# Di-Grignard reagents and metallacycles
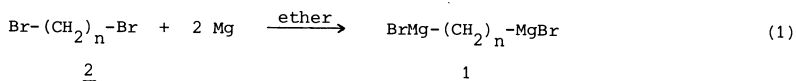
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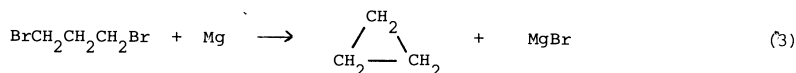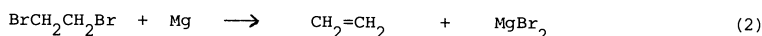
Abstract - Aliphatic $\alpha,\omega$-dibromides can be converted to the corresponding $\alpha,\omega$-di-Grignard reagents; for those members carrying less than four carbon atoms between the functions, special procedures are required. The synthesis, structure and applications of the di-Grignard reagents are discussed; particular emphasis is placed on the structures of the corresponding cyclic dialkylmagnesiums, and on the use of the reagents for the preparation of metalla- and 1,3-dimetallacyclobutanes.

## I INTRODUCTION

Di-Grignard reagents - and the corresponding dilithium reagents - are useful synthons for the preparation of many organic and organometallic compounds; in particular, they are often used for the preparation of metallacycles of various elements (1,2). It is nontrivial to point out that the usefulness of these reagents depends on their availability. The traditional and most convenient way to prepare Grignard reagents is from organic halides and magnesium metal in a basic, aprotic solvent. For di-Grignard reagents ($\underline{1}$) this method is applicable in a straightforward way only when at least four (aliphatic) carbon atoms separate the two functions (eq. 1).
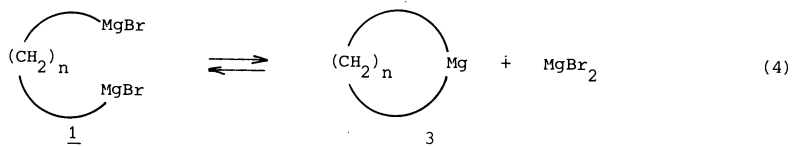
$$Br\text{-}(CH_2)_n\text{-}Br \; + \; 2\ Mg \; \xrightarrow{\text{ether}} \; BrMg\text{-}(CH_2)_n\text{-}MgBr \qquad (1)$$

$$\underline{2} \qquad\qquad\qquad\qquad \underline{1}$$

Already one year after the discovery of the famous reaction bearing his name, V. Grignard (3) recognized that not $\underline{1}$, but other products are formed when 1,2-dibromoethane (eq. 2) or 1,3-dibromopropane (eq. 3) were subjected to the Grignard formation reaction.

$$BrCH_2CH_2Br \; + \; Mg \; \longrightarrow \; CH_2{=}CH_2 \; + \; MgBr_2 \qquad (2)$$

$$BrCH_2CH_2CH_2Br \; + \; Mg \; \longrightarrow \; \overset{CH_2}{\underset{CH_2 - CH_2}{\diagup \diagdown}} \; + \; MgBr \qquad (3)$$

It is of historical interest that the feasibility of eq. 1 became apparent only several years later (4,5) after the corresponding organic dihalides had been made readily accessible by the pioneering work of J. von Braun (5). Shortly afterwards, the synthetic potential of $\underline{1}$ in organometallic chemistry started to be developed (6).

For a number of years, our own research effort in this area was directed towards two objectives. In the first place, we were interested in the isolation of $\underline{1}$ in pure form in order to study their structure and properties. For instance, the Schlenk equilibrium of $\underline{1}$ could be expected to furnish the previously unknown magnesacycloalkanes $\underline{3}$ (eq. 4).

$$\underset{\underline{1}}{(CH_2)_n\!\!\left\langle\begin{matrix} MgBr \\ MgBr \end{matrix}\right.} \;\;\rightleftharpoons\;\; \underset{\underline{3}}{(CH_2)_n\!\!\left\langle\begin{matrix} \\ \end{matrix}\right. Mg} \; + \; MgBr_2 \qquad (4)$$

A second goal was the synthesis and systematic investigation of di-Grignard reagents with short carbon chains containing less than four aliphatic carbon atoms between the two magnesiums;

<u>4</u>, <u>5</u>, and <u>6</u> are illustrations of such compounds. Two of these, i.e. <u>5</u> (7) and <u>6</u> (8,9), had been reported previously, but their organometallic chemistry had not been explored.

$$BrMgCH_2CR_2CH_2MgBr \qquad\qquad CH_2(MgBr)_2$$

<u>4a</u>: R = H
<u>4b</u>: R = Me

BrMg      MgBr
<u>5</u>

<u>6</u>
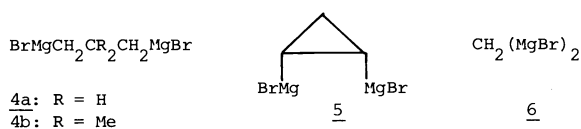
In the following discussion, we will roughly take the descending number of intervening carbon atoms as a guideline.

## II  MAGNESACYCLES

From a combination of eq. 1 and eq. 4, one might conclude that magnesacycles could be obtained from <u>2</u> via <u>1</u> and elimination of magnesium bromide from the latter by the well-known Schlenk procedure, i.e. precipitation of magnesium bromide with dioxane. Although this approach is possible, large amounts of organomagnesium are lost by co-precipitation and the resulting solution is never quite free from (organo)magnesium bromide. In order to obtain pure <u>3</u>, one has to follow a more roundabout route via the organomercurials <u>7</u>, which are converted to <u>3</u> by shaking with magnesium metal in tetrahydrofuran (room temperature, several days)(eq. <u>5</u>).
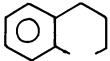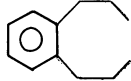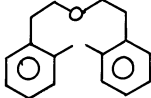


(5)
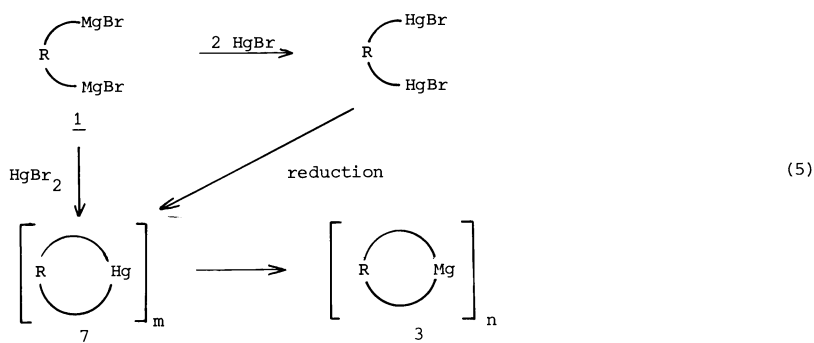
In this way, we have prepared a number of magnesacycles <u>3</u>. An interesting question was whether they were monomeric (eq. 5: n = 1) or more highly aggregated; in other words: are monomeric magnesacyclopentane or magnesacyclohexane capable of existence? Table 1 gives the results of measurements of the empirical degree of association (n in eq. 5) of <u>3</u>.

The results of Table 1 permit a number of interesting conclusions. Contrary to normal monovalent dialkylmagnesiums, which are monomeric in tetrahydrofuran, (cf. diethylmagnesium), magnesacycloalkanes display a strong tendency towards dimerization. A detailed analysis reveals that in different compounds, different structural features are responsible for this behaviour. X-Ray structures of the dimers of <u>3a</u> (12) and <u>3b</u> (16) show the C-Mg-C angle to be rather wide (128° and 141.5°, respectively), which makes the monomeric five- or six-membered ring highly strained, but is easily accommodated in the ten- or twelve-membered ring, respectively, of the dimers. While angle strain is less important in <u>3c</u> and absent in <u>3d</u>, these monomers are disfavoured by the well-known medium-sized ring effect. In the benzo-annelated systems <u>3e</u> and <u>3f</u>, the monomers are increasingly favoured by the absence of antibonding van der Waals interaction compared to <u>3b</u> and <u>3c</u>, respectively: especially in <u>3f</u>, this effect is surprisingly large. It is interesting to point out that due to the rapid exchange between carbon-magnesium bonds, the systems investigated are free to find the energy minimum imposed by geometric and conformational factors by changing their aggregation, which is obviously impossible in e.g. their all-carbon analogs. In contrast to the magnesacycloalkanes proper, the oxygen containing ring systems <u>3g-i</u> occur exclusively as the monomers. This is obviously due to the possibility of forming five-membered (<u>3g</u>) or six-membered (<u>3h</u>, <u>3i</u>) chelate rings. The stabilization due to intramolecular coordination was confirmed by measuring the heat of reaction per carbon-magnesium bond of the magnesacycles with acetic acid. It revealed the expected strain (cf. the footnotes in Table 1) in monomeric <u>3b</u> and <u>3e</u>, slight strain (ca. 11 kJ.mol$^{-1}$) in monomeric <u>3f</u>, and the absence of strain in the dimers of <u>3a</u>, <u>3c</u>, and <u>3d</u> (13). For <u>3g-i</u>, the effects of intramolecular coordination and unfavourable transannular interactions could not be separated, but it could be concluded that the intramolecular oxygen-magnesium bond was stronger than that in the model compound Et$_2$Mg·2 THF (15), even though tetrahydrofuran is a rather strong base towards organomagnesium compounds.

The detailed knowledge of the magnesacycles permitted also interesting conclusions concerning the corresponding di-Grignard reagents <u>1</u> (eq. 4), two of which will be mentioned here. In the first place, the thermodynamic parameters for the Schlenk equilibria are within the limits of error identical for ethylmagnesium bromide ($\Delta H_S$ = 25.6 kJ.mol$^{-1}$, $\Delta S_S$ = 99.2 J.mol$^{-1}$.K$^{-1}$ (17)), <u>1a</u> ($\Delta H_S$ = 31.4 kJ.mol$^{-1}$, $\Delta S_S$ = 123.4 J.mol$^{-1}$.K$^{-1}$ (12)), and <u>1b</u>

TABLE 1.  Degree of association (n) of magnesacycles 3

| Compound | R | n [a] | Ref. |
|---|---|---|---|
| Et$_2$Mg | – | 1 | 10,11 |
| 3a | –(CH$_2$)$_4$– | 2 | 12 |
| 3b | –(CH$_2$)$_5$– | 1-2 [b] | 12,13 |
| 3c | –(CH$_2$)$_6$– | 2 | 13 |
| 3d | –(CH$_2$)$_9$– | 2 | 13 |
| 3e |  | 1-2 [b] | 13 |
| 3f |  | 1 | 13 |
| 3g | –(CH$_2$)$_3$O(CH$_2$)$_3$– | 1 | 14 |
| 3h | –(CH$_2$)$_4$O(CH$_2$)$_4$– | 1 | 15 |
| 3i |  | 1 | 15 |

a. Expressed by quotient of formal concentration of monomer by experimentally determined osmometric concentration. b. Thermodynamic parameters of dimerization: for 3b: $\Delta H = -48.0 \pm 3.0$ kJ.mol$^{-1}$, $\Delta S = -106.0 \pm 10.0$ J.mol$^{-1}$.K$^{-1}$; for 3e: $\Delta H = -48.7 \pm 3.9$ kJ.mol$^{-1}$, $\Delta S = -118.0 \pm 12.0$ J.mol$^{-1}$.K$^{-1}$.

($\Delta H_s = 32.6$ kJ.mol$^{-1}$, $\Delta S_s = 127.6$ J.mol$^{-1}$.K$^{-1}$ (16)). It follows that 1a and 1b are essentially "normal" Grignard reagents, in other words, the influence of the second magnesium center in the molecule on the behaviour of the first one is small, which is in line with the "normal" chemical behaviour of these compounds.

A second conclusion concerns the oxygen containing di-Grignards 1g-i. Association measurements show (14,15) that in tetrahydrofuran solution, these di-Grignards are converted completely to the corresponding dialkylmagnesiums 3g-i, respectively. Apparently, the stabilization of the latter by intramolecular coordination is the driving force for this unusual shift of the Schlenk equilibrium.

## III 1,3-DI-GRIGNARD REAGENTS

We shall discuss the chemistry of 1,3-di-Grignard reagents mainly for the sake of systematics, as the topic has been reviewed recently (18). 1,3-Bis(bromomagnesio)propane (4a) was first prepared by Costa and Whitesides by an elegant, but cumbersome approach which, moreover, gave 4a in low yield and purity (19). A useful application of 4a became possible only after the discovery (20) that it could be prepared directly from 1,3-dibromopropane by slow addition of the dihalide to a large excess of magnesium in diethyl ether; the mediocre yield of ca. 30% 4a is no major obstacle in view of the cheapness of the starting materials; the removal of the side product 1,6-bis(bromomagnesio)hexane (15%), if necessary, can be preformed by extraction with tetrahydrofuran. This treatment affords a pure precipitate with the composition of magnesacyclobutane which, in view of its extremely low solubility, and our experience with higher homologs (see II.), must be oligomeric or polymeric. With one equivalent of magnesium bromide in diethyl ether, 4a is reconstituted and available for further reactions in pure form (eq. 6) (21).
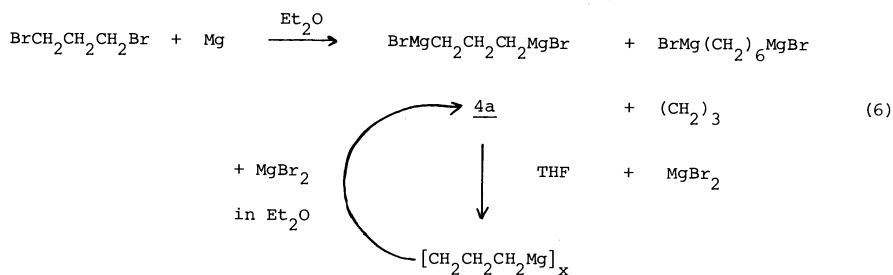


In a similar fashion, the 2,2-dimethyl derivative 4b was prepared (22); the yield of 4b is still lower (ca.18%), but it can directly be used for further applications because it is obtained practically pure from organometallic byproducts (23).

In light of the discussion of section II., it is of interest to point out that <u>4a</u>, like the even shorter homologs (see IV. and V.) have a much higher tendency to disproportionate according to the Schlenk equilibrium (eq. 4); one of the reasons is probably the low solubility of the (oligomeric) diakylmagnesium. Especially in tetrahydrofuran, <u>4a</u> can only be kept in solution in the presence of at least 2 molar equivalents of magnesium bromide which are apparently involved in a complex with <u>4a</u>. In diethyl ether-$d_{10}$, $^1$H NMR spectroscopy revealed the presence of two equivalent (together 90%) and one different (10%) species which have been tentatively assigned the structures <u>4aA</u> and <u>4aB</u> (eq. 7). DNMR furnished the activation parameters $\Delta H^{\ddagger}(1) = 21$ kJ.mol$^{-1}$, $\Delta S^{\ddagger}(1) = -109$ J.mol$^{-1}$.K$^{-1}$ and $\Delta H^{\ddagger}(2) = 28$ kJ.mol$^{-1}$, $\Delta S^{\ddagger}(2) = -117$ J.mol$^{-1}$.K$^{-1}$ for these fast equilibria (24).
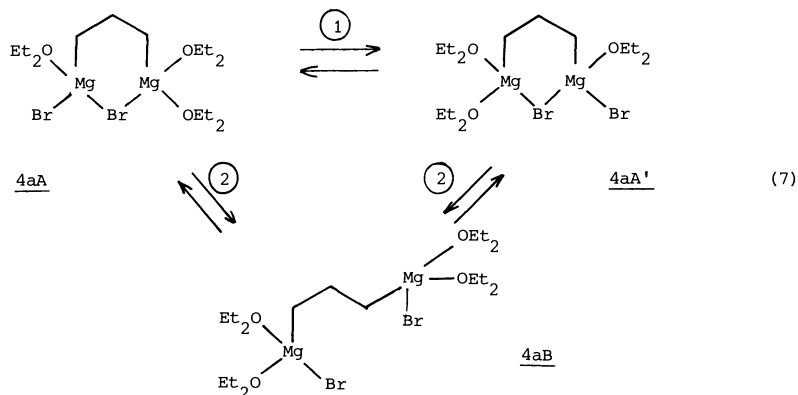


Compound <u>4a</u> and especially <u>4b</u> have been successfully applied in the synthesis of a variety of main group and transition metalorganic compounds (18) such as: 1,3-dimetallopropanes of lithium (22), mercury (20,22) and tin (20); metallacyclobutanes of germanium (21), tin (25), titanium, zirconium, hafnium (26) and vanadium (23) (eq.8).
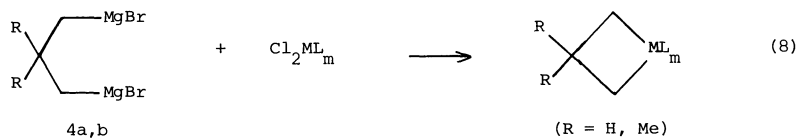


Cyclobutanon was obtained in low yield (13%), but nevertheless in a preparatively attractive fashion by the slow reaction of crude <u>4a</u> with carbon dioxide (eq. 9 (27)).
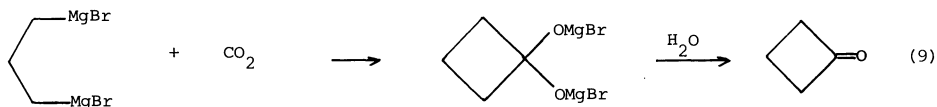


## IV  1,2-DI-GRIGNARD REAGENTS

1,2-Di-Grignard reagents are particularly difficult to synthesize from the corresponding 1,2-dihalides because of the ready elimination of magnesium dihalide (cf. eq. 2). With aromatic 1,2-dihalides, this escape reaction is somewhat retarded, and compounds such as <u>7</u> have been obtained in a round-about fashion by Wittig (28), although direct synthesis with magnesium metal is also possible (29)(eq. 10).
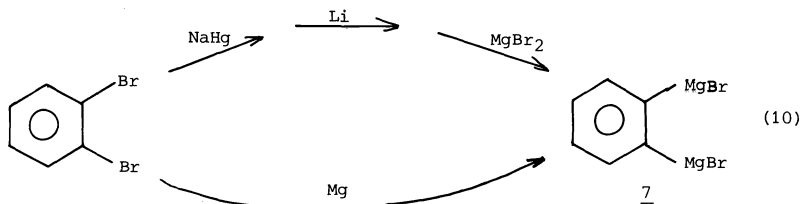


The only case of an aliphatic 1,2-di-Grignard reagent is 1,2-bis(bromomagnesio)cyclopropane (<u>5</u>) which was first prepaired by Wiberg and Bartley (7). We have repeated and extended Wiberg's synthesis and found (30) that from both <u>cis</u>- and <u>trans</u>-1,2-dibromocyclopropane, only the <u>cis</u>-isomer of <u>5</u> is obtained as established from derivatization and from direct observation of <u>5</u> by $^1$H NMR spectroscopy (eq. 11). The yield of <u>5</u> is low (ca. 10%); the elimination product according to eq. 2, i.e. cyclopropene, is the main product. Still, it is remarkable that <u>5</u> is formed at all, as the vicinal combination of an electropositive

$$(11)$$
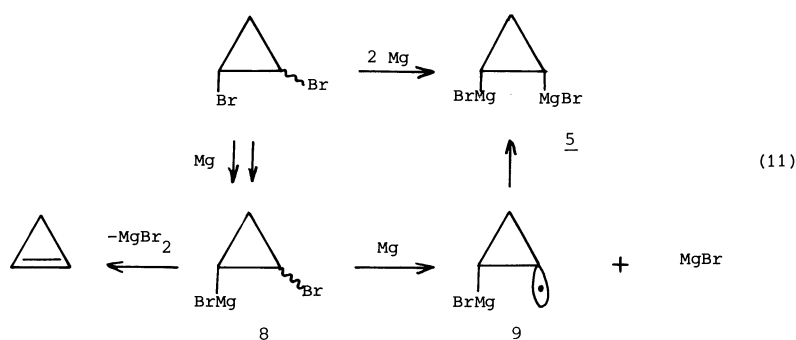
metal and a halogen as in the presumable intermediate $\underline{8}$ is known to be extremely prone towards elimination. Undoubtedly, the fact that $\underline{8}$ survives sufficiently long to undergo the second Grignard formation step to $\underline{5}$ is due to the high strain of the elimination product cyclopropene. The cis-configuration of $\underline{5}$ is probably determined by the preference of the final intermediate radical $\underline{9}$ for the cis-configuration; this is supported by theoretical calculations (31).

Due to the fortunate circumstance that $\underline{5}$ is sparingly soluble in diethyl ether, it could be isolated in pure form. Reminiscent of $\underline{4a}$ is the observation that the solubility of $\underline{5}$ increases on addition of magnesium bromide; again, this indicates complex formation which is probably aided by bridging between the two organomagnesium functions closely arranged next to each other (cf. structure $\underline{4aA}$). Similarly, tetrahydrofuran disproportionates $\underline{5}$ to give a precipitate of the halogen-free dialkylmagnesium which is(at least)oligomeric and dissolves only in HMPT.

## V  1,1-DI-GRIGNARD REAGENTS

The methylene-di-Grignard reagent can be prepared from dibromo- or diiodomethane. It was first described in 1926 by Emschwiller (8) and has been studied by Cainelli et al in view of its use as a Wittig-type carbonyl-methylenation reagent (9). Until recently, it seemed essential to use dilute magnesium amalgam (0.5-1%), and diethyl ether/benzene 1:1 as a solvent (9, 32). We found now that methylenedimagnesium dibromide ($\underline{6}$) can conveniently be prepared from dibromo-methane and magnesium amalgam using di-isopropyl ether; the sometimes disturbing byproduct me-thylmagnesium bromide dissolves, and a slurry of (pure) $\underline{6}$ and magnesium bromide is obtained in 60-80% yield; after decantation, it is dissolved in diethyl ether/benzene 1:1 (33)(eq. 12).

$$CH_2Br_2 + Mg/Hg \xrightarrow{\ (i\text{-}Pr)_2O\ } CH_2(MgBr)_2\downarrow \qquad (12)$$

$$\underline{6}$$
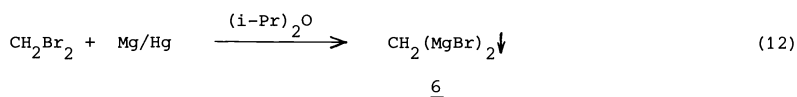
With $\underline{4a}$ and $\underline{5}$, $\underline{6}$ shares the tendency to elimi-nate magnesium bromide and to form polymeric, sparingly soluble solids which approximate the composition of $(MgCH_2)_n$, although in this case, it is difficult to remove all the magnesium bromide which may be due to the formation of mixed complexes such as $\underline{10}$ (32).
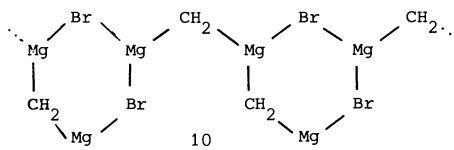


Compound $\underline{6}$ reacts with $Cp_2TiCl_2$ to give $\underline{11}$ (eq. 13) which is an analog of Tebbe's reagent $Cp_2TiCH_2 \cdot AlClMe_2$ ($\underline{12}$) (34) and Eisch's compound $Cp_2TiCH_2 \cdot ZnX_2$ ($\underline{13}$)(35). All these "metal car-bene complexes" react e.g. with alkenes to give titanacyclobutanes ($\underline{14}$); their thermal stability seems to decrease in the sequence $\underline{12} > \underline{13} > \underline{11}$, parallel with increasing electropositivity of the main group metal (36).



$$(13)$$
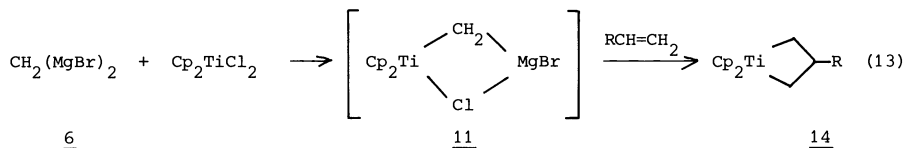
Particularly promising is the use of $\underline{6}$ in the synthesis of 1,3-dimetallacyclobutanes. This has been illustrated for main group and transition metals of group 14 and 4, respectively. Reaction of $\underline{6}$ with $Me_2GeCl_2$ gave $\underline{15a}$ (together with the higher homologous ring systems $\underline{16a}$ and $\underline{17a}$); $Me_2SnCl_2$ furnished only $\underline{16b}$ and $\underline{17b}$ (eq. 14 (32)).



$$(14)$$

a: M = Ge; b: M = Sn
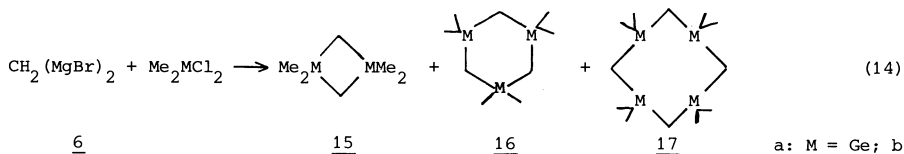
Reaction of $Cp_2TiCl_2$ with 2 molar equivalents of 6 gave the versatile intermediate 18, which is formally a 1,3-di-Grignard reagent!It has been converted to mixed 1,3-dimetallacyclo-butanes 19 of group 4/group 14 (37) or 20 of group 4 (38), respectively (eq. 15).



19a: M = Si

19b: M = Ge

19c: M = Sn

20a: M = Ti

20b: M = Zr

20c: M = Hf
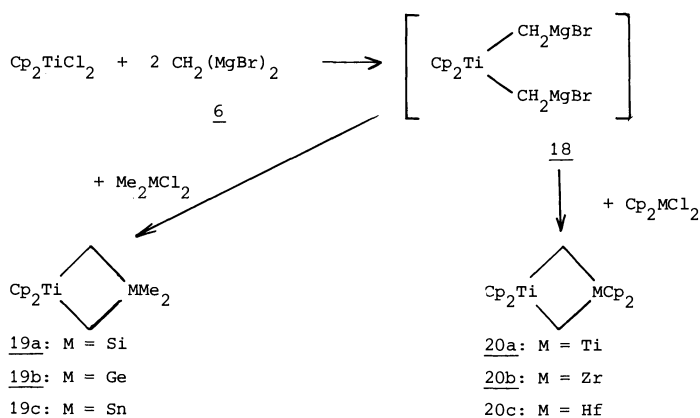
In a similar fashion to $Cp_2TiCl_2$, $Cp_2ZrCl_2$ and $Cp_2HfCl_2$ have been converted to the 1,3-di--Grignard reagents corresponding to 18 and further to all possible analogs of 20 (39).

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