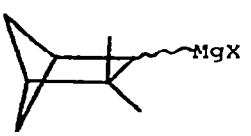
purity suggests that Grignard rearrangement per se does occur. Transition metal catalysis of a portion of the reaction might provide an explanation for some variations in observations which have been reported. In the transition metal-catalyzed process, if the metal exchange is rate-determining, one might expect a reaction rate which is first order in unrearranged alkyl groups, and also first order in total Grignard (since transition metal impurity might be a constant fraction of total magnesium). Thus, linear dependence upon total organomagnesium at higher concentrations might be explained. Also, the rate-decreasing effect of added water or alcohol (or exposure to air) might result from preferential coordination of alkoxide or hydroxide with the catalytic impurity, removing it from circulation. Varying results found by different workers might be explained by differences in magnesium purity, concentration, or success at exclusion of moisture and oxygen. (However, there are other explanations, such as changes in state of aggregation, which may equally well rationalize the effects of partial hydrolysis.)

5. Effect of organometallic composition

a. Halogen in RMgX. In a number of cases, rearrangement rates have been compared for Grignard reagents prepared from corresponding chlorides, bromides, and/or iodides. Minor differences exist, with the chloride most frequently being fastest. Results are summarized in Table II. The results are undoubtedly indirectly influenced by variation in association and the Schlenck equilibrium, and so they may not reflect the direct effect of halogen on the rate of monomeric RMgX.

b. Dialkylmagnesium vs. alkylmagnesium halide. Solutions of Grignard reagents appear to contain dialkylmagnesium species in mobile equilibrium with alkylmagnesium halide [179,180]:

TABLE II. EFFECT OF HALOGEN VARIATION ON GRIGNARD REARRANGEMENT RATES

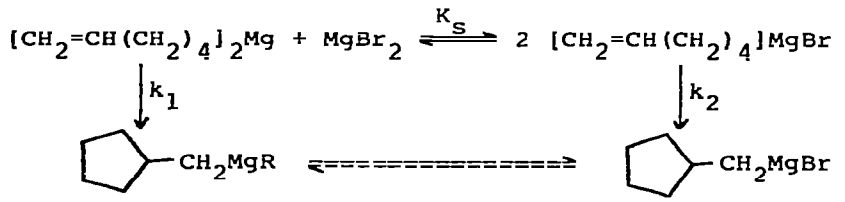
RMgX (conditions)	Relative Rate Cl	Br	I	References
c-$C_4H_7CH_2MgX$ (ether, 52-80°, 0.2 M)	(1)	0.22-0.43[a]	-	138
c-$C_4H_7CH(CH_3)MgX$ (ether, 66-80°, 0.1 M)	(1)	0.3-0.45[a]	-	138
 (ether, 102-126°, 0.06-0.32 M)	(1)	4[b]	-	137
 (ether, 102-126°, 0.06-0.32 M)	(1)	4.5-7.3[b]	-	137
CH_2=CH-$(CH_2)_2$-$CH(CH_3)MgX$ (THF, 110°, 0.4 M)	(1)	-	0.6	132
CH_2=CH-$(CH_2)_3$-$CH(CH_3)MgX$ (THF, 100°)	(1)	-	0.5	178
CH_2=CH-$(CH_2)_4$-MgX (THF, 100°, ~0.4 M)	(1)	0.75	-	92
$CH_3C{\equiv}C$-$(CH_2)_4$-MgX (THF, 100°, ~0.2 M)	(1)	~0.7	-	153
$C_6H_5C{\equiv}C$-$(CH_2)_4$-MgX (THF, 66°, 0.04 M)	(1)	5	6	154

[a]Rates extrapolate to similar values at about 120-125°. [b]An excess of $MgBr_2$ from disproportionation was present.

$$2\ RMgX \rightleftharpoons R_2Mg + MgX_2$$

There is every reason to expect different rearrangement rates from the two organomagnesium species, and indeed such differences are observed in a number of other reactions, with the dialkylmagnesium generally reacting faster [181,182]. In several rearrangement studies, the reaction rate of the Grignard solution has been compared on the one hand with the dialkylmagnesium (usually prepared by dioxan precipitation) and on the other with a Grignard solution containing additional magnesium halide. The result observed has generally been an increased rate for the dialkylmagnesium, and a decrease with added magnesium halide. These studies are summarized in Table III.

The most detailed study made appears to be in the case of eqn 81. The rate was measured for rearrangement of the dialkylmagnesium reagent, and for the Grignard reagent with various



(81)

concentrations of added magnesium bromide. Analysis of rate results yielded the values: $k_1 = 45 \times 10^{-6}$ sec^{-1}; $k_2 \approx 1 \times 10^{-6}$; $K_s = 30\text{-}40$. (The equation, as drawn here, is oversimplified, in that it neglects formation of RMgR'.)

TABLE III. EFFECT OF ORGANOMETALLIC COMPOSITION ON THE RATE OF REARRANGEMENT

Grignard (conditions)	Relative Rate for R_2Mg	Effect of MgX_2	Reference
c-$C_4H_7CH_2MgCl$ (THF, 61.5°, 0.1-1.0 M)	1.2-1.5	decrease	129
CH_2=CH-$(CH_2)_2$-$CH(CH_3)MgCl$ (THF, 110°, 0.6 M)	3	decrease	132
CH_2=CH-$(CH_2)_4$-MgBr (THF, 100°, 0.1-0.2 M)	2.6	decrease	183
CH_2=CH-$(CH_2)_3$-CH=$CHCH_2MgBr$ (ether, 35°, 0.4 M)	"increased significantly"	"little effect"	156
CH_2=$C(CH_3)CH_2CD_2MgBr$			90
(ether, 80°, 0.8-1.0 M)	2[a]	increase[b]	
(THF, 80°, 0.8-1.0 M)	decreased slightly[c]	-	
CH_2=$C(C_6H_5)CH_2CD_2MgBr$			
(ether, 80-100°, 0.3-1.4 M)	0.5-1.5[a]	-	90
(THF, 100°, 0.3 M)	1.2[c]	-	90

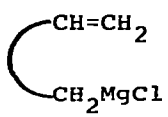
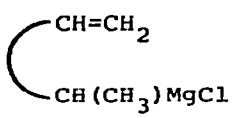
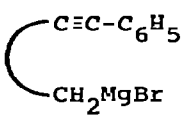
[a]Reaction rate shown to be slower in solvent containing dioxan. [b]Rate increase smaller than that produced by equivalent concentration of RMgX. [c]Reaction solvent contained dioxan.

6. Effect of structure of the rearranging groups

a. Ring size. Cleavage reactions occur much more rapidly with a three-membered than with a four-membered ring. Cyclopropylmethylmagnesium bromide cleaves with a half-life of about 2 hr

at -24°C in dimethyl ether [80], while cyclobutylmethylmagnesium bromide has a half-life of about 150 hr at 52°C in diethyl ether [138]. A rather long temperature extrapolation and an assumption of negligible solvent effect lead to a very crude estimate of a rate difference of as much as 10^8. The difference in ring strain between cyclopropane and cyclobutane appears to be about 2 kcal [134], which corresponds to a rate difference of

TABLE IV. GRIGNARD CYCLIZATION RATES TO RINGS OF VARIOUS SIZES

Compound (conditions)	k_{rel}			
	C_3	C_4	C_5	C_6
 (THF, 100°)	ca. 300[a]	0.007[b]	(1)[c]	-
 (THF, 100°)[c]	-	0.0043	(1)	0.0046
 (DME, 84°)[d]	-	ca. 0.05	(1)	ca. 0.002

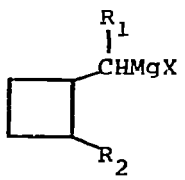
[a]Estimated by extrapolation from data in ref 79 at lower temperatures, and the assumptions $k_{Cl}/k_{Br} = 2$; $k_{ether}/k_{THF} = 25$.
[b]Extrapolated from data at higher temperatures in ref 133.
[c]Ref 148. [d]Ref 154.

only 50-60. Therefore, it may be concluded that a greater relief of strain has occurred in the transition state for cleavage of the three-membered ring; conversely, the transition state for the cyclization (or cleavage) of the four-membered ring is the more strained. Cleavage of the five-membered ring is not observed in simple cases, as the equilibrium strongly favors ring closure. Even with the more highly strained norbornyl system, cleavage apparently is not rapid enough to compete effectively with attack on the solvent.

Relative rates for ring-closure to various ring sizes follow the order $C_3 > C_5 > C_4 > C_6$. The order appears to be reasonably explained on the basis of variation in ring strain and entropy loss or "distance factor" through the series [183]. Table IV gives some relative rates.

b. Alkyl group substitution. The effects of alkyl group substitution (generally methyl) have been determined in a number of systems and for substitution in various positions.

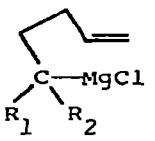
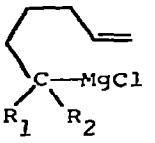
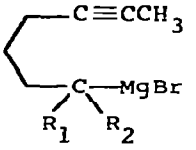
In the cleavage of the cyclobutylmethyl Grignard reagent, the effects of methyl substitution have been studied in the positions shown in 84. Methyl substitution at R_1 has a rather



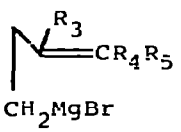
84

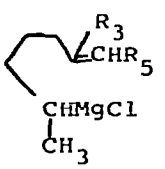
minimal effect. In THF, the secondary Grignard (X = Cl) rearranges about 1.4 times as fast as the primary [129]; in ether, it is about 0.50-0.55 times as fast (X = Cl or Br), and the activation parameters in ether for the primary and secondary compounds are the same within experimental error [138]. Methyl

TABLE V. EFFECTS OF METHYL AND ARYL SUBSTITUTION ON GRIGNARD REAGENT CYCLIZATIONS

	Relative Rates		
1. α-SUBSTITUTION (METHYL)			
	THF, 110°	THF, 100°[a]	THF, 100°[b]
$R_1 = R_2 = H$	5[c] (<1)[d,e]	(1)	(1)
$R_1 = CH_3$; $R_2 = H$	(100)[a,e,f]	41	~4
$R_1 = R_2 = CH_3$	~1[e]	0.34	-

2. DOUBLE BOND SUBSTITUTION (METHYL)

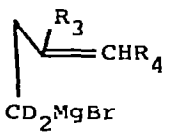
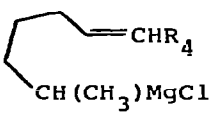
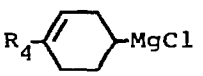




	ether, 80°	ether, 100°	THF, 100°[a]
$R_3 = R_4 = R_5 = H$	(1)[f]	(1)[f]	(1)
$R_3 = CH_3$; $R_4 = R_5 = H$	0.01[g]	-	8.5×10^{-4}
$R_3 = R_5 = H$; $R_4 = CH_3$	-	1.2×10^{-4}[h]	8×10^{-3}
$R_3 = H$; $R_4 = R_5 = CH_3$	-	2×10^{-6}[h]	-

TABLE V (continued)

3. DOUBLE BOND SUBSTITUTION (ARYL)

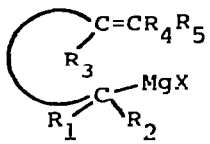
			
	ether, 100°	THF, 100°[i]	THF, 120°
$R_3 = R_4 = H$	(1) ("concentrated solution")[f]	(1)	(1)[j]
$R_3 = C_6H_5$; $R_4 = H$	6×10^{-3} (1.64 M)[g]	-	-
	1.5×10^{-3}[g]		
	4×10^{-4}[i] (0.2 M)		
$R_3 = H$; $R_4 = C_6H_5$	9×10^{-4} (0.28 M)[i]	7	~0.1[k]

[a]Ref 148. [b]Ref 102. [c]Extrapolated from higher temperatures; Ref 133. [d]Based on no observable reaction after 170 hr at 110°. [e]Ref 132. [f]Extrapolated from lower temperatures; Ref 79. [g]Ref 90. [h]Estimated from ref 93. [i]Ref 92. [j]Estimated from data at 80 and 120° in ether, and 80° in THF. [k]Ref 115.

substitution at R_2 has an important effect, in that the cleavage is directed to the side away from the methyl group to an extent of at least 99%, forming primary ring-cleaved Grignard in preference to secondary (eqn 53) [178]. Cleavage rates of cis- and trans-isomers are 0.29 and 0.36, respectively, relative to the unsubstituted compound, compared with a value of 0.5 for cleavage of the unsubstituted compound toward a single ring

methylene group. Additional cases in which ring cleavage leads preferentially to the primary Grignard rather than the secondary or tertiary are shown in eqns 34, 50, 61, and 62.

In the cyclization reaction, methyl substitution has been studied at the positions indicated in 85. A secondary Grignard ($R_1 = CH_3$; $R_2 = H$) appears to be significantly more reactive than primary ($R_1 = R_2 = H$). The tertiary Grignard ($R_1 = R_2 = CH_3$) seems, on the basis of less extensive evidence, to be



85

markedly slower than the secondary. Available data for four- to six-membered rings are summarized in Table V-1. Quantitative comparisons of the α-methyl effect are not available for the three-membered ring, but qualitative observations suggest the likelihood of an increased rearrangement rate for the secondary compound 25 [79,95]. The tertiary Grignard (X = Cl) (eqn 35) rearranges about as fast at 70° in THF as the primary one (X = Br) (eqn 29) does at 27° in ether [96]. The additional gem-dimethyl group in eqn 39 appears to accelerate the cyclization considerably.

Methyl substitution on the double bond produces a consistently large decrease in rate, whether in the R_3 or R_4,R_5 position. Quantitative data are summarized in Table V-2.

c. Other substitution. In ring cleavage reactions, there is little evidence in simple systems for the effects of other kinds of substitution. Only ring-opened products were formed from 2-phenylcyclobutylmethyl chloride on treatment with

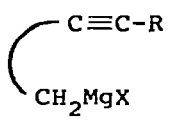
magnesium [131], so either rearrangement is very rapid, or a free radical intermediate in the Grignard formation rearranges quite efficiently. The rearrangements in eqns 65 and 66, in which only ring-cleaved products are formed, may likewise indicate ready cleavage to an allylic or benzylic Grignard. Cleavage products in the reaction of dehydronorbornyl chloride or norbornylmethyl chloride with sodium, or on heating the Grignard corresponding to the latter, indicate an increased tendency to cleave when an allylic organometallic may be generated in the process (eqns 72-74).

In the cyclization reaction, there is evidence for the effects of chlorine and aryl substitution on the double bond. In the conversion of $ClCH{=}CHCH_2CH_2MgBr$ to cyclobutene (eqn 44), it is believed that the rate-determining step is cyclization to a three-membered ring by addition of the Grignard function to the double bond [105]. This rate is slower by a factor of about 1,000 than the isotope-position rearrangement of eqn 29. In a similar reaction (eqn 45), phenylcyclobutene is formed on reaction of $(C_6H_5)C(Cl){=}CHCH_2CH_2Br$ with magnesium; but as indicated previously, the Grignard reagent, 35, does not appear to be an intermediate in formation of most of the phenylcyclobutene [108]. At elevated temperatures, the Grignard reagent does decompose, yielding phenylcyclobutene as a part of the product. Decomposition of the Grignard ($t_{1/2}$ ~ 4 hr at 115°C) appears to be a bit slower than isotope-position rearrangement of the corresponding Grignard, 18a [92], which lacks the chlorine ($t_{1/2}$ ~ 6 hr at 100°C). Again this suggests a rate-retarding effect of chlorine on the double bond.

Phenyl substitution on either end of the double bond (positions R_3 or R_4 in structure 85) appears to have an effect ranging from substantially retarding to modestly accelerating,

depending upon the system. It was thought earlier that the substitution of two phenyl groups on the double bond in eqn 42 led to a large increase in rate, since the two methylene groups were equilibrated by the time of the first observation. However, it now appears that nearly complete equilibration occurs during rather than after formation of the Grignard, and that subsequent reaction is very slow [92]. Relative rates for several systems are summarized in Table V-3.

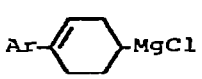
In cyclization by addition to a triple bond (86), R cannot be H, as this would decompose the Grignard. For cyclization to



86

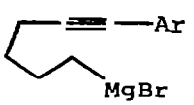
a five-membered ring, the reaction is more rapid with R = phenyl than R = butyl, by factors of about 30-35 in THF or DME [154]. Qualitative observations suggest a similar trend in cyclizations forming four- and six-membered rings.

Substitution in the aryl group has been investigated in two instances. In both cases, positive ρ-values were found, indicating that electroncially the reaction is favored by electron-withdrawing substituents. In both cases, the magnitude of the effect was small.



ρ = +1.4 (THF, 120°)

(H, p-CH_3, m-CF_3) [115]

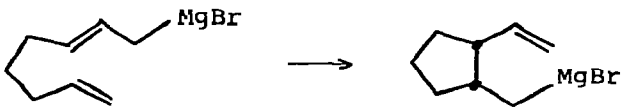


ρ = +0.90 (DME, 84°)

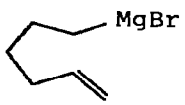
(H, p-F, p-CH_3, p-OCH_3) [154]

In one instance, cyclization has been reported which involves

the addition of an allylic Grignard to a double bond:



$k \approx 10^{-4}$ sec^{-1} (refluxing ether) [156]



$k \approx 10^{-5}$ sec^{-1} (THF, 100°) [148]

The rate is markedly enhanced.

d. Nature of the unsaturated group to which addition occurs. Cyclizations have been studied in which the unsaturated function undergoing addition is a simple olefinic double bond, an acetylic triple bond, or an allenic double bond. Addition to the triple bond appears to be more rapid than addition to the corresponding double bond in the comparisons listed.

$ClMg-(CH_2)_4-C{\equiv}CCH_3$ $t_{1/2}$ ~ 50 hr (THF, 100°) [153]

$ClMg-(CH_2)_4-CH{=}CHCH_3$ $t_{1/2}$ ~ 40 hr (THF, 155°) [151]

$BrMgCH(CH_3)-(CH_2)_3-C{\equiv}CCH_3$ $k = 2.3 \times 10^{-5}$ sec^{-1} (THF, 100°) [148]

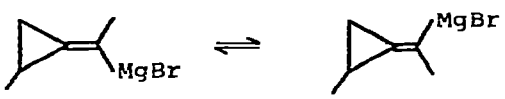
$ClMgCH(CH_3)-(CH_2)_3-CH{=}CHCH_3$ $k = 0.03 \times 10^{-5}$ sec^{-1} (THF, 100°) [148]

$BrMgCH(CH_3)CH_2C{\equiv}CCH_3$ $t_{1/2}$ ~ 8 hr (THF, 100°, 0.3 M) [102]

$ClMgCH(CH_3)CH_2CH{=}CHCH_3$ $t_{1/2}$ ~ 120 hr (THF, 113°, 2 M) [94]

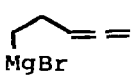
In the last comparison, it is possible that the cyclization rate of the acetylenic compound is greater than the rearrangement rate

cited; if the cyclization and cleavage are stereospecific, the rate of rearrangement might be controlled by the rate of interconversion of intermediates 87 and 88 (see section IVB-8 for discussion of this stereochemical question in other cases).



87 88

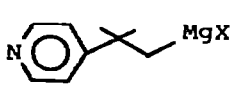
The information available is insufficient to state with certainty whether the allenic function of 28 is more or less reactive than a simple monosubstituted double bond. The



28

cyclization is reported to have a half-life of about 4 days at room temperature in THF, whereas isotope-position rearrangement in eqn 29 has a half-life of 30 hr at 27° in ether. If rearrangement in ether is accelerated by a factor of 25, as found in some cases, the allene would be somewhat more reactive. Additionally, the preparation of the allenic Grignard was accompanied by a large amount of formation of hydrocarbon. Magnesium bromide, formed with the hydrocarbon, might produce an additional decrease in the measured rate.

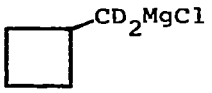
An aromatic ring is another unsaturated group to which cyclization by intramolecular addition might occur. Generally, a phenyl ring appears to be unreactive toward addition of an organomagnesium function. The cyclization of 89 (see eqn 11) involves such an addition to a pyridine ring.



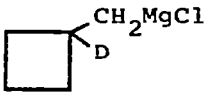
89

7. Isotope effects

Secondary kinetic isotope effects have been studied in ring-cleavage reactions of 90 and 91 [129,177]. Isotope effects



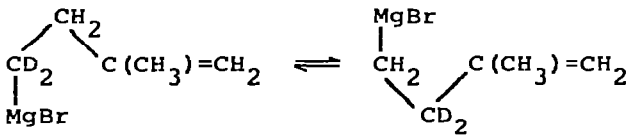
90



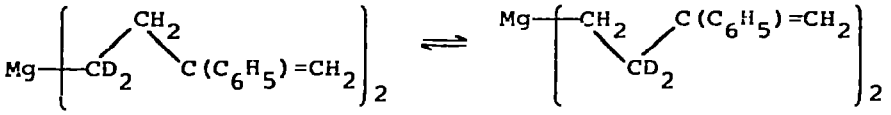
91

(k_H/k_D) of virtually unity were observed (1.02±0.02 and 1.00±0.02, respectively).

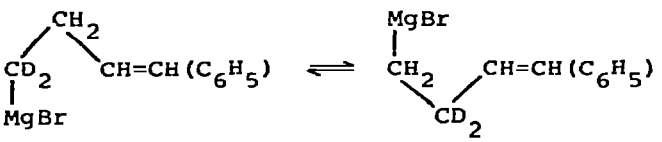
Secondary isotope effects upon equilibria have also been reported, with the following results:



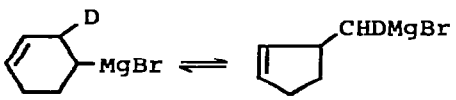
K = 1.09-1.76 (depending upon solvent and concentration) [90].



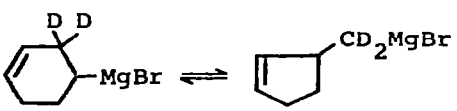
K = 1.41-1.83 (depending upon temperature and concentration) [90]



K = 1.39±0.05 [92]



K_H/K_D = 1.14 [114]



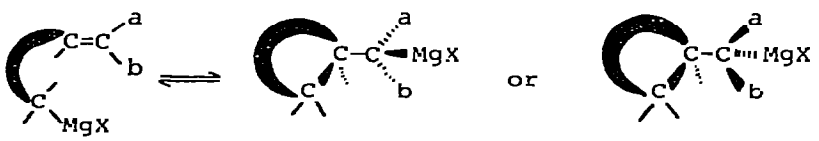
K_H/K_D = 1.20 [114]

The equilibrium isotope effects have been ascribed to the electron-releasing effect of deuterium vs. protium [92,114].

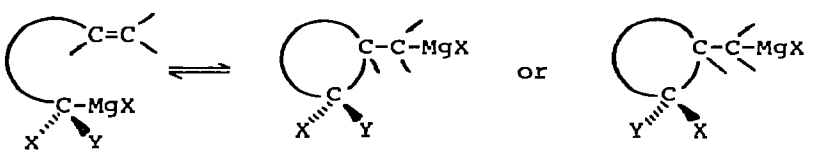
8. Stereochemistry

Several significant questions might be asked concerning the stereochemistry of the cyclization-cleavage rearrangements. Unfortunately, the configurational lability of the carbon magnesium bond precludes a straightforward answer to two which are of considerable mechanistic importance:

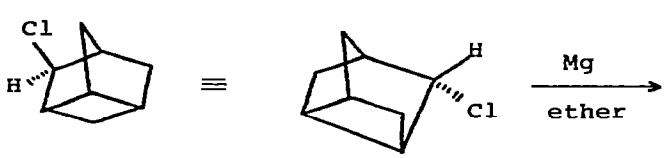
(i) Does the cyclization (or cleavage) occur with cis- or trans- stereospecificity, or with loss of double bond stereochemistry?

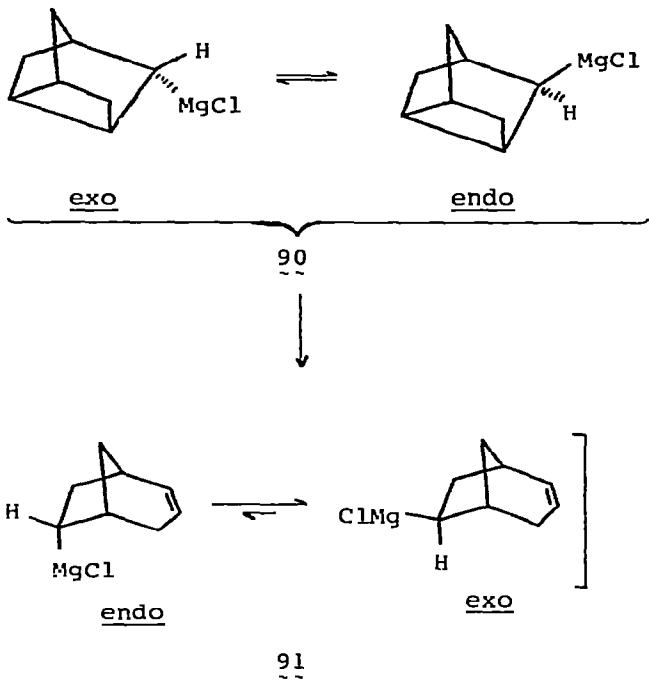


(ii) In the addition, does the carbon atom adding to the double bond react with inversion, retention or racemization?



The ring cleavage reaction of eqn 64, redrawn in eqn 82, illustrates the situation [140]. The exo- chloride or bromide

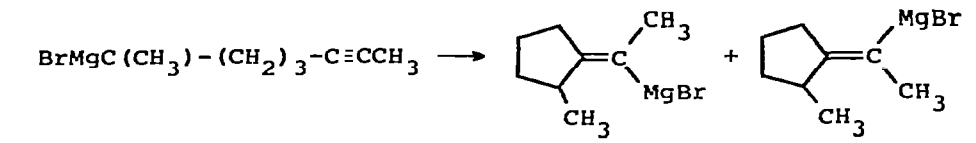




(82)

is converted by magnesium primarily into exo-90, which on heating, equilibrates with its endo- isomer. At longer heating times or higher temperatures, cleavage occurs. The eventual Grignard is mainly exo-91 (as shown by carbonation). Since equilibration of exo- and endo-90 is more rapid than the cleavage, it is not possible to determine whether one or both isomers are cleaving. Similarly, inversion in exo- and endo-91 probably occurs even more rapidly, so that the immediate cleavage product is not established.

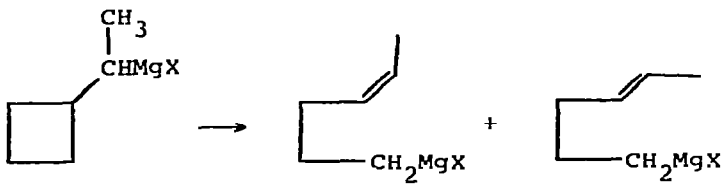
Alkenyl magnesium compounds have greater configurational stability than saturated ones, but here, also, the stereochemistry picture is somewhat confused. Cyclization to a five-membered ring in eqn 68b led to a mixture of two products in a 5:1 ratio, but the stereochemical identities were not established, and it was not known whether this mixture was the product as initially



(68b)

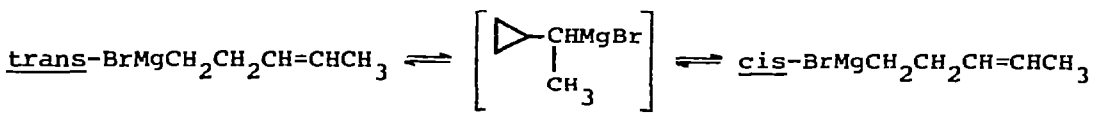
formed, or the consequence of isomerization [102,153]. A similar result (with a 1:1 product mixture) was found for the closure to a six-membered ring (eqn 79).

Stereochemistry at the double bond is also of interest. Cleavage of the 1-cyclobutylethyl Grignard leads to approximately a 1:1 mixture of cis- and trans- isomers [129]:



At the temperature of the reaction, the equilibrium mixture of the 2-hexenes should have a cis:trans ratio of about 1:3, and there is no obvious reason to expect the equilibrium ratio of Grignard products to differ greatly from this. Hence, the transition states leading to cis- and trans- products are equal in energy, although the products differ. Interestingly, the portion of Grignard reagent that had rearranged during formation was almost exclusively cis. In the direction of addition, the only available evidence apparently relates to the chlorine-substituted double bond of 33. The cis- and trans- isomers react at similar rates [105].

Stereochemistry at the double bond is also involved in a cyclization-cleavage rearrangement [93]:

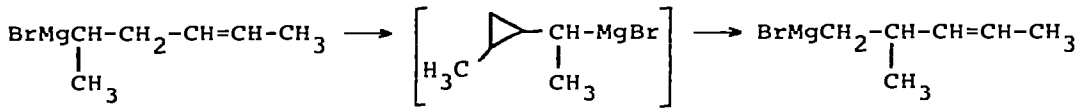


Starting from either side of the equilibrium mixture (cis:trans = 21:79) the same rate of approach to equilibrium was observed. This was of the same order of magnitude as the rate of approach to the equilibrium distribution of deuterium between the methylene groups in the same system:

$$\underline{\text{cis}}\text{-} + \text{BrMgCD}_2\text{CH}_2\text{CH=CHCH}_3 \rightleftharpoons \underline{\text{cis}}\text{-} + \text{BrMgCH}_2\text{CD}_2\text{CH=CHCH}_3$$
$$\underline{\text{trans}}\text{-} \qquad\qquad\qquad\qquad\qquad\qquad \underline{\text{trans}}\text{-}$$

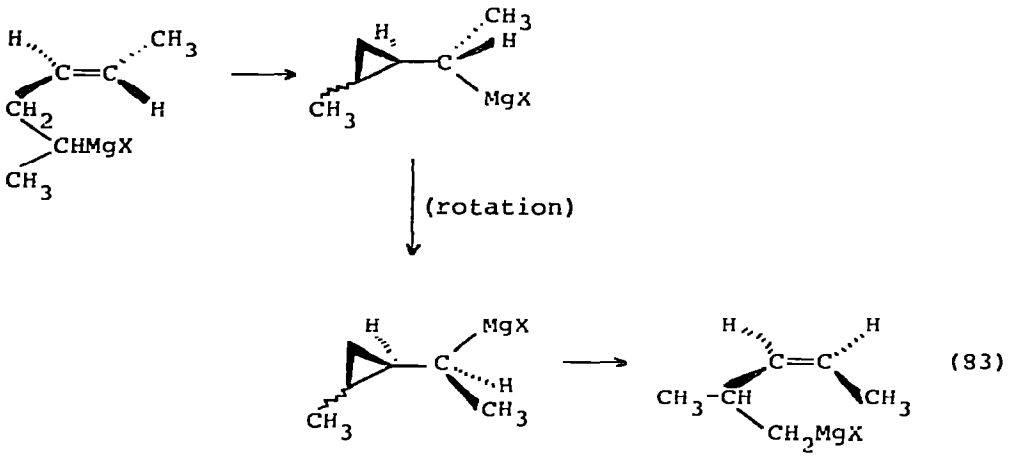
From this result, it was concluded that the cyclic Grignard is a true intermediate in the isotope-position rearrangement, with sufficient lifetime to achieve rotational equilibrium (and hence cis-trans equilibration in the rearrangement product).

In a related experiment, the rearrangement was a "one-way" secondary to primary process [94]:



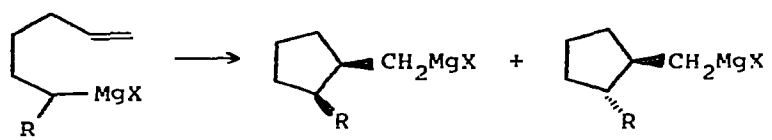
92 93

The product from heating trans-92 in ether was approximately a 1:1 mixture of cis- and trans-isomers, which did not change in composition with additional strong heating. If the rate of inversion of the cyclized Grignard 93 is slower than its rate of ring cleavage, then a stereospecific mechanism for cyclization (and cleavage) should lead exclusively to a cis- double bond in the product. This is illustrated for a cis- mechanism in eqn 83, but a trans- mechanism would give the same result (of course, both addition and cleavage should have the same stereochemistry). Either inversion is faster than cleavage, or reaction is not stereospecific.



(83)

Another aspect of stereochemistry involves the geometric relationship of groups on the ring in the product of a cyclization. This is illustrated for the five-membered ring, but the same situation has been observed for a six-membered ring also:

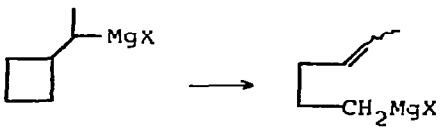
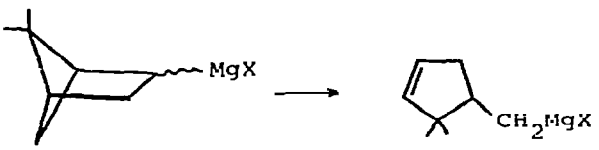
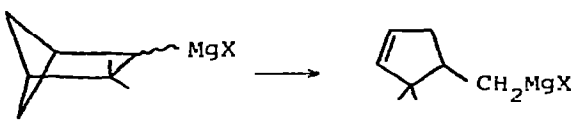
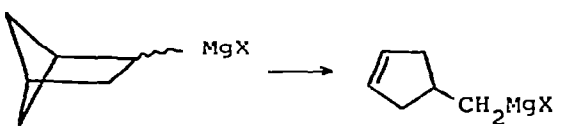
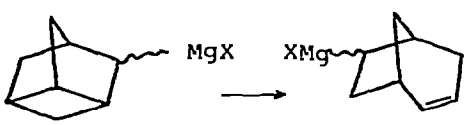
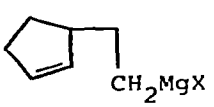
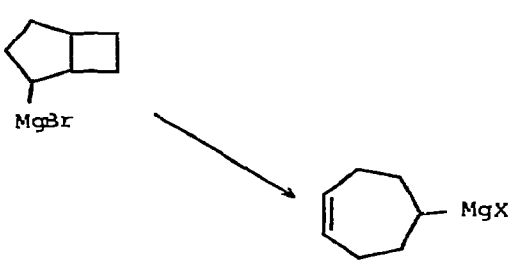


Stereochemical results have been reported for reactions in eqns 67b, 67d, 67g, and 75 [92,148]. The observed result has been a preponderance of the trans- isomer, to an extent ranging from 3:1 to over 10:1. In the course of Grignard reagent formation, cyclized product is formed in competition with unrearranged reagent. Interestingly, in this initially-formed cyclic product, the cis- isomer appears to predominate.

A contrasting result--exclusively (~30:1) formation of cis-product in eqn 70--has been interpreted in terms of a cyclic transition state in that reaction [156].

The rate and course of Grignard cleavage reactions also

TABLE VI. RELATIVE CLEAVAGE RATES OF BICYCLIC AND TRICYCLIC GRIGNARD REAGENTS[a]

Reaction[b]	Relative Rate	$\Delta H^{\ddagger}_{T}$ (kcal/mole)	$\Delta S^{\ddagger}$ (cal/mol deg)
	(1)	---	---
	0.001-0.007	32.1±1.3 (X = Cl) 30.6±1.1 (X = Br)	-1.4±2.1 -1.2±1.7
	0.005-0.07	33.4±2.0 (X = Cl) 28.2±1.9 (X = Br)	5.3±3.2 -4.6±3.0
	0.065	---	---
	0.015	---	---
	0.06	31.6±0.9 (X = Br)	4.3±0.5
	0.005	28 (X = Br)	-10

[a]Refs 137, 138, 140, and 184. [b]Reaction conditions: ether, 100°, ca. 0.2 M).

appears to be significantly influenced by geometrical requirements of the reaction. Thus, some ring-cleavage reactions of bicyclic α-cyclobutylalkyl Grignard reagents appear to be surprisingly slow when compared with simpler analogs, despite the potential for greater relief of ring strain in cleavage of the bicyclic compounds. Some results are listed in Table VI. It may be noted that with the last entry in Table VI, cleavage to a secondary Grignard competes more favorably with cleavage to a primary Grignard than in the 2-methylcyclobutylmethyl system. Strain energy in the two products shown should be comparable.

9. Activation parameters for organomagnesium rearrangements

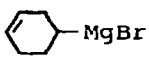
Activation parameters derived from kinetic data are listed in Table VI for bicyclic Grignard cleavages and Table VII for others

C. Mechanism of Organomagnesium Cyclization and Cleavage Rearrangements

The principal mechanistic question which we will address is the detailed nature of the cyclization and cleavage processes. Before considering specific mechanistic proposals, however, some preliminary points mught be made.

In a number of the reactions cited above, cyclization to a three- or four-membered ring is observed only indirectly, by skeletal or isotope-position rearrangement. It is possible that these rearrangements might "by-pass" the intermediate cycloalkylmethyl organometallic, and consist in mechanism (as well as formally) of a simple 1,2- or 1,3-vinyl shift. Several arguments suggest that this is not the case: (a) The existence of both thermodynamically favored cyclizations, and rearrangements which can be formulated as addition-elimination processes, points to the plausibility of similar reaction paths

TABLE VII. ACTIVATION PARAMETERS IN ORGANOMAGNESIUM REARRANGEMENTS[a]

Compound	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (cal/mol deg)	Reference
$CH_2=CHCH_2CD_2MgBr$ (Ether; 27° and 55.5°)	ca 25.5	ca + 3	79
$ClCH=CHCH_2CH_2MgBr$ (THF; 61.5 and 107°)	ca 30	ca + 2	105
$(CH_2=C(C_6H_5)CH_2CD_2)_2Mg$ (ether; 60, 80, 100°)	ca 24.2	ca -12	90
 (ether; 80, 100, 120°; 3.5M)	ca 22	ca -17	114
$CH_2=CHCH_2CH_2CD_2MgCl$ (THF; 140-160°; est'd[b])	ca 28.5	ca -15	133
$CH_2=CHCH_2CH_2CH(CH_3)MgCl$ (THF, 85-110°)	ca 23	ca -24	132
$C_6H_5C\equiv C(CH_2)_4MgBr$ (DME, 51-84°)	19.2	-21	154
C-$C_4H_7CH_2MgCl$			138
(ether, 52-80°)	25.8±0.3	-3.4±0.6	138
(THF, 60-100°)	26.5±0.2	-4.6±0.5	133
C-$C_4H_7CH_2MgBr$ (ether, 52-80°)	31.5±0.7	+11.3±1.2	138
C-$C_4H_7CH(CH_3)MgCl$ (ether, 66-80°)	25.7	-5.8	137
C-$C_4H_7CH(CH_3)MgBr$ (ether, 66-94°)	31.9±0.7	11.1±1.1	137

[a]Results calculated or recalculated from available rate data. Error limits, where given, are standard deviations reported in least squares analysis of rate data. Results are indicated as approximate where data were available at two temperatures only, where no indication of accuracy or reproducibility of data was available, or where scatter in Arrhenius plots was apparent. [b]Obtained from activation parameters for reverse reaction and estimated thermodynamic parameters for equilibrium.

for both. (b) Similarities have been noted in medium, concentration, and structural effects (see sections IVB-1 to IVB-5) among cyclizations, cleavages and the "rearrangements." (c) Thermochemical arguments indicate that the enthalpy of the transition state for the isotope-position rearrangement of eqn 56 is very similar to that for the cleavage of the cyclobutylmethyl Grignard [133]. A similar treatment of published data for the cyclopropylmethyl case gives a like result [177]. (d) The rearrangements of eqns 32c and 33, which lead to double bond cis-trans isomeric mixtures, are best explained by the loss of cis-trans identity in the cyclic intermediate. Hence, it appears reasonable to conclude that a common mechanism applies to cyclizations, cleavages, and rearrangements.

Cleavage, cyclization, and rearrangement reactions have been noted with organometallics of elements other than magnesium, which forms the principal emphasis of the present review. Very substantial differences, reasonably ascribed to the difference in polarity, exist between reaction rates of organomagnesium and organolithium compounds. These might also reflect a change in reaction mechanism. For instance, it is reported for the reaction of eqn 31a that the rearrangement rate of the Grignard decreases in going from ether to THF, while that of the corresponding lithium derivative increases with solvent polarity. It appears that considerable caution should be exercised in comparing results from organosodium compounds, for instance, with those from the more covalent organomagnesium compounds. It might also be wise to be suspicious of comparisons involving reactions carried out under the more vigorous conditions (up to 160°), or reactions in which conjugation with a phenyl group could stabilize a radical or carbanion intermediate.

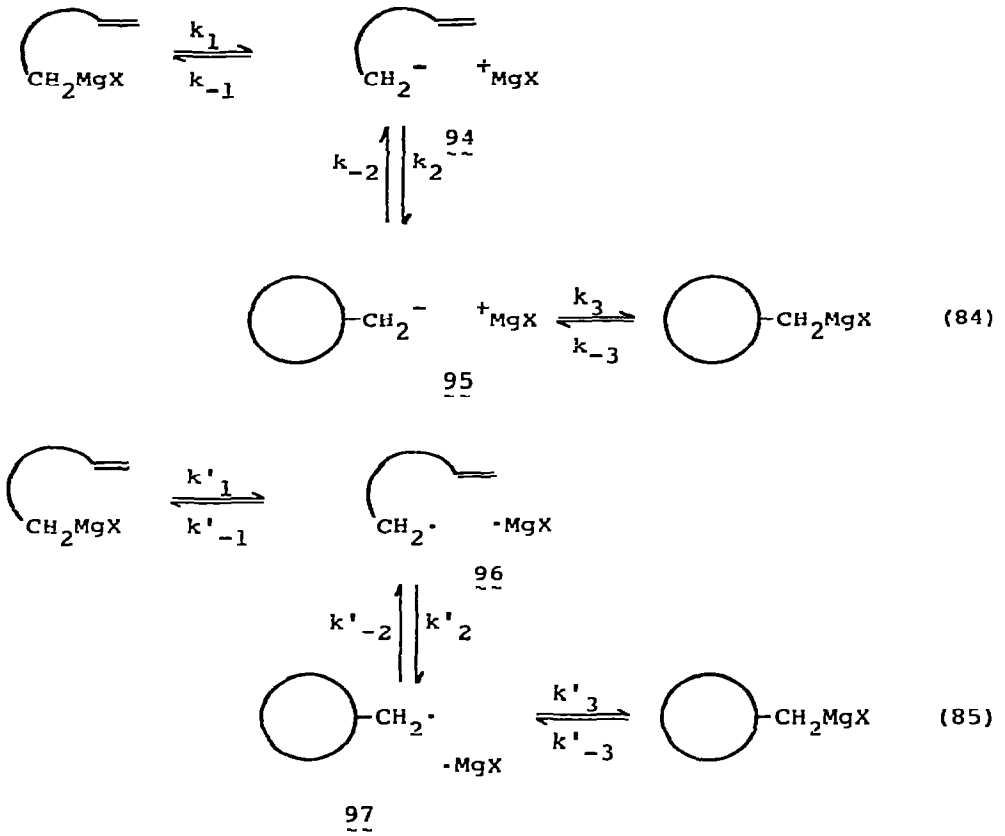
Another uncertainty in mechanisms is raised by the concentration effect observed at higher concentrations (>0.5-1.0 M). In concentrated solution, the rate appears to be roughly linear in total Grignard concentration, and the different rate law might imply a different mechanism. This point will be discussed later (see section IVC-5).

In the discussion to follow, we will generally assume that a common mechanism type is involved in all of the organomagnesium rearrangements, regardless of ring size and the direction of the equilibrium. If, as is the case with three- and four-membered rings, the cleavage is exothermic, then cleavage and cyclization may both be observed within the same system (the latter as "vinyl shift" rearrangement). Cleavage and cyclization mechanisms must (by microscopic reversibility) be identical, but opposite in sequence. With larger rings, the cyclic isomer is favored at equilibrium, and so cyclization is observed directly but cleavage is not seen.

1. The carbanion and radical mechanisms

Conceptually, the two simplest mechanisms for the rearrangement are as illustrated in eqns 84 and 85. They consist, respectively, of heterolytic or homolytic cleavage of the carbon-magnesium bond, followed in turn by ring-cleavage (or cyclization) in the intermediate carbanion or radical, and re-formation of the carbon-magnesium bond.

Either carbanions or radicals would seem to be plausible intermediates in reaction of a Grignard reagent. Much of organomagnesium and other organometallic chemistry is commonly termed "carbanion chemistry"; despite the well-established polar-covalent nature of the carbon-magnesium bond, most reactions of Grignard reagents are basically those expected of a



"coordinated carbanion," and ionization to a carbanion would be the anionic analog of the S_N1 mechanism in carbonium ion chemistry. Radical chemistry is also observed with organomagnesium compounds, though generally not in the fashion of a simple homolytic cleavage of the carbon-magnesium bond.

Several sorts of evidence may be marshalled against these mechanisms. The most telling evidence against the carbanion mechanism comes from the lack of acceleration with increased solvent polarity and the effects of substituents. The radical mechanism, while compatible with the solvent effect, also runs into trouble with substituent effects.

Before dismissing these mechanisms, however, it may be well

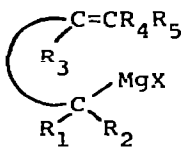
to examine them in a bit more detail. In either carbanion or radical mechanisms, possibilities might be considered in which any one of the three steps is rate-determining. Furthermore, within one of these mechanisms, the rate-determining step might be different for endothermic and exothermic cyclizations.

If the first step (k_1) is rate-determining, then by definition, $k_2 > k_{-1}$. This situation seems somewhat unlikely. Recombination of the caged radical (96) or ion pair (94) should be extremely rapid. In the radical case, the quite exothermic (~-15 kcal) cyclization of the 5-hexen-1-yl radical is rapid ($k \sim 10^5$ sec^{-1}), but not rapid enough to compete with caged radical pair processes [185]. Endothermic cyclizations to cyclobutylmethyl or cyclopropylmethyl radicals are even less likely to compete with recombination. Experimental evidence also indicates that k_1 is not rate-determining. If it were so, the rate of cyclization should be essentially independent of substitution, position, or nature of the unsaturated groups. Yet, as summarized in section IVB-6, the cyclization rate is highly sensitive to precisely these variations in both exothermic and endothermic cases.

If the final recombination step (k_3) is rate-determining, then its transition state must be the highest point in free energy along the reaction coordinate. It again seems somewhat unlikely that this step should be slower than k_{-2}, particularly if the cleavage is endothermic. The most likely situation for this step to be rate-determining would be in systems with a three- or four-membered ring, where step k_{-2} is exothermic. From the Hammond postulate, the transition state for step k_3 (also k_{-3}) should be quite similar in structure to the intermediate 95 or 97. Then, in either the cyclization or the cleavage, any

feature which stabilizes a carbanion or a radical at this position should accelerate either the cleavage or the cyclization. The experimental finding is that in cyclization, the reaction is slowed by phenyl or chlorine substitution at this position, which should stabilize either a carbanion or a radical (see eqns 32a, 42, 45, 50, and 67g), and by methyl, which should stabilize a radical (see eqns 44 and 45). In ring cleavage, methyl has a modest effect, in either direction depending upon the solvent, whereas it should markedly accelerate radical formation and decelerate carbanion formation. It would appear, then, that this step cannot be rate-determining.

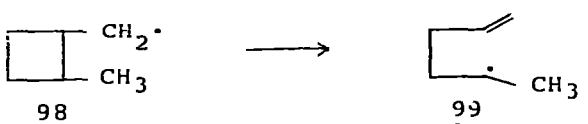
The second step, intramolecular addition of the carbanion or radical (or its reverse), may now be considered. If the addition were carbanion, the predicted rate effects of terminal substituents on the double bond would be the same as for step 3 rate-determining: R_4 = aryl or chlorine should accelerate, and



methyl should retard. The retardation by methyl is observed, but not the accelerations predicted for chlorine or phenyl. The small positive ρ-values found in eqns 50 and 68d (see section IVB-6-c) are consistent with some build-up of negative charge on the terminal carbon, but they are much smaller than expected for a reaction which generates full carbanionic charge in this position. The observed solvent effect, in which rate increases are found with decreasing polarity, is also difficult to reconcile with an ion pair transition state. However, this latter might be tempered with some caution, since the solvent effect appears to be complex,

depending upon coordinating power of the solvent as well as its polarity. It may also include the effect of solvent upon association and exchange equilibria.

For a radical mechanism, terminal substitution of aryl, chlorine, or methyl on the double bond would all be expected to stabilize the cyclized radical, and hence to accelerate rearrangement. This prediction contrasts with the marked decreases noted in most instances. However, alkyl and chlorine substitution are found to have rather small effects on rates of intermolecular radical additions [186]. The small positive ρ-value might be consistent with addition of a nucleophilic alkyl radical. A most telling argument against the radical mechanism comes from the preferential cleavage to primary product (vs. secondary or tertiary), as observed in eqns 53, 34, 50, 61, and 62. Cleavage of an intermediate radical should occur predominantly to give the more highly substituted radical, in direct contrast with experiment. It is found, for instance, that cleavage of the 2-methylcyclobutylmethyl radical 98 leads mainly to 99 [184].



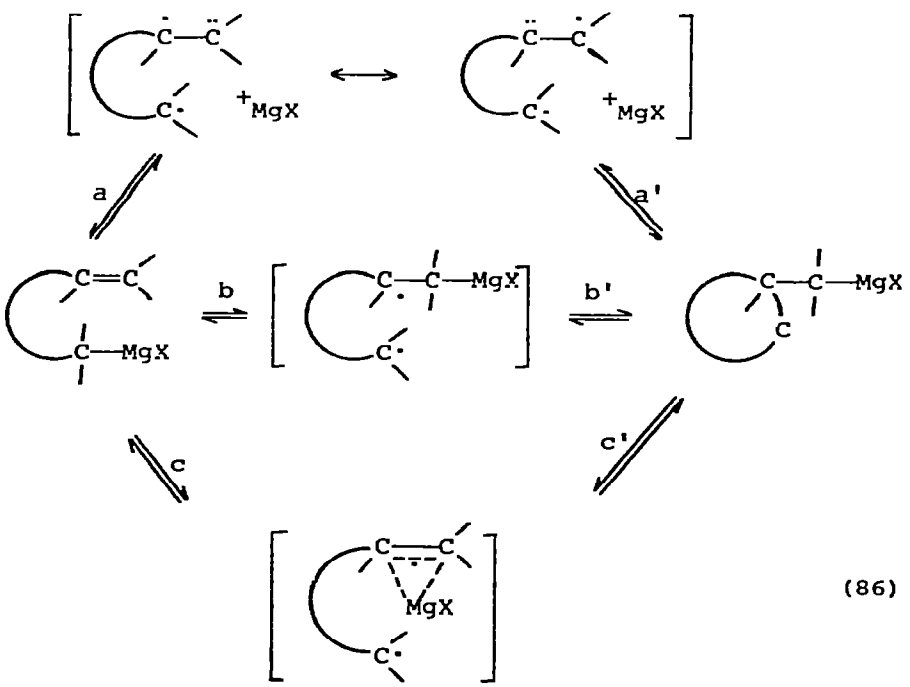
98 99

Other substituent effects are somewhat less clear-cut in relation to the carbanion and radical mechanisms. The rate-retarding effect of either phenyl or methyl in the R_3 position might be ascribed to a steric hindrance to new bond formation at that position, whatever the mechanism. The "irregular" effect of R_1 and R_2 ($1° < 2° > 3°$) substituents may be ascribed to opposing effects of a number of sorts. Alkyl substitution would decrease or increase respectively the equilibrium dissociation to carbanions or radicals, but would have the opposite effect upon reactivity

of these toward the double bond. The net effect upon the product $(k_1k_2)/k_{-1}$ could be the irregular trend observed. This sequence could be further complicated by a steric effect decreasing the rate for the tertiary organometallic. Similar uncertainties cloud the interpretation of the minor rate difference between cleavages of cyclobutylmethyl and cyclobutylethyl Grignard reagents (eqns 52a and 52b) (see section IVB-6-b). In conclusion, it does not appear that the carbanion or radical mechanisms, regardless of which step might be rate-determining, are consistent with the data.

2. The electron-transfer mechanism

A second basic form of mechanism is a process in which electron transfer from the organometallic function to the double bond occurs, followed by formation of the new C-C bond. This mechanism is illustrated in several variations: simple electron



(86)

transfer in eqn 86a, and electron transfer via transfer of the metal atom in eqns 86b and 86c. From another viewpoint, the latter might be considered ligand exchanges on magnesium.

A mechanism of this sort appears to have reasonable analogy. The π^* orbital of an alkene should be capable of accepting an electron, and the σ-electrons of the electron-rich C-Mg bond should be among the most easily ionized of bonding electrons. An electron-transfer mechanism [187] has recently gained popularity in discussions [188,189] of the addition of Grignard reagents to carbonyl compounds (eqn 87), and a similar mechanism has been proposed by two groups for the addition of Grignard

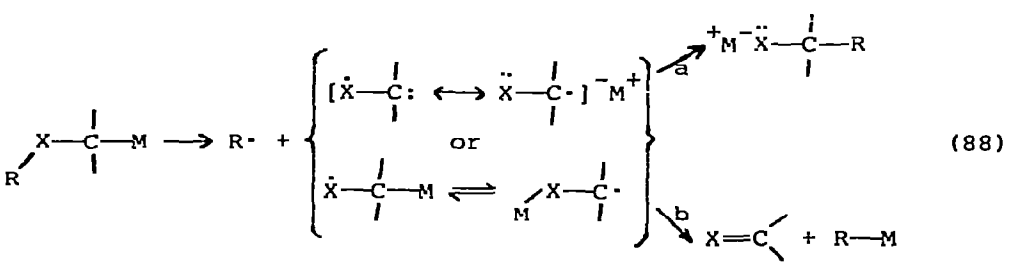
$$RMgX + \rangle C{=}O \longrightarrow R\cdot + \rangle \dot{C}\text{-}OMgX \longrightarrow R\text{-}\overset{|}{\underset{|}{C}}\text{-}OMgX + \begin{matrix}\text{other}\\ \text{products}\end{matrix} \qquad (87)$$

reagents to the multiple bonds of unsaturated alcohols [190,191]. However, there is no general agreement that this mechanism prevails in most Grignard additions. Ashby [192] notes that single electron transfer from methyl Grignard to benzophenone may be attributed largely to transition metal impurities in the magnesium, and is particularly important when there is a large excess of Grignard. It may simply be an unproductive side-reaction. Electron-transfer seems to be most likely (a) for hindered ketones, (b) for ketones with less negative reduction potentials ($Ar_2CO >> R_2CO$), (c) with tertiary or benzyl (as opposed to methyl or phenyl) Grignard, and (d) in polar solvents (ether<THF<HMPT) [193].

The electron-transfer mechanism should be less likely for addition to an alkene than to a carbonyl function. A C=C bond accepts an electron less readily than does a C=O bond. This is apparent in the inertness of unconjugated alkenes toward electrochemical reduction, and the more negative $E_{1/2}$ values for

polarographic reduction of aryl-substituted alkenes, as compared with aryl carbonyl compounds [194,195]. Grignard reagents are known to transfer an electron to those polycyclic aromatic hydrocarbons which are easily enough reduced [196,197]. These include pentacene, tetracene, and perylene; the limit of reducibility under mild conditions appears to be around tetracene in THF and anthracene in DME. However, from polarographic measurements (in dimethylformamide), it appears that the reduction potential of styrene is some 0.4 V more negative than that of anthracene [198,199], and those of unconjugated alkenes are still more negative by a yet unknown amount. It is possible that the electron-transferred intermediates of eqn 86 are higher in energy than the transition state for the Grignard cyclizations. (For example, the relatively rapid cyclization of eqn 29 has an activation energy of about 26 kcal/mol, or about 1.1 eV.)

In the direction of ring cleavage, the electron-transfer mechanism bears analogy both to the radical pair mechanism currently favored for Wittig and Stevens rearrangements, and to the thermal ring-cleavage rearrangements of small-ring hydrocarbons. Pursuing the first analogy in eqn 88, we note



(88)

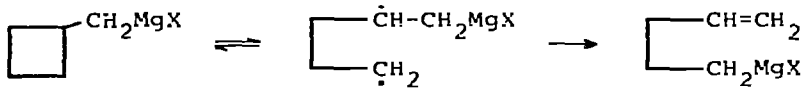
a, X = O

b, X = CR'_2

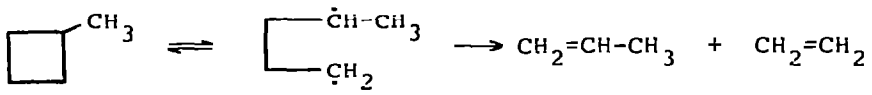
that the intermediate proceeds to products either by recombination (path a) in Wittig rearrangement, or metal or electron transfer

(path b) in the Grignard cleavage. The intermediate (a) in the Wittig rearrangement is stabilized by resonance, which allows a transfer of negative charge from carbon to oxygen. This stabilization is great enough that a C-O single bond (normally with D(C-O) of about 75-85 kcal/mol) [200] cleaves with a modest activation energy (e.g., 16 kcal/mol for the rearrangement of benzyl i-propyl ether) [201].

The relationship to thermal reactions of small-ring compounds is seen by comparison of eqns 89 and 90.



(89)



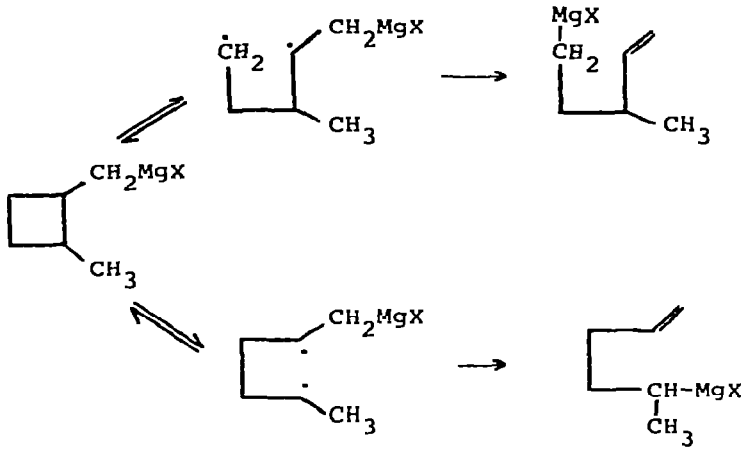
(90)

A thermochemical interpretation of the vapor phase thermal decomposition of cyclobutanes suggests that the diradical intermediate in eqn 90 is 54-56 kcal/mol higher in enthalpy than the starting material [202]; activation energy for its formation is 63 kcal/mol. Other approaches suggest that the diradical may instead be comparable in energy with the transition state [203]. The activation energy for ring cleavage of the cyclobutylmethyl Grignard (eqn 89) is 26.5 kcal/mol. If the diradical is an intermediate in this reaction, the radical center must be stabilized by the β-magnesium (or -carbanion) to the extent of 27-36 kcal/mol - perhaps more if reaction of the diradical intermediate in either direction has a non-zero activation energy. Both of these analogies demand a large amount of stabilization for the intermediate in the electron-transfer mechanism, but there appear to be no good models for judging whether such stabilization is realistic.

Experimentally, the mechanism of eqn 86a, simple electron transfer, encounters serious difficulties on several scores. It is difficult to see why aryl or chlorine substitution on the double bond should not accelerate the cyclization by this mechanism: the intermediate should be greatly stabilized, and the exothermic second step should be relatively insensitive to substitution. The substituent effect [148] on the Grignard carbon (1°<2°>3°) would also be difficult to explain if the first step is rate-determining, since a monotonous 1°<2°<3° order is expected. It could be explained by opposing effects on an equilibrium electron transfer, and a rate-determining ring closure. However, if the second step is rate-determining, the transition state should resemble an ion pair, and the observed solvent effect (see section IVB.1) is inconsistent. (Solvent effects on rates of pure electron-transfer reactions do not seem to follow a very distinctive pattern [204,205], but if the subsequent step is rate determining, a normal solvent effect is expected.)

With the metal-transfer variants, b and c of eqn 86, the substituent and solvent effects may be more satisfactorily rationalized. The intermediate might be sterically destabilized by double bond substituents of varied electronic nature (methyl, aryl or chlorine), and internal substituents on the double bond could hinder the second step. Intermediates in eqn 86b and 86c are not formally ionic or obviously different in polarity from a Grignard reagent, and so the observed small solvent effects seem reasonable.

The ring-cleavage reaction of the 2-methylcyclobutylmethyl Grignard appears to provide quite clear evidence <u>against</u> the electron-transfer mechanism (eqn 91). If the first step in the

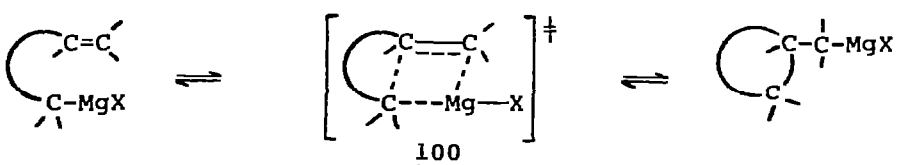


(91)

cleavage is rate-determining, then the secondary Grignard product would be expected to form most rapidly. This is not the case; the product is 99% primary Grignard. The primary Grignard product might be explained if the first steps, yielding primary and secondary radical pair intermediates, are in equilibria. Primary Grignard would result if its rate of formation from the low concentration of primary radical is more rapid than secondary Grignard formation from the larger concentration of secondary radical. However, it is likely that the diradical intermediates (stabilized as they must be) would live long enough to undergo partial rotational equilibrium. Then, uncleaved Grignard should have undergone cis-trans equilibration. This does not occur.

3. The concerted mechanism

A mechanism which appears to avoid most of the problems of substituent and solvent effects is a four-center mechanism, in which bonding changes in the carbon skeleton are effectively concerted with movement of the magnesium (eqn 92). The structure



(92)

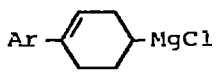
100

100 is envisioned as a transition state, rather than a stable intermediate, making the reaction a one-step process. However, bonding changes need not be entirely synchronous; formation of the new C-C bond might in principle be more or less advanced than formation of the new C-Mg bond. Also, it is not necessary to presuppose that this transition state is entirely nonpolar. Both starting material and product contain polar bonds, and the distribution of charge in the transition state could well be either more or less uneven.

A cyclic four-center mechanism has considerable precedent in organometallic chemistry [206]. The hydroboration reaction is most commonly discussed in terms of such a process [207], and in various modifications it appears to explain most stereochemical features of that reaction [208]. The kinetics of addition of Al-C [209] and Al-H [210] bonds to olefins in the gas phase have been studied carefully, and a "relatively tight quadrupolar four-center" transition state is proposed. Similar mechanisms have been drawn for intramolecular additions of unsaturated organoaluminum compounds [160-164]. Eliminations of metal hydride in pyrolysis of organolithium [211] and -magnesium [212] compounds have also been discussed in terms of four-center mechanisms. Finally, four-center transition states appear regularly in discussions of addition and elimination reactions involving organotransition metal compounds, and in particular, in Ziegler-Natta polymerization [213-218].

A major virtue of the concerted mechanism is that it does not have a strong bias toward a characteristic substituent effect pattern, such as we anticipate for the mechanisms discussed previously. Variations might be devised which are "radical-like," "carbanion-like," "electrophilic" or "nucleophilic," etc. In

the present case, the electronic effect of remote benzene-ring substituents in 101 [115] and 102 [154] (see section IVB.6.c) is consistent with the development of partial anionic or "organometallic" character in the transition state on the carbon



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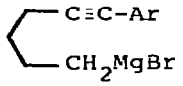


102

adjacent to the aromatic ring. The effect is about a third as large as typically found in clear-cut carbanion-generating reactions, a figure which is comfortably close to the 35% ionic character estimated for a C-Mg bond from Pauling electronegativities.

Most of the other substituent effects may be attributed to a pronounced steric influence of substituents on any of the three carbon atoms taking direct part in the reaction. Thus, phenyl or chlorine should electronically stabilize the forming organomagnesium function, but this is usually over-ridden by steric destabilization in the transition state. In agreement with this line of reasoning, the cyclizations of the type:

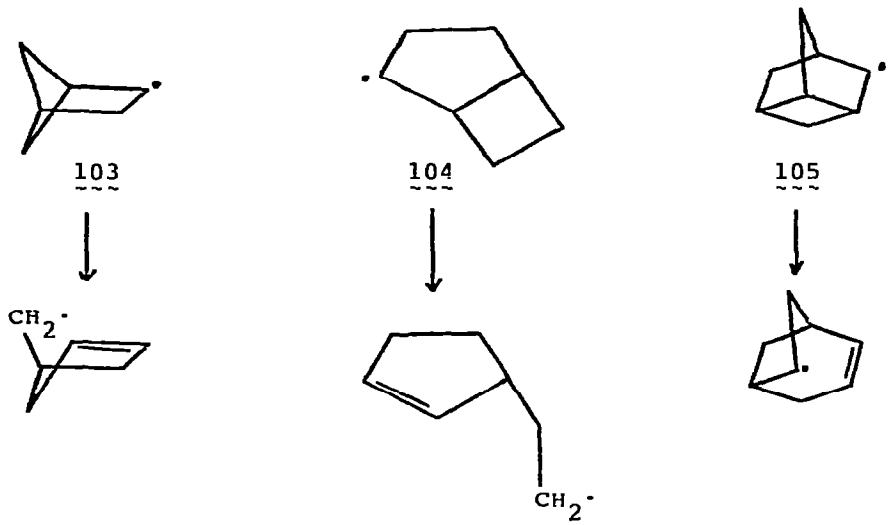
with R = methyl seem to have a larger rate-decreasing effect than R = phenyl, since steric and electronic effects act in the same direction. There is even a small rate increase for R = phenyl in the cyclization to a five-membered ring in eqn 67g [92]. Cyclization to the cyclopentane ring is exothermic, so the transition state may occur earlier along the reaction coordinate, at a point where the steric interaction is less serious.

The trend in substitution α- to the magnesium in cyclization

(1°<2°>3°) may be explained as first, a destabilization of the organomagnesium bond of starting material by methyl, and second, a steric effect in the transition state that becomes more pronounced with the second methyl. The minor effect of R = methyl substitution in the cleavage reaction of eqn 52 may have a similar explanation, while the preferred direction of cleavage in eqns 34, 50, 53, 61, and 62 could result either from an inductive effect or from steric difficulty in transfering magnesium to the more hindered carbon.

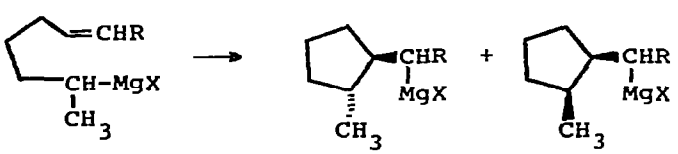
Solvent effects may be similarly "manipulated" for the concerted mechanism. The slight rate decrease in more polar solvents might be ascribed to dispersal of the partial negative charge of the polar C-Mg bond between two carbon atoms in the transition state. We therefore conclude that the concerted mechanism "fits" the experimental results. However, since this mechanism might be fitted to almost any pattern of results, this fit does not provide strong support in favor of the mechanism.

A likely consequence of a cyclic concerted mechanism would be a sensitivity to geometric restriction in the transition state. In a number of cases (noted in section IVB.8), cyclobutane ring cleavages of bicyclic and tricyclic compounds are much slower than those of monocyclic analogs, even though the relief of strain, and hence the driving force for ring cleavage, is greater. The rate decrease might be attributed to distortion of the transition state from its optimum geometry, increasing the distance that the magnesium must bridge in the course of transfer from carbon to carbon, and twisting the incipient double bond. Ring-cleavage reactions of the corresponding radicals 103-105 generated in tri-n-butytin hydride reductions of the halides, were similarly retarded. Therefore, though the concept of steric constraint is quite consistent with the concerted mechanism, it probably does



not serve to distinguish it uniquely from other mechanisms.

Another variety of steric result is somewhat more difficult to explain by the concerted mechanism. In the simplest conception of this mechanism, the three carbon atoms and the magnesium undergoing bonding changes might be supposed to lie in the same plane. This would maximize overlap of the orbitals involved in forming and breaking bonds. Their arrangement might be "roughly square," distorted somewhat from a regular shape by varying bond lengths. In several cases, it may be seen by examination of models that the coplanar, "roughly square" transition state for a concerted reaction is not consistent with experimental results. In the clearest and most consistently documented situation, Richey has found that the predominant product formed on cyclization to a five-membered ring is the trans-isomer, as shown in eqn 93, R = H, CH_3, C_6H_5 [92,148]. On the surface, this would seem to be the



(93)

expected result, since the trans- isomer should be the more stable. However, manipulation of models or examination of figure 1 will show that the transition state leading to trans- isomer has a severe steric interaction which is absent in that leading to the cis.

Another case where the coplanar concerted model appears to run afoul of experiment is the bicyclo[3.2.0]heptyl system (eqn 62), in which primary and secondary Grignard are formed in a ratio of 63:61 = 10:1. Conformational factors seem to lead to puckered four- and five-membered rings in this bicyclic system [219,220]. However, an approximately planar transition state structure leading to 63 can be achieved without much bending of valence angles. It appears to be little less favorable than that from the 1-cyclobutylethyl Grignard. On the other hand, it is impossible to achieve anything approximating a planar arrangement for cleavage to 61. Yet as much as 10% of the product is formed by this route. In contrast, only 1% of the product from 2-methylcyclobutylmethylmagnesium chloride is the secondary Grignard (eqn 53), where it is possible to obtain an "optimum" planar transition state.

Another result which is troublesome to explain via the planar concerted mechanism is the relative rate of ring closure reactions to three- and four-membered rings. As pointed out previously (section IVB.6.a) the transition state in the cyclopropylmethyl case must be less strained than in the cyclobutylmethyl. The rate of ring closure in the former is more rapid by 10^4 to 10^5, and much of the difference arises from a lower activation energy. However, examination of models suggests that a greater distortion of valence angles is necessary in the former case to reach a roughly rectagular planar configuration. (Some cyclization

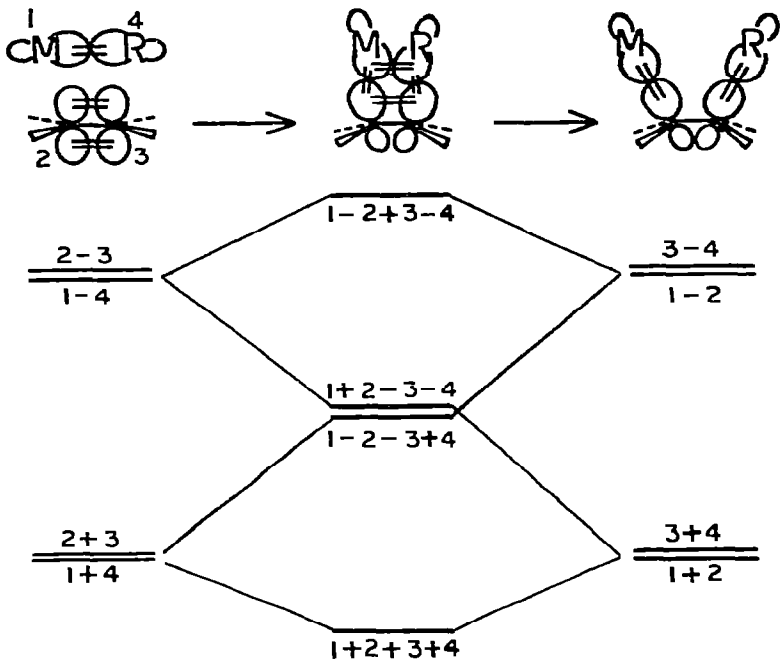


Figure 2(a)

Figure 2. Orbital correlation diagrams for concerted four-centered addition reactions. (a) Reaction utilizing only four orbitals. (b) Reaction utilizing p-orbital on metal. (c) Reaction via π-complex. Scale used for diagrams assume all atomic orbitals have equal coulomb integral; all bonds of starting material and products have equal resonance integral β; all partial bonds of transition state and π-complex have resonance integral 0.75 β.

reactions occurring by internal nucleophilic displacement proceed with a lower activation energy for formation of a four- than a three-membered ring [221,222].)

It is likely that some of the stereochemical objections to a planar concerted mechanism might be relieved in a four-center transition state with some other preferred geometry. Further

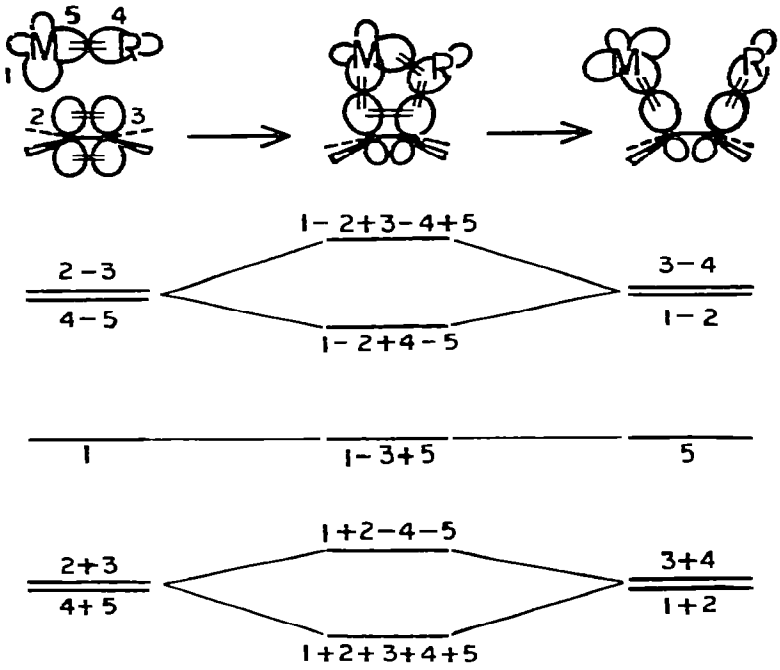


Figure 2(b)

consideration will be given to this possibility in the next section.

Another potential difficulty with the concerted four-center mechanism arises from orbital symmetry considerations. Formally, the mechanism is a $[_{\sigma}2_s + _{\pi}2_s]$ cycloaddition, forbidden by orbital symmetry [223-226]. On this basis, it has been asserted that the hydroboration of alkenes cannot follow such a mechanism, and must instead involve an intermediate π-complex [227] (see next section). An orbital correlation diagram, as in figure 2a, is helpful in discussing the situation, utilizing the approach described by Zimmerman as "MO Following" [228]. In the idealized situation, consisting of a square array of atomic orbitals with identical electronegativities and equal resonance integrals around the ring, the anti-aromatic "cyclobutadiene-like" set of orbitals is

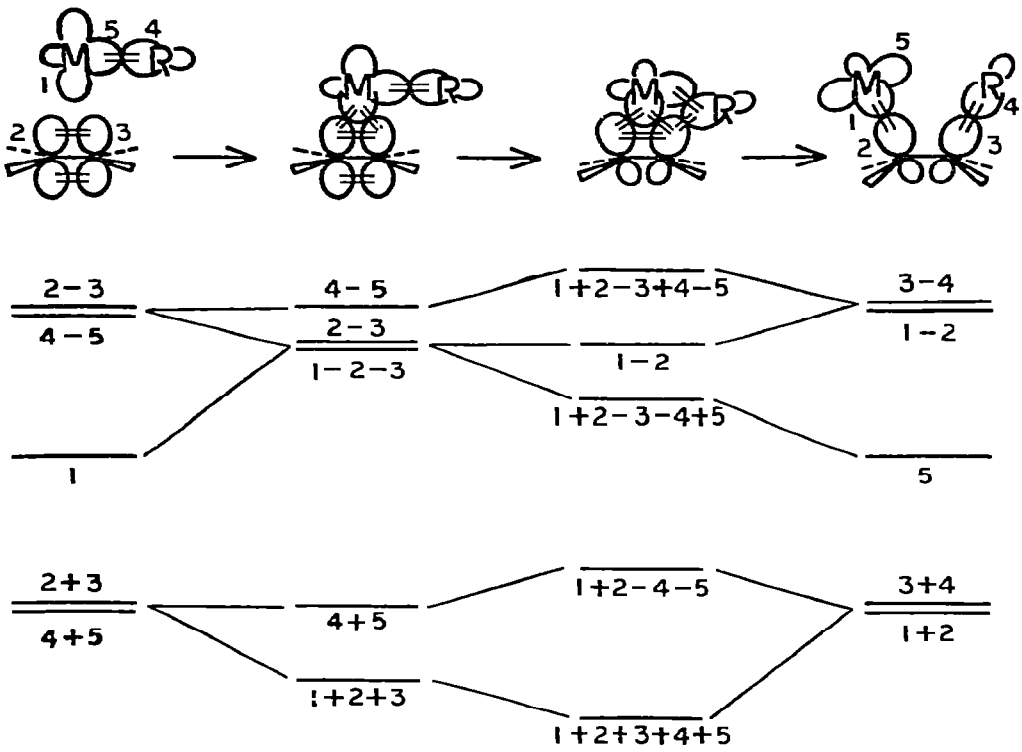


Figure 2(c)

generated in the transition state. In this view, only the orbitals of the π-bond and of the M-R σ-bond are involved. The energy barrier rendering the reaction "forbidden" results from the necessity of placing an electron pair into one of the degenerate orbitals located at the nonbonding level. Symmetry considerations dictate also that the transition state orbital in which this electron pair is placed correlates with a bonding orbital of the reactants, but with an antibonding orbited product [223]. Rigorous preservation of orbital symmetry through the addition would lead to formation of product in a doubly excited electronic state. It is generally considered that electron interaction will prevent crossing of the electronic states and allow correlation of ground state with ground state [223,227,229]. Yet, a substantial activation barrier persists.

If the transition state is less symmetrical, the center levels are split apart, lowering the activation barrier [228,230-232]. Such splitting occurs, for instance, when the reaction is made polar by altering the electronegativity of one or both of the atoms being added, or when the bonds differ in strength. The common view appears to be that such electronic distortions do not usually remove the "forbiddenness" to a sufficient extent that the formally forbidden pathway becomes the preferred one [223]. However, it has recently been proposed that concerted [$2_s + 2_s$] processes are important in a number of <u>polar</u> addition reactions for just this reason [231,232].

Another way in which the [2 + 2] cycloaddition may become allowed is if it is "antarafacial" in one of the components [223]. In the present case of addition of an M-R bond to a carbon-carbon double bond, this could be satisfied by <u>trans</u> addition to the double bond ($[_\sigma 2_s + _\pi 2_a]$), or inversion of configuration at either M or R ($[_\sigma 2_a + _\pi 2_s]$).* Physically, either possibility may be sterically prohibitive. However, examination of models does suggest that such a mechanism (with inversion at carbon) could explain the preference for <u>trans</u> product noted above in cyclization to the cyclopentylmethyl Grignards (eqn 93).

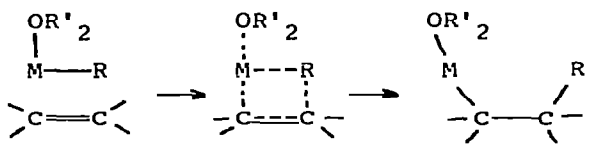
A more realistic transition state model utilizing a vacant metal p-orbital is illustrated in figure 2b. A similar possibility has been considered for hydroboration [231,233]. The set of orbitals generating the transition state is a linear rather than a cyclic array, since the two metal orbitals involved (p and the hybrid orbital used for the M-R bond) are necessarily orthogonal. The transition state MO's are now formalistically the orbitals of

---

* In the special case of metal hydride addition (hydroboration), inversion is, of course, impossible at the hydrogen.

the pentadienyl cation, with the two end atomic orbitals being the two metal orbitals. A smooth transition occurs from starting materials through transition state to product; in particular, the higher filled orbital is bonding throughout, and its nodal form represents an intermediate stage between starting state and product orbitals.

A possible difficulty with this interpretation may be that, in ether solvents, we expect magnesium to be tetra-coordinated, using up all low energy orbitals. It might be necessary to free an orbital to interact with the double bond, either by loss of a solvent molecule in a prior equilibrium, or by partial displacement or weakening of coordination in the transition state:

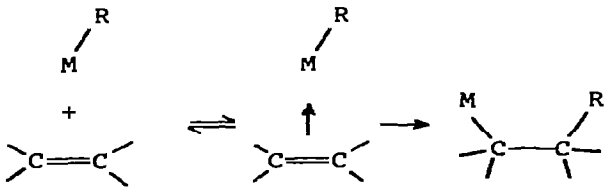


This question has been considered in hydroboration [233], in alkyl group exchange reactions [234], and is known to be an important factor in the reactivity of organoaluminum compounds (see, for example, [235,236]).

It thus appears that orbital symmetry concerns are not prohibitive of the concerted four-center mechanism, though some modification from the simplest model for such a mechanism may be preferred, and geometries other than a coplanar array of reacting atoms might be considered.

4. The π-complex mechanism

Related to the four-center mechanism is one that involves a π-complex intermediate, formed by interaction of the olefinic π-electrons with the metal. Rearrangement of the π-complex would probably be rate-determining.



Again, proposal of such a mechanism has ample precedent in organometallic chemistry. A π-complex mechanism was proposed to account for a stereochemical [237] and other [238] results in the hydroboration of alkenes, and was considered to be consistent with orbital symmetry restrictions [227]. A variety of kinds of evidence in the addition of triphenylaluminum to alkynes have been considered in accord with a π-complex mechanism, in which electrophilic attack by the aluminum is the dominant feature [239,240]. Nmr evidence for such a complex has been reported [241]. For the gas-phase addition of trialkylaluminum compounds to ethylene, it was concluded that kinetic parameters required π-complex formation before conversion to products via a four-center transition state [242]; later data were interpreted to favor a direct one-step mechanism [243]. Ethylene coordination to an alkyllithium tetramer was considered a likely stage in addition [244]. The accepted mechanism for alkene polymerization by Ziegler-Natta catalysts appears to involve coordination of alkene to the transition metal component of the catalyst, followed by rearrangement which effectively inserts the alkene into a carbon-transition metal bond [215-218,245,246]. π-Complex intermediates appear also to be involved in decomposition of transition metal alkyls via metal hydride elimination [247] and insertion of alkenes into a transition metal-carbon bond [248]. In a review of π-complexes as reaction intermediates [249], the distinction between well defined and stable transition metal-olefin π-complexes, and weaker "molecular complexes" has been

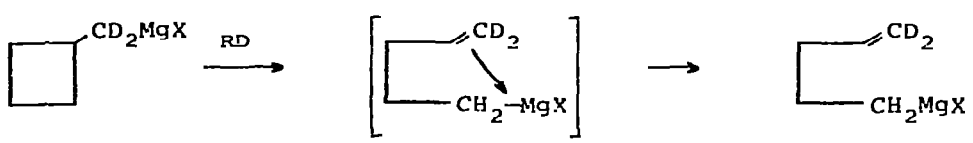
noted. It was concluded that there is little evidence justifying such intermediates except in the case of transition metals, where π-bonding from filled metal d-orbitals to vacant olefin π*-orbitals provides additional stabilization. However, it might be noted that SCF calculations on a methyl-titanium-ethylene complex taken as a model for the intermediate in polymerization suggest little or no dative back-bonding from titanium to ethylene [250], of the sort generally considered to stabilize transition metal π-complexes.

Discussion of the π-complex mechanism might well begin with a continuation of the orbital-following considerations from the previous section. Figure 2c follows orbital changes in proceeding from metal alkyl plus olefin to π-complex to product. The formation of π-complex occurs readily with no complication. In the transition from π-complex to adduct, the orbitals are formally those of the vinylcyclopropenyl cation [251]. This π-system has two low-energy orbitals of nodal form that appear to provide smooth evolution through the course of the reaction. It may be noted in passing that in the previously mentioned calculations on a methyl-titanium-ethylene complex [250], migration of the methyl from titanium to an ethylene carbon occurs smoothly, without loss of binding to the metal in the process. In that case, however, the metal-alkyl bonding utilizes principally metal d-orbitals for σ-bond formation, and transfer of the alkyl group from metal to carbon appears to be facilitated by the presence of an additional vacant d-orbital on the metal (which is out of the consideration for the lighter elements).

We would like to note at this point that the transition state configuration shown in figure 3c for rearrangement of the π-complex to product could be achieved directly from olefin plus metal, without the necessity of a π-complex as a potential <u>minimum</u> along

the reaction coordinate. This corresponds to a direct, one-step, four-center addition process very similar to that described earlier. The significant difference is that we now allow direct interaction of the metal with both olefinic carbon atoms in the transition state, instead of only one. Such interaction would be maximized by approach of the metal atom toward the mid-point of the alkene π-bond, at the expense of some loss in interaction of the M-R σ-bond with the olefin. This might be referred to as a concerted mechanism with "π-complex character." Even in an "approximately square" planar four-center transition state, some interaction of the metal orbital with the second olefinic p-orbital should be present as a second-order stabilizing effect, although overlap might be fairly slight. From this vantage point, the four-center and π-complex mechanisms may be viewed as extremes in a spectrum of similar mechanisms, varying in the degree of overlap and strength of bonding between the metal atom and second end of the carbon-carbon π-bond.

The π-complex mechanism for the Grignard rearrangement was originally suggested as a possible explanation for two experimental observations on the ring-cleavage rearrangement of the cyclobutylmethyl Grignard [129]. First, the kinetic α-deuterium isotope effect for the rearrangement of 90 is unity, within experimental error. In reactions where as sp^3 carbon is changing hybridization



90

to sp^2, the isotope effect k_H/k_D is frequently in the vicinity of 1.1 per deuterium [252-254] in a variety of reactions ranging from carbonium ion, through radical and concerted, to carbanion. There

is also an equilibrium isotope effect $k_H/k_D < 1$ for formation of iodine- or transition metal ion-olefin π-complexes [255,256]. If the rate-determining step of the cyclobutylmethyl Grignard cleavage is formation of the π-complex, the isotope effect on π-complex stability might compensate the expected isotope effect for $sp^3 \rightarrow sp^2$ hybridization change, leading to the observed value of approximately unity. However, recent results on the equilibrium isotope effect on Grignard reagent stability (see section IVB.7) indicate that $-CH_2MgX$ is affected in the same direction as $=CH_2$ by deuterium substitution. Hence, a smaller effect (or perhaps none at all) should result from this compensation, and the isotope effect results may not provide any support for a π-complex.

The second observation was the formation of cis- and trans-isomers in equal amounts in eqn 52 (R = CH_3). It might be expected that the more stable trans isomer should be formed preferentially, as in the pyrolytic cis-elimination from 2-butyl acetate, where the product ratio of 2:1 in favor of trans approximates the equilibrium mixture [257,258]. cis-Alkenes generally have larger equilibrium constants for formation of π-complexes than trans [255,256]. Formation of cis- isomer of the Grignard, in excess of the equilibrium proportion, could result if the transition state leading to that isomer is preferentially stabilized by the same factors that stabilize the π-complex of cis-alkenes. However, trans:cis ratios within the group of related E-2 eliminations of 2-alkyl derivatives vary from greater than the equilibrium value to less than unity as structures and conditions are changed [259]. Since it is not clear precisely what stereochemical result should be expected in the absence of a π-complex, the observed stereochemistry does not provide convincing evidence in favor of one.

There does appear to be experimental evidence for intramolecular interaction of an olefinic double bond with a non-transition metal organometallic function. The first such evidence was from spectroscopic studies on 3-butenyllithium, $CH_2=CHCH_2CH_2Li$ [260,261]. The nmr spectrum showed downfield shifts of olefinic resonances relative to 1-butene when studied in cyclopentane or benzene solution, but these absorptions were shifted back to higher field on addition of dimethyl ether. Shifts to low frequency were observed in the infrared C=C stretch and vinyl deformation modes, and evidence was also noted in the ultraviolet. Similar indication of interaction was found in nmr and ir spectra of unsaturated alkylaluminum compounds 106 (n = 3) [262]. cis-106 (n = 3; R = CH_3) was found to be monomeric. When

$$RCH=CH(CH_2)_nAl(i\text{-}Bu)_2$$

106

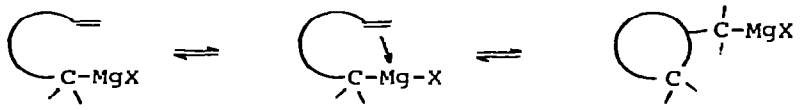
R = H, CH_3

the aluminum is further removed from the double bond, or when ether is the solvent, spectroscopic evidence does not indicate interaction [162,262]. Shifts in the nmr attributed to metal-double bond interaction have also been reported for di-(4-pentenyl)zinc, $(CH_2=CHCH_2CH_2CH_2)_2Zn$; interaction appears to be reduced by addition of 2,2'-bipyridine. The results were interpreted in terms of weak dipole-dipole interaction, rather than a stable π-complex [263,264].

Interaction of magnesium with a double bond may also be indicated, although it has not been specifically studied or thoroughly documented. In several cases, we have observed the olefinic hydrogens of unsaturated Grignard reagents at lower field in the nmr spectra than those of the hydrocarbon obtained

by hydrolysis of the Grignard, even though those observations were made in ether and THF solutions, which should complex effectively with the magnesium.

If the mechanism of Grignard cyclization is represented by eqn 94 (with a π-complex either as a reaction intermediate or as a configuration along the reaction coordinate close to the

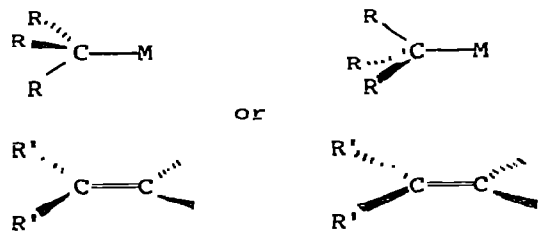


(94)

transition state), electrophilic interaction of magnesium with the double bond might show up in electronic substituent effects on the reaction rate. A number of reactions of substituted styrenes which may involve π-complex intermediates or electrophilic interaction of a metal with the double bond have ρ-values ranging around -1±0.5 [115]. The addition of triphenylaluminum to substituted diphenylacetylenes is favored by electron-releasing substituents [265]. Combination of rate results with data on product distribution suggest that electrophilic attack by the metal is important in that reaction. In the two instances where similar information is available on the electronic effect of aryl substituents on the Grignard cyclization (see section IVB.6.c), the small positive ρ-value indicates that the nucleophilic component of attack on the double bond dominates in determining the substituent effect.

In the preceding discussion of the concerted mechanism, it was pointed out that several experimental findings may be inconsistent with a planar transition state. If the reaction mechanism involves initial approach of the metal to the double bond, followed by shift of the alkyl group, there would seem to be less of a requirement for a coplanar geometry. Indeed, this

mechanism might be preferred generally on steric grounds, since it may be seen in 107 that the coplanar approach for a concerted



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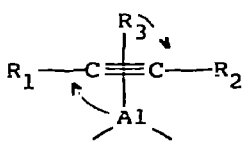
addition will produce interactions between the adding alkyl group and groups attached to the double bond. Eisch has previously proposed that the addition of aluminum derivatives to alkynes may involve the perpendicular geometry of 108 in the initial



108

interaction of reactants, with the reaction coordinate consisting partly of the torsional motion shown. This description of the mechanism comes very close to a π-complex or a π-complex-like transition state. Examination of models suggests that a reaction coordinate tending toward such a non-planar geometry would probably reconcile the stereochemical questions raised earlier. Indeed, as shown in figure 3, the bicyclo[3.2.0]heptyl--cycloheptenyl conversion (eqn 62) may be forced to pass through the perpendicular configuration.

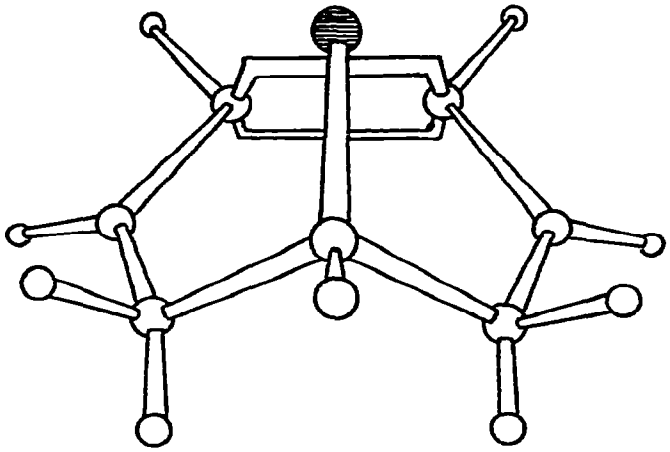


Figure 3. Conformation of cyclohepten-5-yl organometallic. Metal atom is shaded. Solvation and other coordination on metal is omitted.

5. Concentration effect and reaction mechanism

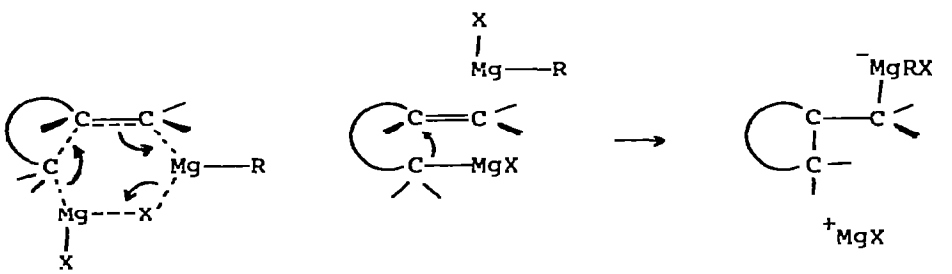
It was noted previously (see section IVB.2) that the rate of a number of Grignard rearrangements increases markedly at higher concentrations. The rate change, in which the high concentration rate seems to be roughly second order (first order each in total Grignard and in unrearranged alkyl group), may imply a change in mechanism at higher concentrations.

Maercker [90] has proposed that "ate-complexes" [267] may be involved at high concentrations (eqn 95). It is not unlikely that one of the species in this equilibrium should have a higher

$$RMg^+ + RMgX_2^- \rightleftharpoons 2\ RMgX \rightleftharpoons R_2MgX^- + MgX^+ \qquad (95)$$

reactivity than the RMgX molecule (whether by the same, or by a different mechanism). If these species exist as ion pairs, the second-order rate dependence would be explained. Alternatively,

the rate increase at higher concentration could reflect a larger concentration of ionic species at the higher dielectric constant known to exist in concentrated Grignard solutions. Another possibility is an actual bimolecular rearrangement step, of which possibilities are shown in 109 and 110 (note that 110 must involve an "ate" complex at some stage [114]).



109 110

The ions of "ate-complexes" have generally been invoked to explain electrochemistry and electrical conductivity of Grignard solutions [268,269]. There is also experimental evidence for complexes of the type $Li^+R_3Mg^-$ produced by interaction of organolithium and dialkylmagnesium compounds [270].

At present, there does not appear to be any evidence to make fruitful a further discussion of possibilities for a high concentration mechanism. (As indicated earlier in section IVB.5, catalysis by transition metal impurities could also lead to second-order rate dependence.) Except for the rate increase, other characteristics of the reaction (such as substituent effects) do not show any obvious differences with concentration. For this reason, our discussions above have not considered a bimolecular mechanism for the rearrangements, and we have implicitly assumed that the mechanism at high concentration is not fundamentally different in nature from that at low

concentration. However, this is an area of uncertainty at the present time.

6. Summary

From the foregoing discussion, we would like to summarize conclusions relating to the mechanism of Grignard cyclization-cleavage rearrangements. The carbanion and radical mechanisms seem wholly inadequate to rationalize the substituent and solvent effects on rearrangement rate. They should probably be discarded completely, except, perhaps, for reactions occurring under forcing conditions. The electron-transfer (or more properly, magnesium-transfer) mechanism may be consistent with most of the data. However, it encounters very serious problems with cleavage of the 2-methylcyclobutylmethyl Grignard, and may have to be discarded for this reason. The concerted mechanism, more or less by default, seems best able to account for experimental results, provided non-coplanar variations are considered. Finally, although there is no evidence which requires a π-complex mechanism, the non-planar concerted mechanism may be nearly indistinguishable from it. Furthermore, there is ample indication that at least weak intramolecular interaction between a double bond and a non-transition metal group may occur.

7. Relationship to intermolecular additions of Grignard reagents to carbon-carbon multiple bonds

In previous sections of this review, it has been noted that the most prominent rearrangements of organomagnesium compounds consist of intramolecular cyclization by addition to a multiple bond, or the cleavage reaction which is the reverse of the cyclization. These intramolecular processes also have their

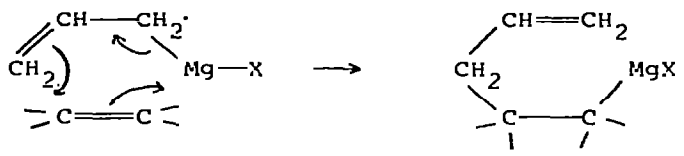
intermolecular analogs, which have become much more prominent in the past few years.

While additions of organolithium and -aluminum compounds to ethylene and other alkenes have been well established for some years [271], additions of organomagnesium compounds to unconjugated double bonds do not occur readily [272], and the first examples have been observed only recently. In 1970, Lehmkuhl first reported that allylic Grignard reagents add to ethylene and 1-alkenes [273]. In subsequent work, additions of isopropyl, tert-butyl and benzyl Grignard reagents were studied, and norbornene and norbornadiene were found to undergo additions [157,135,136]. Grignard reagents have also been added to the strained double bond of cyclopropenes [274]. Processes have been patented for adding secondary, tertiary, and allylic Grignard reagents [275] and diallylmagnesium compounds [276] to ethylene and other alkenes, and for aligomerizing ethylene by treatment with a primary Grignard at high temperature and pressure [277]. 1-Butene, formed in the pyrolysis of ethyl Grignard, is believed to be formed by addition to the ethylene generated in the reactions [278].

No mechanistic studies of the intermolecular reaction have been reported. However, it is observed qualitatively that the reactions are faster using ether-free Grignard in a non-basic solvent than with an ethereal Grignard solution. The solvent effect on addition rates appears to follow the order THF < ethyl ether < isopropyl ether. By analogy with additions of organo-aluminum and -lithium compounds, a cyclic, four-center mechanism, perhaps involving a π-complex, might be imagined. There does not appear to be an obvious reason for believing that intramolecular and intermolecular additions occur by different processes.

For the allylic Grignard, whose additions are particularly

facile and occur predominantly with "inversion" of the allylic groups, a six-center cyclic mechanism has been proposed [157].



(On the other hand, as noted previously in this review, the analogous six-center mechanism for addition of allylic Grignard reagents to carbonyl compounds has been seriously criticized.) A similar cyclic mechanism has been proposed also for an intramolecular addition of an allylic Grignard [156] (see section IVA.4), and is consistent with the observed stereochemistry, and the lack of catalysis by magnesium bromide. The facile addition of dicrotylzinc to alkenes has recently been reported [279].

Another principal class of additions, also recently discovered, involves addition to allylic or propargylic alcohols [190,191,280, 281] and other alkenes containing basic groups [282,283]. These additions, too, are most facile with allylic Grignard reagents, but have been observed in certain instances with benzylic [190,280], vinyl [191,281,284], or tertiary [190] ones. They occur much more readily than the additions just discussed, where the basic group is lacking. Additions of lithium reagents (allylic and otherwise) [285-289] and allylic zinc reagents [282,290,291] to carbon-carbon double and triple bonds are also facilitated by polar groups in allylic or more distant positions.

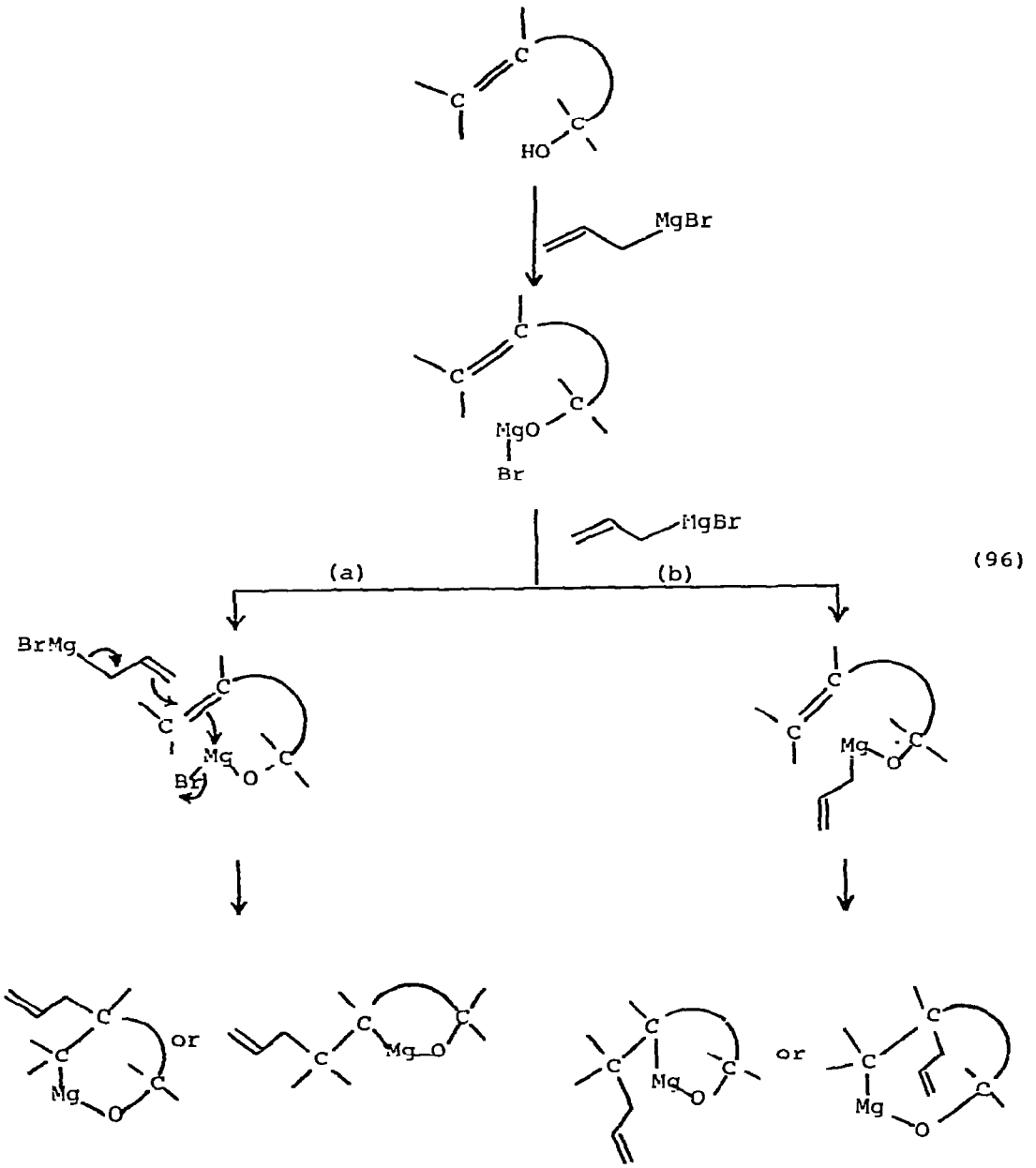
There does <u>not</u> appear to be a consistent trend in reactivity, orientation, or stereochemistry running through all of these reactions, which would imply a common mechanism for all situations. However, coordination of the magnesium (or other metal) to the basic functional group would seem to be a prerequisite for any

mechanism. Two general varieties of mechanism which have been discussed are illustrated in eqn 96 for an unsaturated alcohol reacting with allylmagnesium bromide. Variations within these might be envisioned, ranging from concerted four- or six-center to radical, carbanion or electron-transfer processes. With an ether, thioether or tertiary amine, simple coordination (rather than salt-formation) with the basic group would occur. These additions, particularly those *via* mechanism b, may be thought of as intramolecular additions. In various cases, both of these mechanisms have been supported by experimental evidence including stereospecificity, regiospecificity, and kinetics [292], and it appears that the mechanism may depend upon the particular system. It seems that a close mechanistic relationship between the organomagnesium rearrangements and the additions to allylic alcohols and related compounds is not demonstrated.

A number of cases are also recorded of facile addition of Grignard reagents to vinyl derivatives, such as vinyl silanes [293], halogenated alkenes [294-296], and vinyl organometallic compounds [297]. However, there appears to be little evidence available to permit any mechanistic comparisons.

V. RADICAL REARRANGEMENTS IN ORGANOMAGNESIUM FORMATION AND REACTION

Previous segments of this review have been concerned with rearrangements of organomagnesium compounds--that is, rearrangements in which one organomagnesium compound is converted to another. In a number of additional cases, rearrangements have been noted during the process of forming a Grignard reagent, or during the reaction of the organometallic with some other reactant. In most instances, these appear to be free radical reactions, and the observation of



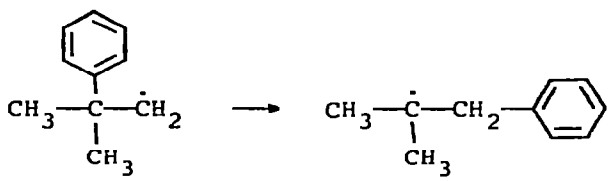
(96)

rearrangement has on occasion been used as supporting evidence for the radical nature of the reaction. In this portion of the review, rearrangements so observed will be summarized. However, there will not be an attempt to present a comprehensive survey of either

radical reactions of Grignard reagents or rearrangements of free radicals.

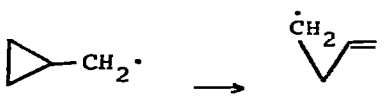
A. Radical Rearrangements

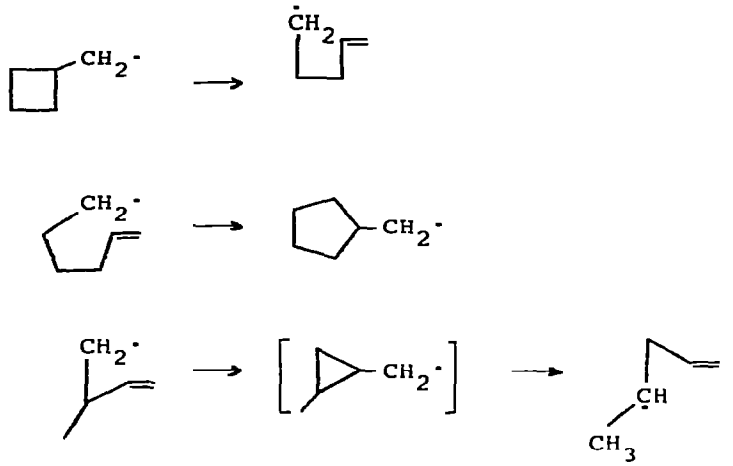
As in "carbanion chemistry," rearrangements also are quite limited in variety in radical chemistry [298,299]. Generally, the rearrangements found parallel quite closely those of "carbanions." 1,2-Shifts are important only when the rearranging group is aryl (or a heteroatom group). These likely occur *via* intramolecular radical addition to the aromatic ring. The prototype of these rearrangements is that of the neophyl radical **111** [300,301]. Intramolecular hydrogen-abstractions from more remote positions have been observed.



111

The other major class of radical rearrangements comprises ring cleavages, and their reverse, intramolecular additions to a double bond. Some simple cases observed include cleavage of the cyclopropylmethyl [302], and cyclobutylmethyl [303] radicals, cyclization of the 5-hexenyl radical [304,305], and apparent vinyl group rearrangements which have been shown to occur *via* an addition-cleavage sequence [306]:





B. Rearrangements During Grignard Reagent Formation

Evidence from a number of sources strongly suggests that free radicals are involved in the process of Grignard reagent formation [307-309], though there may yet be some question as to whether an alternative competing pathway exists which avoids the intermediacy of radicals. Along with the Grignard reagent, reactions of organic halides with magnesium generally produce hydrocarbon by-products in varying amounts, which may be formally derived by dimerization and disproportionation of radicals, or by their abstraction of hydrogen from solvent. One form of a radical mechanism for Grignard formation is shown in eqn 97; the radical anion of the alkyl halide is shown as an intermediate, but might

$$RX \xrightarrow[Mg]{e^-} [RX\cdot^-] \longrightarrow R\cdot + X^- \xrightarrow{Mg} RMgX \qquad (97)$$

$R\cdot \rightarrow$ by-product

not have a finite lifetime. Evidence has been presented that electron-transfer is rate-determining [309]. Radical precursors to by-products might be free, or bound in some fashion to the

magnesium surface. A number of elaborations and variations from this scheme have been discussed in relation to experimental evidence.

If the radical has sufficient lifetime before further reduction to Grignard reagent or reaction to yield by-products, it may, if suitably constituted, rearrange. One of the first-noted cases of rearrangement products was in preparation of the Grignard reagent from neophyl chloride [310]. Rearranged hydrocarbon by-products were formed in amounts ranging from 1 to 6%, in addition to Grignard reagent (eqn 98). The amount of rearrangement

$$C_6H_5\text{-}\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}\text{-}CH_2Cl \xrightarrow{Mg} C_6H_5\text{-}\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}\text{-}CH_2MgCl + C_6H_5C(CH_3)_3 +$$

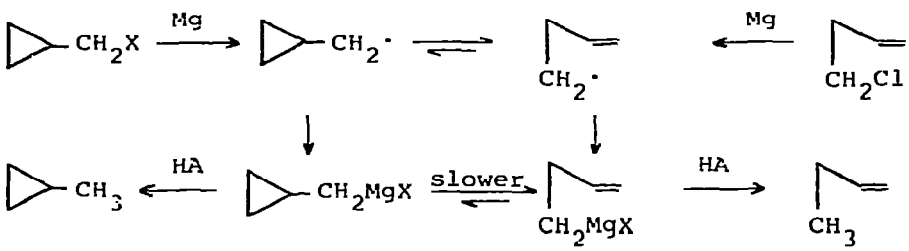
$$C_6H_5CH_2CH(CH_3)_2 + C_6H_5CH{=}C(CH_3)_2 + C_6H_5CH_2\dot{C}(CH_3){=}CH_2 + \text{dimers} \quad (98)$$

was not consistently affected by magnesium purity or by the addition of catalytic amounts of cobalt(II) chloride. The Grignard formed appeared to be entirely unrearranged, though indications of less than 1% of rearranged Grignard were obtained in other work [311]. About 5% of rearranged organometallic is formed in the preparation of neophyllithium [312].

In a number of systems where Grignard rearrangements have been studied, rearrangement during formation of the Grignard was also noted. As indicated above (section IVA), it is uncertain in some cases whether rearranged products result from rapid Grignard rearrangement, or from rearrangement during formation. We will note here only those instances where rearrangement clearly is shown to occur <u>during</u> Grignard formation.

When cyclopropylmethyl halides were allowed to react with

magnesium in ether containing an acid [80], between 4 and 33% of the hydrocarbon product was methylcyclopropane (along with 1-butene from ring-opened Grignard). The amount depended upon the halogen and the reaction conditions. When the acid was added <u>after</u> Grignard formation, less than 0.1% of methylcyclopropane was formed. In dimethyl ether, the cyclopropylmethyl Grignard cleaves slowly, but still the methylcyclopropane never exceeded 55% of the product. It was concluded that substantial amounts of ring-cleaved Grignard are formed directly from the halide, presumably <u>via</u> free radical cleavage (eqn 99). Preparation of



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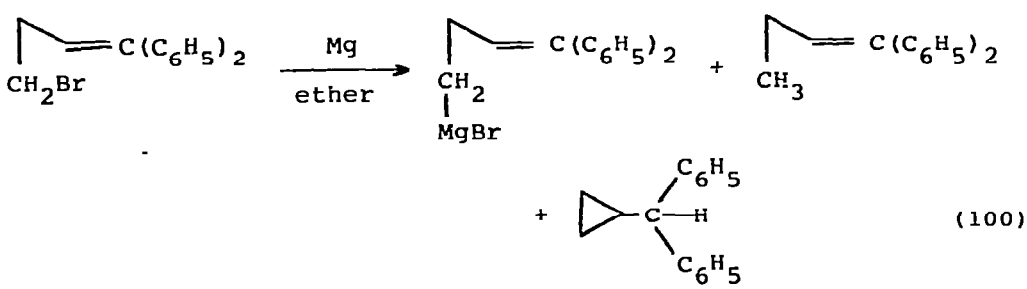
Grignard from 4-chloro-1-butene in the presence of acid yielded traces of methylcyclopropane.

Several percent of cyclopropane products also appear to be formed in eqn 100. However, reaction of the Grignard solution with



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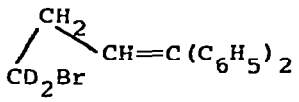
carbon dioxide, mercuric bromide, or D_2O gave entirely open-chain derivatives, indicating that the hydrocarbons are generated during Grignard formation. It was reported that the Grignard prepared

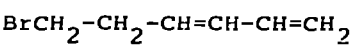
from deuterated bromide 112 had undergone complete equilibration



112

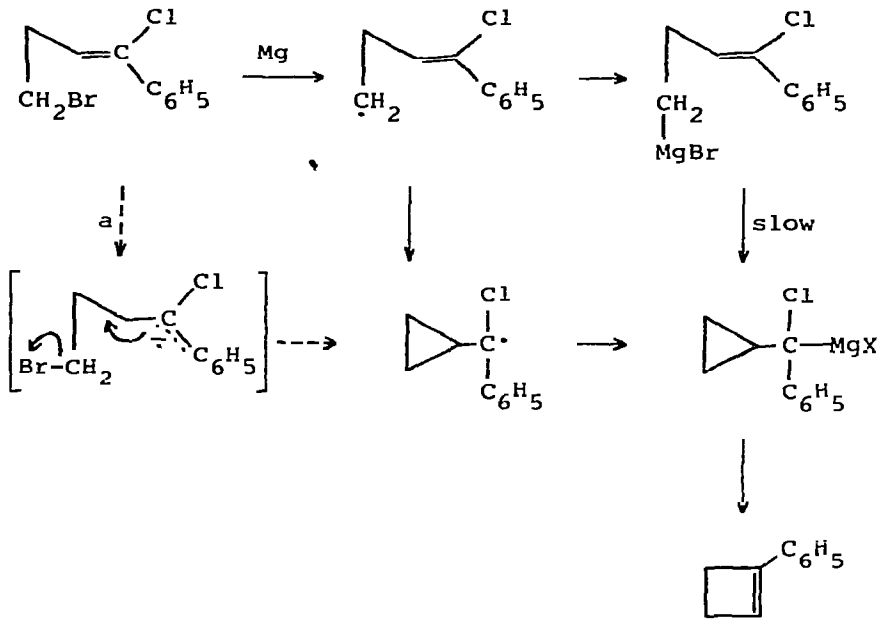
of methylene groups by the time of first observation, and was concluded from this that the phenyl groups enhance the rate of ring closure of the Grignard. It now appears [92] that the equilibration was probably during, rather than after, formation of Grignard.

Monomeric and dimeric hydrocarbons containing cyclopropane rings are produced in Grignard formation from 113 [103]. These appear to have a similar origin in free radical intermediates in the Grignard formation process.



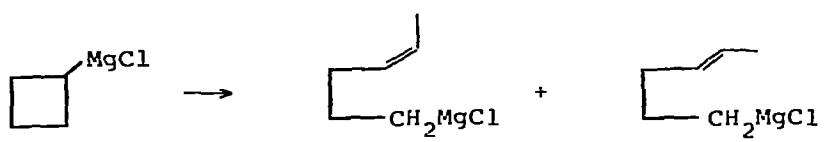
113

Another instance in which free radical intermediates during Grignard formation appear to lead to rearranged product is in the reaction of 4-bromo-1-chloro-1-phenyl-1-butene with magnesium [108]. Phenylcyclobutene is generated only slowly on heating of the Grignard, yet it is a major product produced during the Grignard formation. The following mechanism for its formation was proposed:



An alternative mechanism (indicated above by path a), proceding via intramolecular nucleophilic displacement in the radical anion of starting material, was considered less likely.

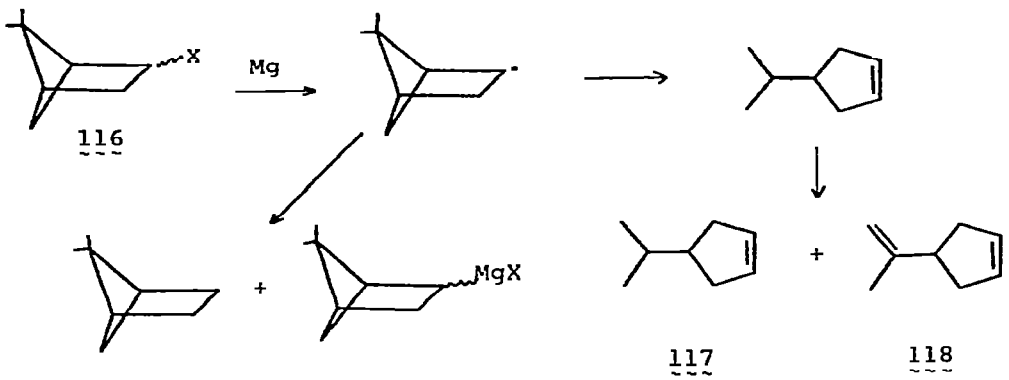
Radical cleavage of a four-membered ring during Grignard formation has also been observed. The Grignard reagent from 1-cyclobutylethyl chloride cleaves to form an approximately 1:1 mixture of Grignard reagents 114 and 115. When the Grignard



114 115

reagent was prepared in ether, about 10-20% of the Grignard had rearranged structure immediately on formation [138]. Interestingly, this was almost exclusively cis in configuration at the double bond. Preparation of Grignard reagents from 116 (X = Cl, Br) led to

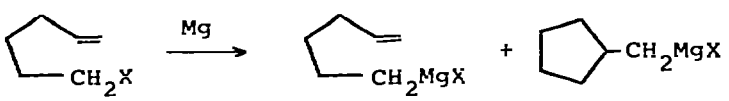
substantial amounts of hydrocarbon by-products [137]. These included 4-isopropylcyclopentene (117) and 4-isopropenylcyclopentene (118) as major components. It may be noted that cleavage



116 117 118

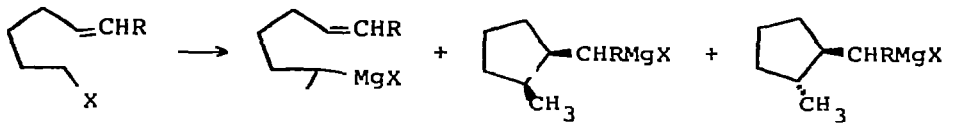
of the cyclobutane occurred in the direction to lead to a tertiary radical. Cleavage of the Grignard, once formed, involves only the alternative ring bond, yielding the primary Grignard.

Radical cyclization to form a cyclopentane ring during Grignard formation is also observed. Grignard reagent formed from 6-halo-1-hexenes is about 5% cyclized (eqn 101), with



(101)

further cyclization occurring very slowly at the same temperature [147-151]. CIDNP signals observed during formation of this Grignard are considered to indicate radical pairs, particularly in formation of the cyclized Grignard [313]. Cyclization to a cyclopentane ring observed in more highly substituted cases leads to an interesting stereochemical result, as shown in eqn 102 [92,148]. Cyclization during formation gave more cis-isomer than trans. However, subsequent cyclization of formed Grignard produced almost entirely the trans-isomer. A similar preference for cis-produ has been reported in a well characterized radical cyclization [314].



(102)

R = H, CH_3, C_6H_5 major minor

C. Rearrangements During Reactions of Organomagnesium Compounds

Although organomagnesium compounds do not appear to undergo ready homolytic cleavage to free radicals, a number of their reactions do appear to involve free radicals. In most cases, radical generation appears to result by electron-transfer from the organomagnesium compound to a reagent capable of accepting an electron. Rearrangement of the radical from the Grignard is expected for suitably constituted radicals, provided their lifetime is sufficiently long.

Most of the rearrangements that have been reported have been found in autoxidation of Grignard reagents. This reaction is believed to occur via a free radical chain mechanism:

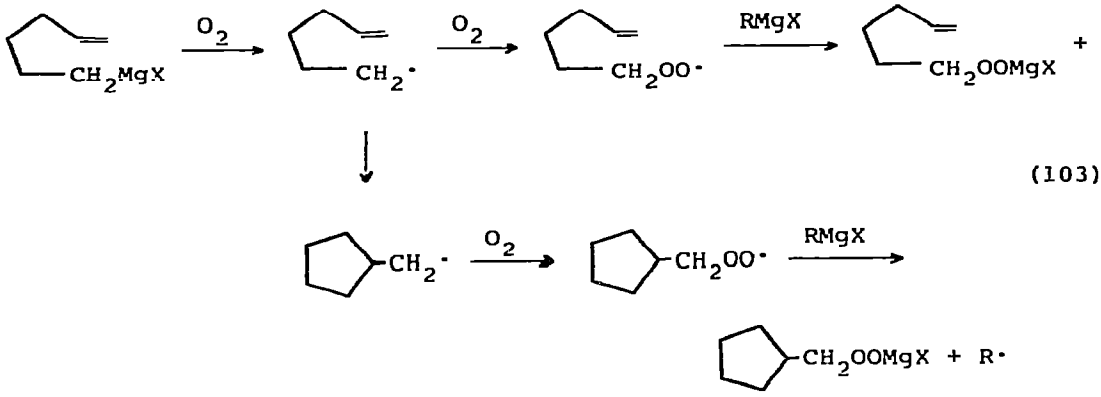
$$RMgX \xrightarrow{O_2} R\cdot \quad \} \text{ initiation}$$

$$R\cdot + O_2 \longrightarrow ROO\cdot$$

$$ROO\cdot + RMgX \longrightarrow R\text{-}OOMgX + R\cdot \quad \Big\} \text{ chain process}$$

$$ROOMgX + RMgX \longrightarrow 2\ ROMgX$$

Details of the initiation are uncertain. A carefully studied case [149,315] involves cyclization to cyclopentylmethyl (eqn 103). Carbonation, hydrolysis, and oxidation with di-t-butyl peroxide all lead to about 5% of cyclic product, resulting from Grignard cyclized during formation. However, oxygenation of the Grignard gave up to 40% of cyclic product. The amount of cyclization

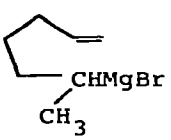


(103)

increases with decreased oxygen concentration, as expected from the mechanism shown, in which there is competition between cyclization and reaction of the radical with oxygen. The last step of the autoxidation, reaction of peroxide salt with more Grignard, apparently does not involve free radicals, so that observation of 40% of cyclic product implies nearly 80% of cyclization of the 5-hexenyl radicals. The results are not consistent with a cage radical process as a major pathway for oxidation:

$$RMgX + O_2 \longrightarrow \overline{R\cdot + \cdot O_2MgX} \longrightarrow ROOMgX$$

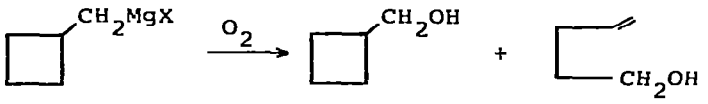
The radical rearrangement is not rapid enough to compete with cage processes [185,316], and the dependence on oxygen concentration would not be predicted. Interestingly, no cyclic product was found in the oxygenation of 119 [317].



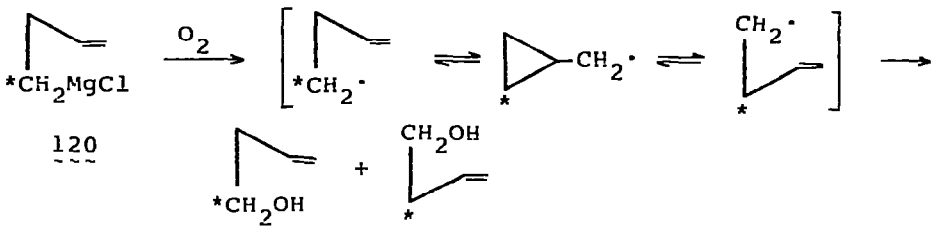
119

Rearranged products have been noted in other Grignard

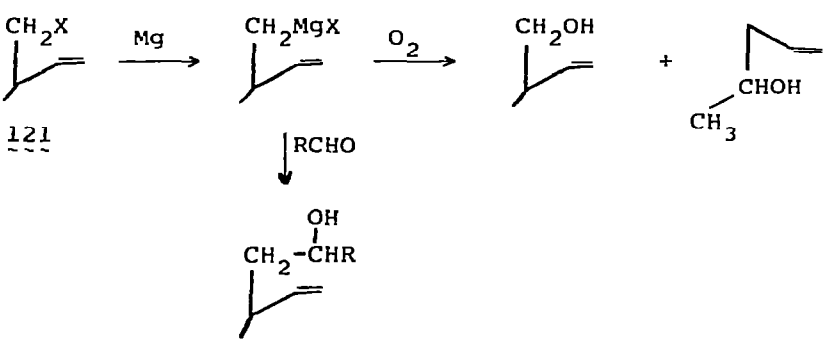
oxygenations. Up to 12% of ring-cleaved product was found in oxygenation of the cyclobutylmethyl Grignard [184]:



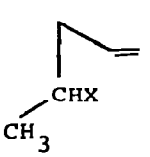
In several instances rearrangements involving three-membered rings have been reported. Labelled Grignard 120 leads to equal amounts of normal and rearranged alcohol [79]. Reaction of the



Grignard reagent from 121 with an aldehyde gives only product with unrearranged skeleton [95]. However, the oxygenation product

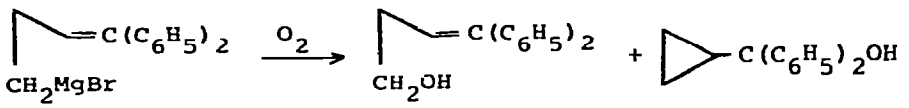


is partly rearranged (0-12%), depending upon halogen and solvent. Oxygenation of the Grignard reagent from 122 leads to mixture of



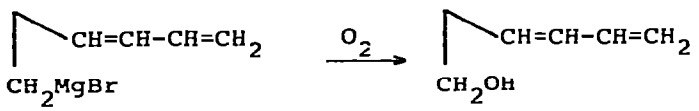
122

the same products, but the interpretation is less clear, since the product reflects rearrangement during and after Grignard formation, as well as that during oxygenation. When the cyclic radical was resonance-stabilized [104], some cyclic products were found on oxygenation, as indicated in eqns 104 and 105.

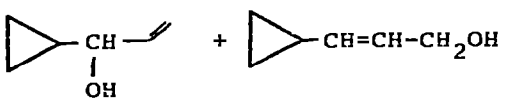


(104)

2.5 1.0



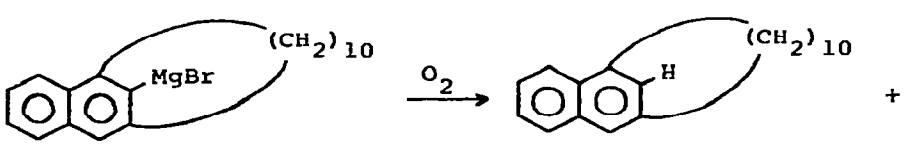
1.0



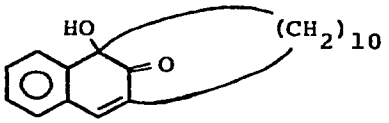
(105)

1.0 1.0

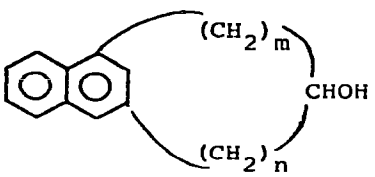
An interesting case, involving rearrangement by an apparent transannular hydrogen abstraction is shown in eqn 106 [318].



42%



+



(106)

16%

34%

(m + n = 9, mixture of four isomers)

Oxygenation of neophyllithium also led to apparent radical rearrangement [319].

Another class of reaction of Grignard reagents for which radical intermediates have often been invoked are reactions involving transition metal salts. Most familiar is the Kharasch reaction of Grignard reagent with alkyl halides, catalyzed by transition metal salts. Depending upon the Grignard reagent, organic halide and metal salt used, a variety of products of coupling, disproportionation and hydrogen abstraction from solvent are found. From the earliest discussion of these reactions, there appears to have been fairly general agreement that metal exchange occurs first to produce an organotransition metal compound:

$$RMgX + m\text{-}X \longrightarrow R\text{-}m + MgX_2 \qquad (107)$$

Beyond this stage, disagreement arises. Mechanisms have been written proposing radical formation by decomposition of the organotransition metal compound, and mechanisms with non-radical decomposition to similar products:

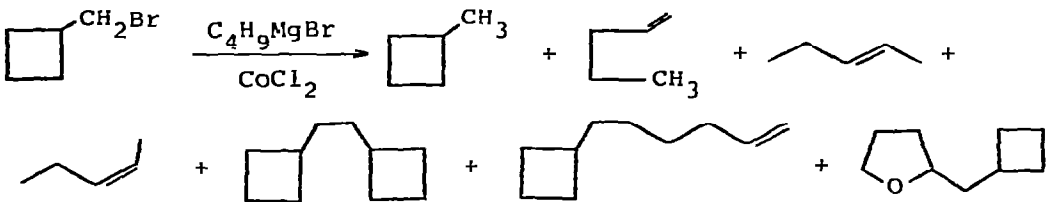
$$R\text{-}m \longrightarrow m + RH + R(-H) \quad \text{or} \quad R\text{-}R \qquad (108)$$

The reduced form of the metal produced in this step appears to be oxidized by organic halides, generating radicals from the halide in the process:

$$m + R'\text{-}X \longrightarrow R'\cdot + m\text{-}X \qquad (109)$$

Rearrangement of the radical from eqn 109 has been observed. The finding of rearranged products from the reaction of neophyl chloride with phenyl magnesium bromide in the presence of cobaltous chloride was the first recorded observation of rearrangement of the neophyl radical [300].

Rearrangement has also been observed in the $CoCl_2$-catalyzed reaction of cyclobutylmethyl bromide with butylmagnesium bromide in THF [320]:



About half of the C_5 product was ring-opened. The 2-pentenes are formed by transition metal-catalyzed isomerization of 1-pentene.

In contrast, decomposition of the transition metal intermediate in eqn 108 appears to involve most commonly non-radical routes. Thus, when a small amount of cobaltous chloride was added to cyclobutylmethylmagnesium chloride, some methylenecyclobutane was formed, but hydrolysis produced no increase in 1-pentene or coupling product beyond that generated during original formation [320]. Reaction of this solution with butyl bromide gave C_5 products which indicated about 5% of ring opening during the reaction. The small amount of ring opening could result from some radical decomposition, or from metal-catalyzed functional exchange between the Grignard and butyl bromide. Similarly, there is little cyclization of 5-hexenyl groups in decomposition of the correspondin alkyl copper(I) phosphine complex [321] or reaction of the Grignard with manganese(II) chloride [322]. Homolytic cleavage of the carbon-transition metal bond may occur, as shown by rearrangement

of neophyl radicals in thermal decomposition of neophyl copper or silver [323]. However, it has been concluded that the instability of organo-transition metal compounds may more frequently be attributed to other facile reaction paths, rather than to inherent weakness or ready cleavage to radicals [324].

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REFERENCES

1. H. E. Zimmerman, in P. de Mayo (Ed.), Molecular Rearrangements, Interscience Publishers, New York, 1963, pp 372-400.
2. E. H. White and D. J. Woodcock, in S. Patai (Ed.), The Chemistry of the Amino Group, Interscience Publishers, New York, 1968, pp 417-423.
3. D. V. Banthorpe, in S. Patai (Ed.), The Chemistry of the Amino Group, Interscience Publishers, New York, 1968, pp 612-623.
4. C. K. Ingold, Structure and Mechanism in Organic Chemistry (2nd edition), Cornell University Press, Ithaca, N. Y., 1969, pp 787-792.
5. D. J. Cram, Fundamentals of Carbanion Chemistry, Academic Press, New York, 1965, pp 223-238.
6. H. E. Zimmerman and A. Zweig, J. Amer. Chem. Soc., 83 (1961) 1196.
7. N. F. Phelan, H. H. Jaffé, and M. Orchin, J. Chem. Educ., 44 (1967) 626.

8. R. B. Woodward and R. Hoffman, The Conservation of Orbital Symmetry, Verlag Chemie, GmbH, Weinheim/Bergstr., Germany, 1971, pp 114-132.

9. S. I. Miller, Advances in Physical Organic Chemistry, 6 (1968) 185; viz. pp 235-237, 287-293.

10. U. Schöllkopf, Angew. Chem. Internat. Edit., 9 (1970) 763.

11. J. E. Baldwin and J. E. Patrick, J. Amer. Chem. Soc., 93 (1971) 3556.

12. V. Rautenstrauch, Helv. Chim. Acta, 55 (1972) 2233.

13. J. E. Baldwin, J. Bernardis, and J. E. Patrick, Tetrahedron Lett., (1970) 353.

14. S. H. Pine, J. Chem. Educ., 48 (1971) 99.

15. E. Grovenstein, Jr., and L. P. Williams, Jr., J. Amer. Chem. Soc., 83 (1961) 2537.

16. E. Grovenstein, Jr., and G. Wentworth, J. Amer. Chem. Soc., 85 (1963) 3305; 89 (1967) 1852.

17. J. J. Eisch and C. A. Kovacs, J. Organometal. Chem., 30 (1971) C97.

18. E. Grovenstein, Jr., J. Amer. Chem. Soc., 79 (1957) 4985.

19. H. E. Zimmerman and F. J. Smentowski, J. Amer. Chem. Soc., 79 (1957) 5455.

20. E. Grovenstein, Jr. and G. Wentworth, J. Amer. Chem. Soc., 89 (1967) 2348.

21. J. J. Eisch and C. A. Kovacs, J. Organometal. Chem., 25 (1970) C33.

22. J. J. Eisch, C. A. Kovacs, and S.-G. Rhee, J. Organometal. Chem., 65 (1974) 289.

23. G. Fraenkel and J. W. Cooper, J. Amer. Chem. Soc., 93 (1971) 7228.

24. E. Grovenstein, Jr., S. Akabori, and J.-U. Rhee, J. Amer. Chem. Soc., 94 (1972) 4734.

25. G. Fraenkel, C. C. Ho, Y. Liang, and S. Yu, J. Amer. Chem. Soc., 94 (1972) 4732.

26. H. F. Ebel, V. Dörr, and B. O. Wagner, Angew. Chem. Internat. Edit., 9 (1970) 163.

27. W. G. Young and J. D. Roberts, J. Amer. Chem. Soc., 68 (1946) 649, 1472.

28. R. H. De Wolfe and W. G. Young, Chem. Revs., 56 (1956) 753.

29. R. A. Benkeser, Synthesis, (1971) 347.

30. J. E. Nordlander and J. D. Roberts, J. Amer. Chem. Soc., 81 (1959) 1770.

31. H. E. Zieger and J. D. Roberts, J. Org. Chem., 34 (1969) 1976.

32. P. West, private communication.

33. J. E. Nordlander, W. G. Young, and J. D. Roberts, J. Amer. Chem. Soc., 83 (1961) 494.

34. G. M. Whitesides, J. E. Nordlander, and J. D. Roberts, J. Amer. Chem. Soc., 84 (1962) 2010.

35. D. A. Hutchison, K. R. Beck, R. A. Benkeser, and J. B. Grutzner, J. Amer. Chem. Soc., 95 (1973) 7075.

36. W. H. Glaze and C. R. McDaniel, J. Organometal. Chem., 51 (1973) 23.

37. D. Leibfritz, B. O. Wagner, and J. D. Roberts, Justus Liebig's Ann. Chem., 763 (1972) 173.

38. L. A. Fedorov, Uspekhi Khimii, 39 (1970) 1389; Russian Chemical Reviews, 39 (1970) 655.

39. P. West, J. I. Purmort, and S. V. McKinley, J. Amer. Chem. Soc., 90 (1968) 797.

40. R. Waack and M. A. Doran, J. Amer. Chem. Soc., 85 (1963) 1651.

41. D. Seyferth and T. F. Jula, J. Organometal. Chem., 8 (1967) 13.

42. E. R. Dolinskaya, I. Ya. Poddubnyi, and I. Yu. Tsereteli, Dokl. Akad. Nauk SSSR, 191 (1970) 862; Dokl. Phys. Chem., 191 (1970) 279.

43. F. B. Bates, D. W. Gosselink, and J. A. Kaczynski, Tetrahedron Lett., (1967) 205.

44. V. R. Sandel, S. V. McKinley, and H. H. Freedman, J. Amer. Chem. Soc., 90 (1968) 495.

45. W. H. Glaze, J. E. Hanicak, M. L. Moore, and J. Chaudhuri, J. Organometal. Chem., 44 (1972) 39.

46. W. H. Glaze, J. E. Hanicak, J. Chaudhuri, M. L. Moore, and D. P. Duncan, J. Organometal. Chem., 51 (1973) 13.

47. H. Lehmkuhl and D. Reinehr, J. Organometal. Chem., 23 (1970) C5.

48. G. Wilke, B. Bogdanović, P. Hardt, P. Heimbach, W. Keim, M. Kröner, W. Oberkirch, K. Tanaka, E. Steinrücke, D. Walter, and H. Zimmermann, Angew. Chem. Internat. Ed. Engl., 5 (1966) 151.

49. V. S. Bogdanov, V. F. Pazdner, G. V. Lagodzinskaya, and B. M. Mikhailov, Theorei. Exper. Khim., 3 (1967) 488; Theoretical and Experimental Chemistry, 3 (1967) 282.

50. V. S. Bogdanov, Yu. N. Bubnov, M. N. Bochkareva, and B. M. Mikhailov, Dokl. Akad. Nauk SSSR, 201 (1971) 605; Proceedings of the Academy of Science of the USSR, 201 (1971) 950.

51. B. M. Mikhailov, Organometal. Chem. Rev. A, 8 (1972) 1.

52. E. J. Lanpher, J. Amer. Chem. Soc., 79 (1957) 5578.

53. G. Davidson, Organometal. Chem. Rev. A, 8 (1972) 303.

54. H. F. Ebel and B. O. Wagner, Chem. Ber., 104 (1971) 307, 320.

55. L. D. McKeever and R. Waack, J. Organometal. Chem., 28 (1971) 145.

56. W. Hanstein and T. G. Traylor, Tetrahedron Lett., (1967) 4451.

57. H. E. Zieger and J. D. Roberts, J. Org. Chem., 34 (1969) 2826.

58. G. Courtois and L. Miginiac, J. Organometal. Chem., 69 (1974) 1.

59. R. H. De Wolfe and W. G. Young, in S. Patai (Ed.), The Chemistry of Alkenes, Interscience Publishers, New York, 1964, pp 727-731.

60. M. Andrac and C. Prevost, Bull. Soc. Chim. Fr., (1964) 2284

61. M. Andrac, F. Gaudemar, M. Gaudemar, B. Gross, L. Miginiac, P. Miginiac, and C. Prevost, Bull. Soc. Chim. Fr., (1963) 1385.

62. Y. Gault, C. R. Acad. Sci., Paris, Ser. C, 250 (1960) 2584.

63. H. Felkin and G. Roussi, Tetrahedron Lett., (1965) 4153.

64. H. Felkin, C. Frajerman, and G. Roussi, Bull. Soc. Chim. Fr., (1970) 3704.

65. H. Felkin and C. Frajerman, Tetrahedron Lett., (1970) 1045.

66. H. Felkin, C. Frajerman, and G. Roussi, Ann. Chim. (Paris), 6 (1971) 17.

67. H. Felkin, C. Frajerman, and Y. Gault, Chem. Commun., (1966) 75.

68. N. T. Anh, Chem. Commun., (1968) 1089.

69. J. Mathieu, Bull. Soc. Chim. Fr., (1973) 807.

70. H. Felkin, Y. Gault, and G. Roussi, Tetrahedron, 26 (1970) 3761.

71. G. A. Holmberg and R. Sjoholm, Acta Chem. Scand., 24 (1971) 3490.

72. R. A. Benkeser, W. G. Young, W. E. Broxterman, D. A. Jones, Jr., and S. J. Piaseczynski, J. Amer. Chem. Soc., 91 (1969) 132.

73. S. Bank, A. Schriesheim, and C. A. Rowe, Jr., J. Amer. Chem. Soc., 87 (1965) 3244.

74. M. Cherest, H. Felkin, and C. Frajerman, Tetrahedron Lett., (1971) 379.

75. R. A. Benkeser and W. E. Broxterman, J. Amer. Chem. Soc., 91 (1969) 5162.

76. P. Miginiac, Bull. Soc. Chim. Fr., (1970) 1077.

77. J. D. Roberts and R. H. Mazur, J. Amer. Chem. Soc., 73 (1951) 2509.

78. L. I. Smith and S. McKenzie, Jr., J. Org. Chem., 15 (1950) 74.

79. M. S. Silver, P. R. Shafer, J. E. Nordlander, C. Rüchardt, and J. D. Roberts, J. Amer. Chem. Soc., 82 (1960) 2646.

80. D. J. Patel, C. L. Hamilton, and J. D. Roberts, J. Amer. Chem. Soc., 87 (1965) 5144.

81. P. T. Lansbury, V. A. Pattison, W. A. Clement, and J. Sidler, J. Amer. Chem. Soc., 86 (1964) 2247.

82. P. T. Lansbury and V. A. Pattison, J. Amer. Chem. Soc., 85 (1963) 1886.

83. E. A. Hill, H. G. Richey, Jr., and T. C. Rees, J. Org. Chem., 28 (1963) 2161.

84. C. L. Bumgardner, K. L. Martin, and J. P. Freeman, J. Amer. Chem. Soc., 85 (1963) 97.

85. C. L. Bumgardner and J. P. Freeman, Tetrahedron Lett., (1964) 737.

86. C. L. Bumgardner and H. Iwerka, J. Amer. Chem. Soc., 88 (1966) 5518.

87. R. W. Hoffmann and K. R. Eichen, Chem. Ber., 100 (1967) 1465.

88. C. H. DePuy, Accounts Chem. Res., 1 (1968) 33.

89. C. L. Bumgardner and J. G. Carver, J. Org. Chem., 37 (1972) 407.

90. A. Maercker and K. Weber, Angew. Chem. Internat. Ed., 8 (1969) 912; Justus Liebig's Ann. Chem., 756 (1972) 43.

91. A. Maercker and K. Weber, Justus Liebig's Ann. Chem., 756 (1972) 20.

92. H. G. Richey, Jr., and H. S. Veale, personal communication; and J. Amer. Chem. Soc., 96 (1974) 2641; H. S. Veale, Ph.D. Thesis, The Pennsylvania State University, 1973.

93. A. Maercker and W. Streit, Angew. Chem. Internat. Edit., 11 (1972) 542.

94. E. A. Hill, K. Hsieh, and D. Elgas, unpublished work.

95. P. Miginiac and B. Cousseran, J. Organometal. Chem., 28 (1971) C5; see also M. Julia and Y. Noël, Bull. Soc. Chim. Fr., (1968) 3749.

96. A. Maercker, P. Guthlein, and H. Wittmayr, Angew. Chem. Internat. Edit., 12 (1973) 774.

97. P. Miginiac, C. R. Acad. Sci., Paris, Ser. C, 264 (1967) 1417.

98. W. Reeve and R. S. Bianchi, J. Org. Chem., 34 (1969) 1921.

99. E. L. McCaffery and S. W. Shalaby, J. Organometal. Chem., 3 (1965) 101; 8 (1967) 17.

100. H. G. Richey, Jr. and W. C. Kossa, Jr., Tetrahedron Lett., (1969) 2313.

101. M. Santelli and M. Bertrand, C. R. Acad. Sci., Paris, Ser. C, (1970) 757.

102. H. G. Richey and A. M. Rothman, personal communication; A. M. Rothman, Ph.D. Thesis, The Pennsylvania State University, 1969.

103. A. Maercker and J. D. Roberts, J. Amer. Chem. Soc., 88 (1966) 1742.

104. M. E. H. Howden, A. Maercker, J. Burdon, and J. D. Roberts, J. Amer. Chem. Soc., 88 (1966) 1732.

105. E. A. Hill, J. Amer. Chem. Soc., 94 (1972) 7462.

106. M. S. Newman and G. Kaugars, J. Org. Chem., 30 (1965) 3295.

107. A. J. Fry and R. H. Moore, J. Org. Chem., 33 (1968) 425.

108. E. A. Hill and M. R. Engel, J. Org. Chem., 36 (1971) 1356.

109. J. L. Derocque, U. Beisswenger, and M. Hanack, Tetrahedron Lett., (1969) 2149.

110. J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, J. Amer. Chem. Soc., 72 (1950) 3116.

111. D. O. Cowan, N. G. Krieghoff, J. E. Nordlander, and J. D. Roberts, J. Org. Chem., 32 (1967) 2639.

112. H. Demole, Helv. Chem. Acta, 47 (1964) 319.

113. G. W. Klumpp, Rec. Trav. Chim Pays-Bas, 87 (1968) 1053.

114. A. Maercker and R. Geuss, Angew. Chem. Internat. Edit., 9, (1970) 909; Chem. Ber., 106 (1973) 773.

115. E. A. Hill and G. E.-M. Shih, J. Amer. Chem. Soc., 95 (1973) 7764.

116. A. Maercker and W. Theysohn, Justus Liebig's Ann. Chem., 759 (1972) 132.

117. A. Maercker, Angew. Chem. Internat. Edit., 6 (1967) 557.

118. E. E. Schweitzer, J. G. Thompson, and T. A. Ulrich, J. Org. Chem., 33 (1968) 3082.

119. T. Teraji, I. Moritani, E. Tsuda, and S. Nishida, J. Chem. Soc., C, (1971) 3252.

120. P. R. Brook and B. V. Brophy, Chem. Commun., (1969) 1397.

121. M. J. Perkins and P. Ward, Chem. Commun., (1971) 1134.

122. R. Kosta, S. Arora, and P. Binger, Angew. Chem. Internat. Edit., 8 (1969) 205.

123. E. Breuer, E. Segall, Y. Stein, and S. Surel, J. Org. Chem., 37 (1972) 2242; (see other references therein).

124. A. Maercker, Justus Liebig's Ann. Chem., 732 (1970) 151.

125. A. Maercker, Justus Liebig's Ann. Chem., 730 (1970) 91.

126. R. M. Magid and S. E. Wilson, Tetrahedron Lett., (1971) 19.

127. E. Dunkelblum and S. Brenner, Tetrahedron Lett., (1973) 669.

128. E. A. Hill, H. G. Richey, Jr., and T. C. Rees, J. Org. Chem., 28 (1963) 2161.

129. E. A. Hill and J. A. Davidson, J. Amer. Chem. Soc., 86 (1964) 4663.

130. E. A. Hill and R. A. Doughty, unpublished results.

131. E. A. Hill and R. Wagner, unpublished results.

132. T. C. Rees, Ph.D. Thesis, Pennsylvania State University, 1966.

133. E. A. Hill and H.-R. Ni, J. Org. Chem., 36 (1971) 4133.

134. S. Kaarsemaker and J. Coops, Rec. Trav. Chem. Pays-Bas, 71 (1952) 261.

135. H. Lehmkuhl and D. Reinehr, J. Organometal. Chem., 57 (1973) 29.

136. H. Lehmkuhl, D. Reinehr, D. Henneberg, and G. Schroth, J. Organometal. Chem., 57 (1973) 49.

137. E. A. Hill, R. J. Theissen, and K. Taucher, J. Org. Chem., 34 (1969) 3061.

138. E. A. Hill, R. J. Theissen, and R. M. Miller, unpublished results; R. J. Theissen, Ph.D. Thesis, University of Minnesota, 1966; preliminary results reported by E. A. Hill

and R. J. Theissen, 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March, 1966, Abstracts p. 19-K.

139. E. A. Hill, R. Guthrie, and R. Miller, unpublished results.

140. E. A. Hill and K. Hsieh, unpublished results; K. Hsieh, M. S. Thesis, University of Wisconsin-Milwaukee, 1968.

141. T. W. Gibson and W. F. Erman, J. Amer. Chem. Soc., 91 (1969) 4771; Tetrahedron Lett., (1967) 905.

142. L. Hörner, P. V. Subramanian, and K. Eiben, Justus Liebig's Ann. Chim., 714 (1968) 91.

143. R. Possi and P. Diversi, Tetrahedron, 26 (1970) 5033.

144. A. G. Anderson, Jr. and M. T. Wills, J. Org. Chem., 32 (1967) 3241 and 33 (1968) 3046.

145. W. R. Moore, L. N. Bell, and G. P. Daumit, J. Amer. Chem. Soc., 92 (1970) 6680.

146. K. L. Erickson, B. E. Vanderwaart, and J. Wolinski, Chem. Commun., (1968) 1031; K. L. Erickson, J. Org. Chem., 38 (1973) 1463.

147. H. G. Richey, Jr. and T. C. Rees, Tetrahedron Lett., (1966) 4297.

148. W. G. Kossa, Jr., T. C. Rees, and H. G. Richey, Jr., Tetrahedron Lett., (1971) 3455.

149. R. C. Lamb, P. W. Ayres, M. K. Toney, and J. F. Garst, J. Amer. Chem. Soc., 88 (1966) 4261.

150. V. N. Drozd, Yu. A. Ustynyuk, M. A. Tsel'eva, and L. B. Dmitriev, Zh. Obshch. Khim., 38 (1968) 2114 and 39 (1969) 1991.

151. E. A. Hill, R. J. Theissen, A. Doughty, and R. Miller, J. Org. Chem., 34 (1969) 3681.

152. J. St. Denis, T. Dolzine, and J. P. Oliver, J. Amer. Chem. Soc., 94 (1972) 8260.

153. H. G. Richey and A. M. Rothman, Tetrahedron Lett., (1968) 1457; A. M. Rothman, Ph.D. Thesis, Pennsylvania State University, 1969.

154. J. K. Crandall and W. J. Michaely, personal communication; W. J. Michaely, Ph.D. Thesis, Indiana University, 1971.

155. S. A. Kandil and R. E. Dessy, J. Amer. Chem. Soc., 88 (1966) 3027.

156. H. Felkin, J. D. Umpleby, E. Hagaman, and E. Wenkert, Tetrahedron Lett., (1972) 2285.

157. H. Lehmkuhl and D. Reinehr, J. Organometal. Chem., 34 (1972) 1.

158. P. K. Freeman, D. E. George, and V. N. M. Rao, J. Org. Chem., 28 (1963) 3234; 29 (1964) 1682.

159. P. K. Freeman, V. N. M. Rao, D. E. George, and G. L. Fenwick, J. Org. Chem., 32 (1967) 3958.

160. G. Hata and A. Miyake, J. Org. Chem., 28 (1963) 3237.

161. K. Ziegler, in H. H. Zeiss (Ed.), Organometallic Chemistry, Reinhold, New York, N. Y., 1960, pp. 220-231.

162. T. W. Dolzine and J. P. Oliver, personal communication (in publication).

163. J. J. Eisch and G. R. Husk, J. Org. Chem., 31 (1966) 3419.

164. G. Zweifel, G. M. Clark, and R. Lynd, Chem. Commun., (1971) 1593.

165. E. Marcus, D. L. MacPeek, and S. W. Tinsley, J. Org. Chem., 36 (1971) 381.

166. E. Marcus, D. L. MacPeek, and S. W. Tinsley, J. Org. Chem., 34 (1969) 1931.

167. H. Pines, N. C. Sih, and E. Lewicki, J. Org. Chem., 30 (1965) 1457.

168. L. H. Slaugh, J. Org. Chem., 32 (1967) 108.

169. P. T. Lansbury and F. J. Caridi, Chem. Commun., (1970) 714.

170. T. W. Dolzine, A. K. Hovland, and J. P. Oliver, J. Organometal. Chem., 54 (1974) C1.

171. R. A. Finnegan and R. S. McNees, J. Org. Chem., 29 (1964) 3234.

172. H. Lehmkuhl, D. Reinehr, J. Brandt, and G. Schroth, J. Organometal. Chem., 57 (1973) 39.

173. C. Walling and M. S. Pearson, J. Amer. Chem. Soc., 86 (1964) 2262.

174. A. L. J. Beckwith, G. E. Gream, and D. L. Struble, Aust. J. Chem., 25 (1972) 1081.

175. C. L. Karl, E. J. Maas, and W. Reusch, J. Org. Chem., 37 (1972) 2834.

176. M. Julia, Accounts Chem. Res., 4 (1971) 386.

177. E. A. Hill, unpublished results.

178. H. G. Richey, Jr. and W. C. Kossa, Jr., personal communication; W. C. Kossa, Jr., Ph.D. Thesis, Pennsylvania State University, 1971.

179. G. E. Parris and E. C. Ashby, J. Amer. Chem. Soc., 93 (1971) 1206 .

180. H. O. House, R. A. Latham, and G. M. Whitesides, J. Org. Chem., 32 (1967) 2481.

181. T. Holm, Tetranedron Lett., (1966) 3329.

182. E. C. Ashby, L.-C. Chao, and H. M. Neumann, J. Amer. Chem. Soc., 95 (1973) 4896.

183. D. Lloyd, Alicyclic Compounds, American Elsivier Publishing Co., Inc., New York, 1963, p. 30.

184. E. A. Hill and A. T. Chen, unpublished results; A. T. Chen, M. S. Thesis, University of Wisconsin-Milwaukee, 1969.

185. D. J. Carlsson and K. U. Ingold, J. Amer. Chem. Soc., 90 (1968) 7047.

186. D. C. Nonhebel and J. C. Walton, Free-radical Chemistry, Cambridge University Press, Cambridge, 1974, pp. 158-170, 210-238.

187. F. F. Blicke and L. D. Powers, J. Amer. Chem. Soc., 51 (1929) 3378.

188. C. Blomberg, R. M. Salinger, and H. S. Mosher, J. Org. Chem., 34 (1969) 2385.

189. T. Holm and I. Crossland, Acta. Chem. Scand., 25 (1971) 59.

190. J. J. Eisch and J. H. Merkley, J. Organometal. Chem., 20 (1969) P27.

191. H. G. Richey, Jr., and F. W. von Rein, J. Organometal. Chem., 20 (1969) P32.

192. E. C. Ashby, H. M. Neumann, F. W. Walker., J. Laemmle, and L.-C. Chao, J. Amer. Chem. Soc., 95 (1973) 3330.

193. J.-F. Fauvargue and E. Rouget, C. R. Acad. Sci., Paris, Ser. C, 267 (1968) 1355.

194. I. M. Kolthoff and J. J. Lingane, Polarography, Interscience Publishers, New York and London, 1952, pp. 634-686.

195. C. K. Mann and K. K. Barnes, Electrochemical Reactions in Nonaqueous Systems, Marcel Dekker, Inc., New York, 1970, pp. 31-53, 177-189.

196. F. J. Reinders and R. Prins, J. Organometal. Chem., 25 (1970) C41.

197. C. Chevrot, M. Troupel, J.-C. Folest, and J. Perichon, C. R. Acad. Sci., Paris, Ser. C, (1971) 493.

198. H. A. Laitinen and S. Wawzonek, J. Amer. Chem. Soc., 64 (1942) 1765.

199. S. Wawzonek and H. A. Laitinen, J. Amer. Chem. Soc., 64 (1942) 2365.

200. J. A. Kerr, Chem. Rev., 66 (1966) 465.

201. H. Schäfer, U. Schöllkopf, and D. Walter, Tetrahedron Lett., (1968) 2809.

202. H. E. O'Neal and S. W. Benson, J. Phys. Chem., 72 (1968) 1866.

203. L. M. Stephenson, T. A. Gibson, and J. I. Brauman, J. Amer. Chem. Soc., 95 (1973) 2849.

204. W. G. Espersen and R. Kreilick, J. Amer. Chem. Soc., 92 (1970) 3894.

205. O. I. Micic and B. Cerek, J. Phys. Chem., 78 (1974) 285.

206. R. E. Dessy and W. Kitching, Adv. Organometal. Chem., 4 (1966) 267.

207. For example, see D. J. Pasto, B. Lepeska, and T.-C. Cheng, J. Amer. Chem. Soc., 94 (1972) 6083, and references therein.

208. See W. R. Moore, H. W. Anderson, and S. D. Clark, J. Amer. Chem. Soc., 95 (1973) 835, and references therein.

209. K. W. Egger, J. Chem. Soc., Faraday Trans. 1, 68 (1972) 1072.

210. K. W. Egger, Helv. Chem. Acta, 55 (1972) 1502.

211. R. A. Finnegan and H. W. Kutta, J. Org. Chem., 30 (1965) 4138.

212. M. Lefrancois and Y. Gault, J. Organometal. Chem., 16 (1969) 7.

213. E. J. Arlman and P. Cossee, J. Catalysis, 3 (1964) 99.

214. D. F. Hoeg in The Stereochemistry of Macromolecules, A. D. Ketley, ed., Marcel Dekker, Inc., New York, 1967, p. 47.

215. P. Cossee in The Stereochemistry of Macromolecules, A. D. Ketley, ed., Marcel Dekker, Inc., New York, 1967, p. 145.

216. G. Allegra, Macromol. Chem. , 145 (1971) 235.

217. W. L. Carrick, Advances in Polymer Science, 12 (1973) 65.

218. D. R. Armstrong, P. G. Perkins, and J. J. P. Stewart, J. Chem. Soc., Dalton Trans., (1972) 1972.

219. F. P. Boer and P. P. North, J. Chem. Soc., Perkins Trans. 2, (1972) 416.

220. P. R. Brook, A. J. Duke, and J. R. C. Duke, Chem. Commun., (1970) 574.

221. J. F. Lam and H. W. Heine, J. Amer. Chem. Soc., 73 (1951) 1348.

222. H. W. Heine, A. D. Miller, W. H. Barton, and R. W. Greiner, J. Amer. Chem. Soc., 75 (1953) 4778.

223. R. B. Woodward and R. Hoffmann, The Conservation of Orbital Symmetry, Verlag Chemie, Gmb H, Weinheim/Bergstr., Germany, 1971, pp. 10-37; 65-113.

224. R. G. Pearson, Accounts Chem. Res., 4 (1971) 152.

225. L. Salem, J. Amer. Chem. Soc., 90 (1968) 543, 553.

226. K. Fukui, Bull. Chem. Soc. Japan, 39 (1966) 498.

227. P. R. Jones, J. Org. Chem., 37 (1972) 1886.

228. H. E. Zimmerman, Accounts Chem. Res., 5 (1972) 393.

229. H. C. Longuet-Higgins and E. W. Abrahamson, J. Amer. Chem. Soc., 87 (1965) 2045.

230. L. M. Raff and R. N. Porter, J. Chem. Phys., 51 (1969) 4701.

231. R. A. Jackson, J. Chem. Soc. B , (1970) 58.

232. N. D. Epiotis, J. Amer. Chem. Soc., 95 (1973) 191.

233. D. J. Pasto and S.-Z. Kang, J. Amer. Chem. Soc., 94 (1972) 6083.

234. J. Soulati, K. L. Henold, and J. P. Oliver, J. Amer. Chem. Soc., 93 (1971) 5694.

235. J. J. Eisch and C. K. Hordis, J. Amer. Chem. Soc., 93 (1971) 4496.

236. P. E. M. Allen and R. M. Lough, J. Organometal. Chem., 61 (1973) 7.

237. A. Streitwieser, Jr., L. Verbit, and R. Bittman, J. Org. Chem., 32 (1967) 1530.

238. K. Sisido, M. Naruse, A. Saito, and K. Utimoto, J. Org. Chem., 37 (1972) 733.

239. J. J. Eisch and R. Amtmann, J. Org. Chem., 37 (1972) 3410.

240. J. J. Eisch and S. G. Rhee, J. Organometal. Chem., 31 (1971) C49.

241. P. E. M. Allen and R. M. Lough, J. Chem. Soc., Faraday I, (1973) 849.

242. K. W. Egger and A. T. Cocks, Trans. Faraday Soc., 67 (1971) 2638.

243. K. W. Egger, Trans. Faraday Soc., 68 (1972) 1017.

244. P. D. Bartlett, C. V. Gobel, and W. P. Weber, J. Amer. Chem. Soc., 91 (1969) 7425.

245. P. Cossee, J. Catalysis, 3 (1964) 80.

246. E. J. Arlman and P. C. Cossee, J. Catalysis, 3 (1964) 99.

247. G. M. Whitesides, J. F. Gaasch, and E. R. Stedronsky, J. Amer. Chem. Soc., 94 (1972) 5258.

248. For example, H. C. Clark and R. J. Puddenphatt, Inorg. Chem., 10 (1971) 18.

249. D. V. Banthorpe, Chem. Rev., 70 (1970) 295.

250. D. R. Armstrong, P. G. Perkins, and J. J. P. Stewart, J. Chem. Soc., Dalton Trans., (1972) 1972.

251. A. Streitwieser, Jr. and J. I. Brauman, Supplemental Tables and Molecular Oriented Calculations, Pergamon Press, Oxford, 1965, p. 3.

252. E. A. Halevi, Progress in Physical Organic Chemistry, 1 (1963) 109.

253. C. J. Collins and N. S. Bowman, ed., Isotope Effects in Chemical Reactions, Van Nostrand Reinhold Company, New York, 1970.

254. A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, J. Amer. Chem. Soc., 80 (1958) 2326.

255. R. J. Cvetanovic, F. J. Duncan, W. E. Falconer, and W. A. Sander, J. Amer. Chem. Soc., 88 (1966) 1602.

256. F. R. Hartley, Chem. Rev., 73 (1973) 163.

257. D. H. Froemsdorf, C. H. Collins, G. S. Hammond, and C. H. DePuy, J. Amer. Chem. Soc., 81 (1959) 643.

258. W. O. Haag and H. Pines, J. Org. Chem., 24 (1959) 877.

259. R. A. Bartsch, G. M. Pruss, D. M. Cook, R. L. Buswell, B. A. Bushaw, and K. E. Wiegers, J. Amer. Chem. Soc., 85 (1973) 6745.

260. J. P. Oliver, J. B. Smart, and M. T. Emerson, J. Amer. Chem. Soc., 88 (1966) 4101.

261. J. B. Smart, R. Hogan, P. A. Scherr, M. T. Emerson, and J. P. Oliver, J. Organometal. Chem., 64 (1974) 1.

262. G. Hata, Chem. Commun., (1968) 7.

263. J. St. Denis, J. P. Oliver, T. W. Dolzine, and J. B. Smart, J. Organometal. Chem., 71 (1974) 315.

264. J. St. Denis, J. P. Oliver, and J. B. Smart, J. Organometal. Chem., 44 (1972) C32.

265. J. J. Eisch and C. K. Hordis, J. Amer. Chem. Soc., 93 (1971) 2974.

266. J. J. Eisch and R. Amtmann, J. Org. Chem., 37 (1972) 3410.

267. G. Wittig, Quart. Rev. (London), 20 (1966) 191.

268. See T. Psarras and R. E. Dessy, J. Amer. Chem. Soc., 88 (1966) 5132.

269. L. Martinot, Bull. Soc. Chim. Belges, 76 (1967) 617.

270. L. M. Seitz and T. L. Brown, J. Amer. Chem. Soc., 88 (1966) 4140.

271. See G. E. Coates, M. L. H. Green, and K. Wade,

Organometallic Compounds, Methuen and Co., Ltd., London, 1967, v. 1., for pertinent references.

272. M. S. Kharasch and O. Reinmuth, Grignard Reactions of Nonmetall Substances, Prentice-Hall, Inc., New York, N. Y., 1954, pp. 87-

273. H. Lehmkuhl and D. Reinehr, J. Organometal. Chem., 25 (1970) C47.

274. M. Yu. Lukina, T. Yu. Rudavshevskaya, and O. A. Nesmeyanova, Dokl. Akad. Nauk SSSR, 190 (1970) 1109.

275. L. H. Shepherd, Jr., U. S. Patent 3,597,488; C.A. 75 (1971) 88751c.

276. L. H. Shepherd, Jr., U. S. Patent 3,641,186; C.A. 76 (1972) 99815y.

277. L. H. Shepherd, Jr., U. S. Patent 3,597,487; C.A. 75 (1971) 118398n.

278. M. Lefrancois and Y. Gault, J. Organometal. Chem., 16 (1969) 7.

279. H. Lehmkuhl and H. Nehl, J. Organometal. Chem., 60 (1973) 1.

280. M. Cherest, H. Felkin, C. Frajerman, C. Lion, G. Roussi, and G. Swierczewski, Tetrahedron Lett., (1966) 875.

281. F. W. von Rein and H. G. Richey, Jr., Tetrahedron Lett., (1971) 3777.

282. B. Mauzé, C. Nivert, and L. Miginiac, J. Organometal. Chem., 44 (1972) 69.

283. H. G. Richey, Jr., W. F. Erickson, and A. S. Heyn, Tetrahedron Lett., (1971) 2183.

284. K. Suga, S. Watanabe, Y. Yamaguchi, and M. Tohyama, Synthesis, 2 (1970) 189.

285. J. K. Crandall and A. C. Clark, Tetrahedron Lett., (1969) 325.

286. H. Felkin, G. Swierczewski, and A. Tambuté, Tetrahedron Lett., (1969) 707.

287. J. K. Crandall and A. C. Clark, J. Org. Chem., 37 (1972) 4236.

288. D. R. Dimmel and S. Huang, J. Org. Chem., 38 (1973) 2756.

289. A. H. Veefkind, F. Bickelhaupt, and G. W. Klumpp, Rec. Trav. Chim., 88 (1969) 1058.

290. B. Mauzé, G. Courtois, and L. Miginiac, C. R. Acad. Sci., Paris, Ser. C, 269 (1969) 1225.

291. G. Courtois and L. Miginiac, J. Organometal. Chem., 52 (1973) 241.

292. H. Felkin and C. Kaeseberg, Tetrahedron Lett., (1970) 4587.

293. G. R. Buell, R. Carriu, C. Guerin, and L. Spialter, J. Amer. Chem. Soc., 92 (1970) 7424.

294. P. Tarrant and D. A. Warner, J. Amer. Chem. Soc., 76 (1954) 1624.

295. Le. D. Trung, J. Mordini, P. Q. Tho, and A. Guyot, Eur. Polym. J., 6 (1970) 1187.

296. J. D. Park, T. S. Croft, and R. W. Anderson, J. Organometal. Chem., 64 (1974) 19.

297. M. Gaudemar, C. R. Acad. Sci., Paris, Ser. C, 273 (1971) 1669.

298. C. Walling, in Molecular Rearrangements, Vol. I, P. de Mayo, Ed., Interscience Publishers, New York, 1963, Chapter 7.

299. R. Kh. Freidlina, Advan. Free-Radical Chem., (1965) 211.

300. W. H. Urry and M. S. Kharasch, J. Amer. Chem. Soc., 66 (1944) 1438.

301. S. Winstein and F. H. Seubold, Jr., J. Amer. Chem. Soc., 69 (1947) 2916.

302. E. Renk, P. R. Shafer, W. H. Graham, R. H. Mazur, and J. D. Roberts, J. Amer. Chem. Soc., 83 (1961) 1987.

303. L. Kaplan, J. Org. Chem., 33 (1968) 2531.

304. S. Arai, S. Sato, and S. Shida, J. Chem. Phys., 33 (1960) 1277.

305. R. C. Lamb, P. W. Ayers, and M. K. Toney, J. Amer. Chem. Soc., 85 (1963) 3483.

306. L. K. Montgomery and J. W. Matt, J. Amer. Chem. Soc., 89 (1967) 934, 3050.

307. H. W. H. J. Bodewitz, C. Blomberg, and F. Bickelhaupt, Tetrahedron Lett., (1972) 281.

308. H. M. Walborsky and M. S. Aronoff, J. Organometal. Chem., 51 (1973) 31.

309. R. J. Rogers, H. L. Mitchell, Y. Fujiwara, and G. M. Whitesides, J. Org. Chem., 39 (1974) 857.

310. C. Rüchardt and H. Trautwein, Chem. Res., 95 (1962) 1197.

311. A. H. Fainberg and S. Winstein, J. Amer. Chem. Soc., 78 (1956) 2763.

312. E. Grovenstein, Jr. and Y.-M. Cheng, Chem. Commun., (1970) 101.

313. H. W. H. J. Bodewitz, C. Blomberg, and F. Bickelhaupt, Paper presented at the Sixth International Conference on Organometallic Chemistry, 1973, abstract no. 29.

314. A. L. J. Beckwith, I. Blair, and G. Phillipou, J. Amer. Chem. Soc., 96 (1974) 1613.

315. C. Walling and A. Cioffari, J. Amer. Chem. Soc., 92 (1970) 6609.

316. J. F. Garst and F. E. Barton, II, Tetrachem. Lett., (1969) 587.

317. J. Sauer and W. Braig, Tetrahedron Lett., (1969) 4275.

318. W. E. Parham, R. W. Davenport, and J. K. Rinehart, J. Org. Chem., 35 (1970) 2662.

319. E. J. Panek and G. M. Whitesides, J. Amer. Chem. Soc., 94 (1972) 8768.

320. E. A. Hill, C. Kummer and H.-R. Ni, Abstracts of Papers, 160th National Meeting, American Chemical Society, September, 1970, Abstract ORGN-161.

321. G. M. Whitesides, E. R. Stedronsky, C. P. Casey, and J. San Fillippo, Jr., J. Amer. Chem. Soc., 92 (1970) 1426.

322. M. Tamura and J. K. Kochi, J. Organometal. Chem., 29 (1971) 111.

323. G. M. Whitesides, E. J. Panek, and E. R. Stedronsky, J. Amer. Chem. Soc., 95 (1973) 232.

324. P. S. Braterman and R. J. Cross, J. Chem. Soc., Dalton, (1972) 657.