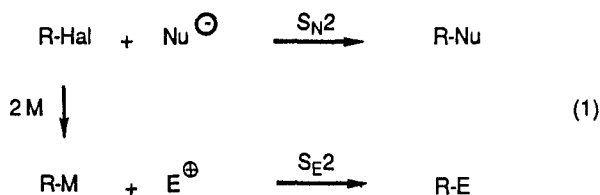# New trends in dimetallic synthons

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Abstract - In principle, organic molecules bearing two reactive organometallic functionalities are valuable synthons for the introduction of the organic moiety as a bifunctional *nucleophilic* reagent; in this regard, they supplement the better known and more widely applied organic dihalides (or their equivalents), which find use as bifunctional *electrophilic* reagents. While a number of simple larger dimetallic species have been known and applied for a long time, much less was known until recently on *small* dimetallic species in which the organometallic functions are separated by one, two, or three carbon atoms only. We have been engaged in a programme to make such small dimetallic species available, in particular in the field of 1,1-, 1,2- and 1,3-di-Grignard reagents and, to a lesser extent, their dilithio analogues. Up till now, a large part of our effort has been devoted to the development of these reagents, either by improving known syntheses or, in many cases, by making the reagents accessible for the first time. The synthetic utility of these reagents has been demonstrated by a broad range of novel organometallic compounds; the exploration of purely organic applications has also been initiated.
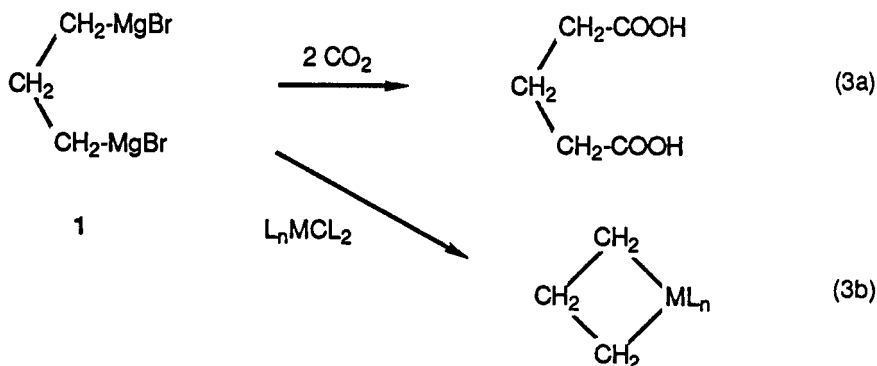
INTRODUCTION

In preparative chemistry, the organometallic compounds of the more electrophilic metals are used essentially as *nucleophilic* synthons. In this regard, they complement the organic halides, in particular the aliphatic halides, the organic rest of which is a wellknown *electrophilic* synthon in the S_N1 or S_N2 reactions. As organometallic compounds, especially those of the synthetically important organolithiums and organomagnesiums, are most often prepared from the corresponding organic halide, the latter is the starting material for important preparative applications either directly (S_N reactions) or indirectly via umpolung to the organometallic reagent followed by S_E2 reaction (eq. 1)

$$R\text{-Hal} \quad + \quad Nu^{\ominus} \quad \xrightarrow{\;S_N2\;} \quad R\text{-Nu}$$

$$2M \downarrow \qquad\qquad\qquad\qquad\qquad (1)$$

$$R\text{-M} \quad + \quad E^{\oplus} \quad \xrightarrow{\;S_E2\;} \quad R\text{-E}$$

In principle, this concept is easily transferred from mono- to di- or polyvalent organic halides. There are numerous examples of their use in nucleophilic substitutions as exemplified by a synthesis of adiponitrile (eq. 2).

$$Br\text{-}CH_2CH_2CH_2CH_2\text{-}Br \quad + \quad 2\,CN^- \quad \rightarrow \quad NC\text{-}CH_2CH_2CH_2CH_2\text{-}CN \qquad (2)$$
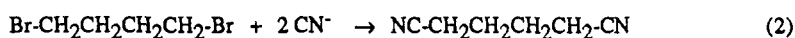
For the corresponding dilithium or di-Grignard reagents, a large number of analogous applications are known. Of special interest is the possibility of reacting not only monovalent, but also divalent electrophiles with the diorganometallic reagent. This is illustrated for the 1,3-di-Grignard reagent 1 of propane: reaction with CO_2 as a *monovalent* electrophile gives the bifunctional product glutaric acid (eq. 3a), while with a metal dihalide as a *divalent* electrophile (eq. 3b), the formation of a four-membered metallacycle is expected.

$$\underset{\textbf{1}}{\overset{\displaystyle CH_2\text{-MgBr}}{\underset{\displaystyle CH_2\text{-MgBr}}{CH_2}}} \quad \xrightarrow{\; 2\,CO_2 \;} \quad \underset{\displaystyle CH_2\text{-COOH}}{\overset{\displaystyle CH_2\text{-COOH}}{CH_2}} \tag{3a}$$

$$\xrightarrow{\; L_nMCL_2 \;} \quad \underset{\displaystyle CH_2}{\overset{\displaystyle CH_2}{\underset{\displaystyle CH_2}{CH_2}}}ML_n \tag{3b}$$

RESULTS AND DISCUSSION

For the higher homologues of 1 having four or more carbon atoms between the metals, both types of reactions are amply documented (1-3). However, for 1 and other (aliphatic) 1,3-dimetallic reagents, these simple reactions were unknown for the trivial reason that such compounds were not known or exceedingly difficult to prepare (4). In recent years, we have succeeded (3) in preparing 1, its substituted derivative 2 (5), the analogues 3 (6) and 4 (7) as well as smaller homologues such as the 1,2-di-Grignard reagents 5 (8,9) and 6 (10) and the 1,1-di-Grignard reagents 7 (11-13), 8 (14) and 9 (15). In most cases, it was possible to apply the original Grignard approach starting from the readily available organic dihalides and magnesium (3); the best results were obtained with a special, sublimed form of the metal (6).
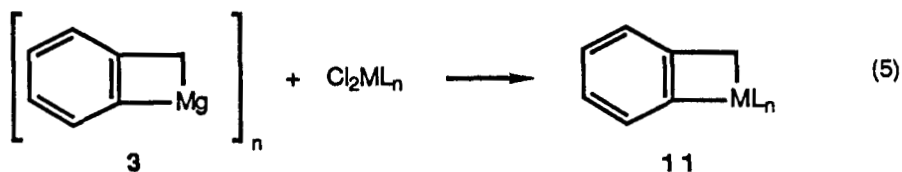

2

3

4

BrMg-CH₂CH₂-MgBr

5

6

7 : R' = R" = H
8 : R' = Me₃Si, R" = H
9 : R' = R" = Me₃Si
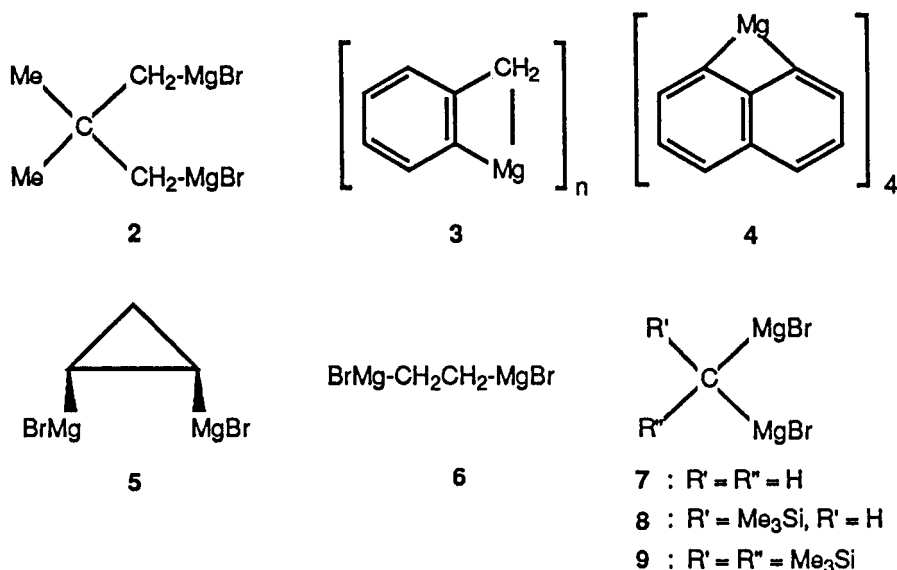
The new or improved short dimetallic reagents 1-4 and 6-9 open up interesting possibilities as synthons both in organic and in organometallic synthesis; 5 and 6 are still difficult to prepare in useful yields. So far, the of applications in organometallic chemistry have received most of our attention, both for the preparation of main group and transition metal organic analogues and small metallacycles. A few examples will suffice to illustrate the scope of this approach which still has by no means been fully explored.
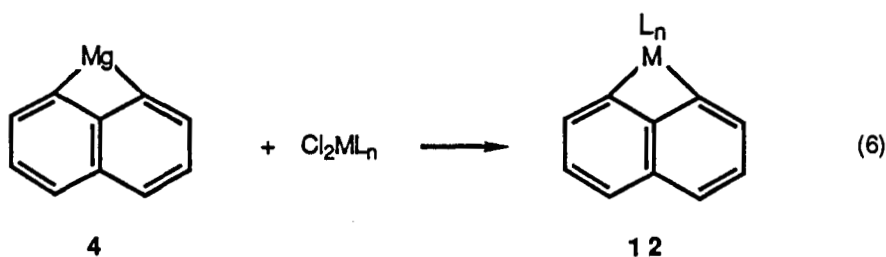
It turned out, for instance, that the principle of cyclization of di-Grignard reagents with metal dihalides to metallacycles works nicely for the 1,3-di-Grignard reagents (or their corresponding diorganylmagnesiums) 1-4 to furnish (derivatives of) metallacyclobutanes (cf. eq. 3b):
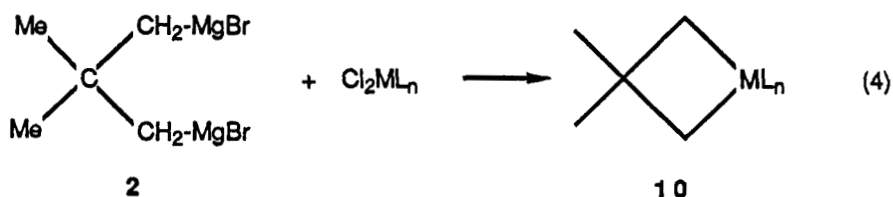
$$M = \text{Ge, Sn, Ti, } \mathbf{Zr, Hf, V, Mo, W, Re, Rh,} \text{ (Ni ?, } \mathbf{Pd} \text{ ?), } \mathbf{Pt}$$

(4)

$$M = \text{Si, } \mathbf{Ge,} \text{ (Sn ?),} \mathbf{Tl, Zr, Hf, Mo, W, Re, Rh,} \mathbf{Pt}$$

(5)

$$M = \mathbf{Ge, Tl,} \mathbf{Pt}$$

(6)

It is beyond the scope of this paper to discuss all these reactions in detail. The four-membered metallacycles of the metals shown in **bold** (eq. 4-6) were prepared for the first time by this diorganometallic approach; it thus appears to be a rather general one (3). In a few cases, the corresponding diorganolithiums have also been used, especially in the case of 4. Sometimes, instead of or besides the four-membered ring product, the dimeric eight-membered or higher homologues are formed. Illustrative is the example of 4 · 4 THF which itself has a unique tetrameric structure both in solution and in the crystal: each magnesium atom is single bonded to one naphthalene, and bridges two others; the molecule has S_4 symmetry and may be considered to consist of two dimeric subunits with eight-membered rings which are connected by four bridging magnesiums.
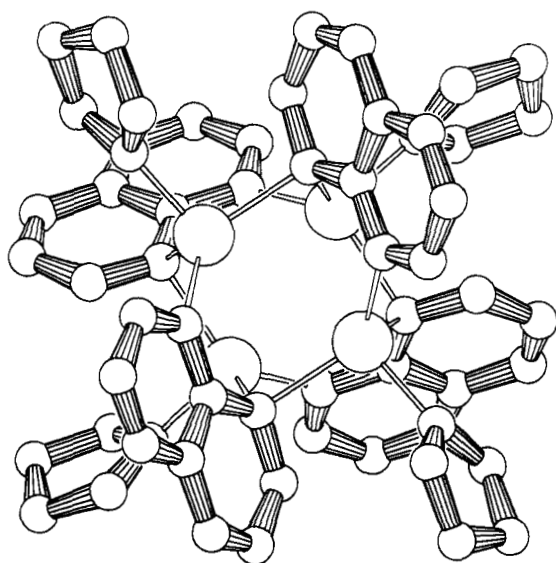

4

From **4** or its dilithio derivative, the monomeric **12** have been obtained for $ML_n=CH_2$ (**16**), $SiMe_2$ (**17**), $GeMe_2$, $TiCp_2$ and $Pt(PPh_3)$ (**7**); the dimetallic eight-membered dimers were formed for $ML_n=GeMe_2$ (**7**), $SnMe_2$ (**18**) and Hg (**19**).

A great deal of interest in metallacyclobutanes stems from their being intermediates in olefin metathesis, a reaction of both theoretical and practical importance (**20**). The direct approach to such - often evasive ! - intermediates by the 1,3-diorganometallic route promises more insight in the mechanism of this reaction.
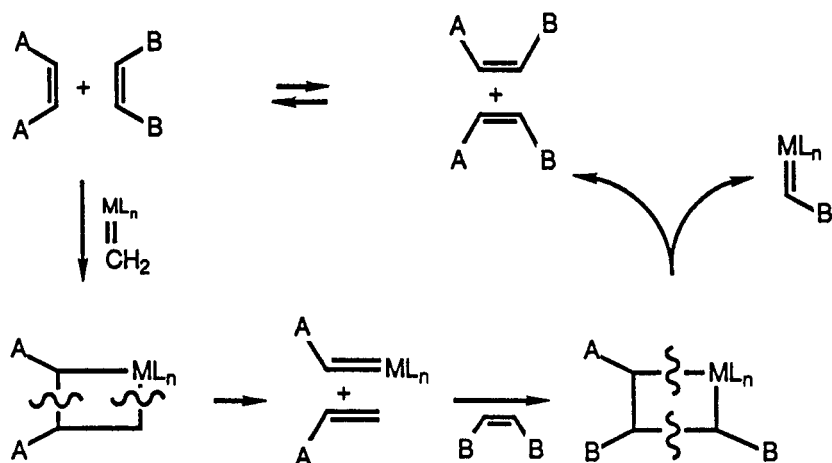
Another interesting class of intermediates in this reaction are the metal-carbene complexes (or metallaalkenes) $L_nM=CH_2$ etc., which are often quite unstable and e.g. dimerize to 1,3-dimetallacyclobutanes **13** (eq. 7).
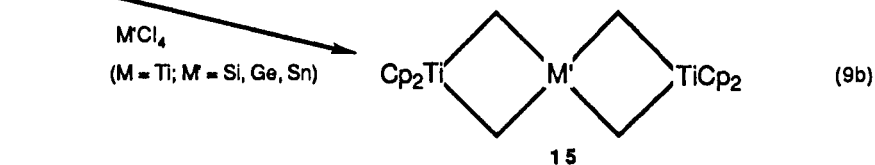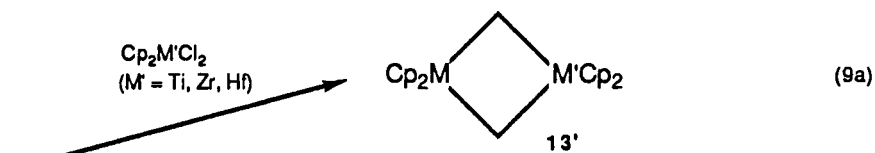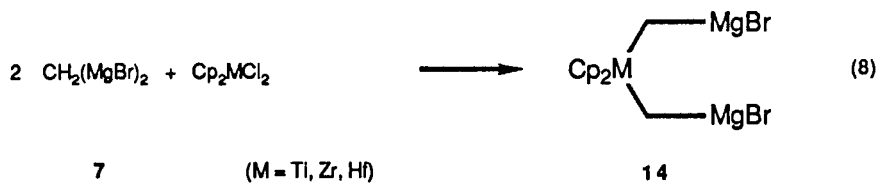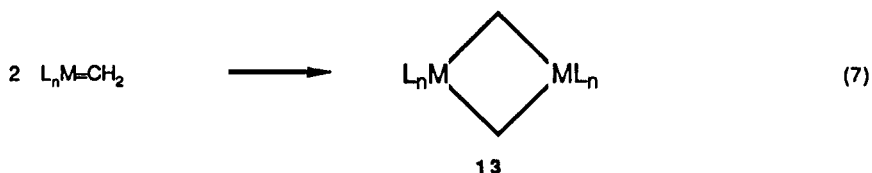
Such dimetallacyclobutanes can also be obtained from the 1,1-di-Grignard reagents **7** and **8** by the route shown in eq. 8 and 9; not o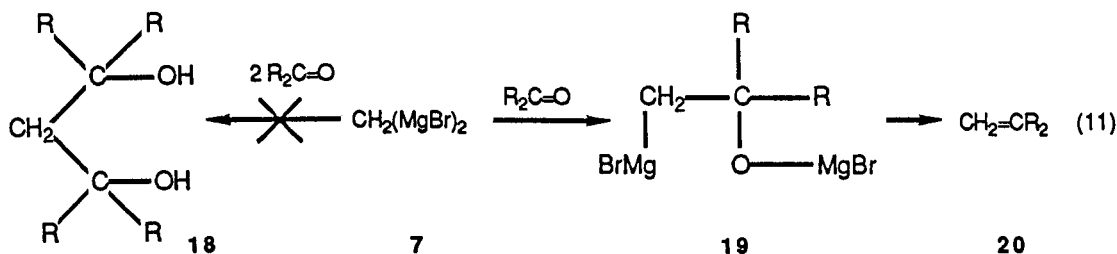nly symmetrical **13** with the same metal are thus available, but also unsymmetrical **13'** (eq. 9a) and interesting spiro compounds **15** (eq. 9b) and **16** (eq. 10) (21-25). Even free, phosphine stabilized metal carbene complexes **17** have been prepared from **7** (eq. 10) (25).

$$Cp_2TiCl \ + \ CH_2(MgBr)_2 \ \rightleftharpoons \ Cp_2Ti \overset{Br}{\underset{Br}{\diamondsuit}} Mg \overset{Br}{\diamondsuit} TiCp_2 \ \xrightarrow{PMe_3} \ Cp_2Ti=CH_2 \qquad (10)$$

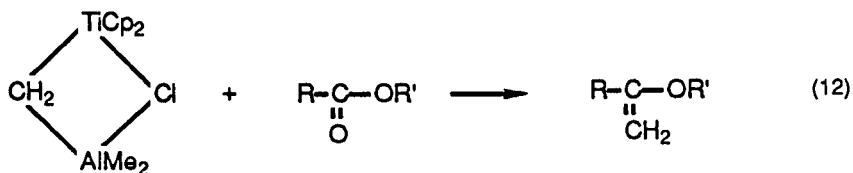$$\textbf{7} \qquad\qquad\qquad \textbf{15} \qquad\qquad\qquad \textbf{16}$$
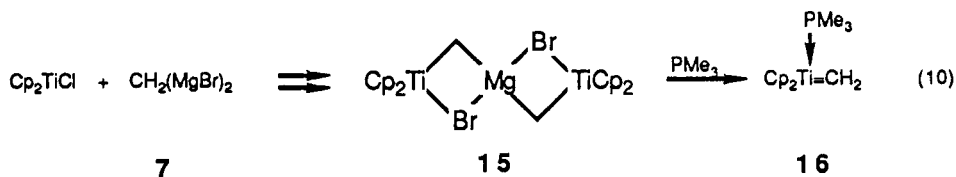
Successful as this approach may appear, it has, of course, some limitations: some of the four-membered metallacycles are just not sufficiently stable as such under the conditions of their formatiom, for instance **10** (M = Ni; Pd) or **11** (M = Sn); in some cases, especially with **1** as starting material, the rapid decomposition of half-reacted intermediates such as $BrMg\text{-}CH_2CH_2CH_2\text{-}ML_n$ may be detrimental (3).

Similar reservations are appropriate for the application of short dimetallic synthons in purely organic synthesis. This area is just beginning to be investigated, and several useful possibilities have been found, but again, some limitations have become apparent, too.

The most simple short di-Grignard reagent, the methylene di-Grignard **7**, has been the first one to be discovered (in 1926 (11)), and its utility has been explored by several authors, especially by Cainelli et al. (12). It was never found to react with two carbonyl compounds to give the diadduct **18**, because the intermediate addition product **19** rapidly eliminates magnesium oxide bromide to give the Wittig-type carbonyl olefination product **20** (eq. 11).

$$R_2C(OH) \cdots CH_2 \cdots C R_2(OH) \quad \overset{2R_2C=O}{\underset{\times}{\longleftarrow}} \quad CH_2(MgBr)_2 \quad \xrightarrow{R_2C=O} \quad CH_2\text{-}\underset{O\text{---}MgBr}{\overset{R}{\underset{|}{C}}}\text{-}R \quad \longrightarrow \quad CH_2=CR_2 \qquad (11)$$

$$\textbf{18} \qquad\qquad \textbf{7} \qquad\qquad\qquad \textbf{19} \qquad\qquad \textbf{20}$$
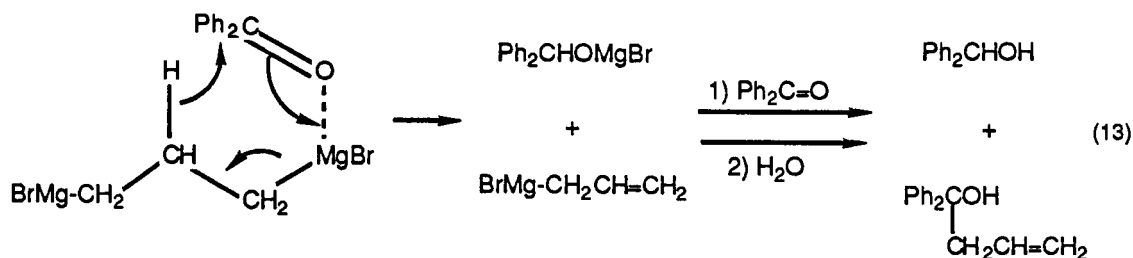
In our experience, this is not only caused by the explosive combination of a strongly carbanionic center with a leaving group in **19** (although in this case, it is admittedly a rather poor one !), but also to the fact that this carbanionic center carries *two* electropositive metals. It seems to be a rather general phenomenon that the reactivity of a carbanion is reduced when it is substituted by two or more metals. Thus, in competiton experiments, **7** clearly looses from CH_3MgBr; this trend continues from **7** via **8** to **9**, so that the latter reacts only slowly with benzaldehyde and hardly with benzophenon (15). Nevertheless, useful applications of 1,1-dimetallic reagents are possible; another illustration is the preparation of enol ethers from esters with Tebbe's reagent (26) (eq. 12).

$$CH_2 \overset{TiCp_2}{\underset{AlMe_2}{\diamondsuit}} Cl \ + \ R\text{-}\underset{O}{\overset{||}{C}}\text{-}OR' \ \longrightarrow \ R\text{-}\underset{CH_2}{\overset{||}{C}}\text{-}OR' \qquad (12)$$

Organic reactions of 1,2-dimetallics such as **5** and **6** have not yet been investigated because of the difficult accessibility of these reagents.
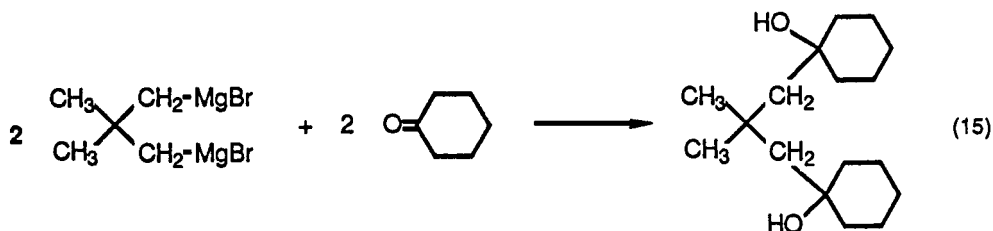
Organic applications of **1** are limited to reactions with hard electrophiles; towards soft electrophiles, such as ketones, the β-hydride reduction, known as a side reaction in ordinary Grignard chemistry, dominates completely (eq. 13).

$$\text{(structure)} \longrightarrow \quad Ph_2CHOMgBr \quad + \quad BrMg\text{-}CH_2CH\text{=}CH_2 \quad \xrightarrow[\text{2) } H_2O]{\text{1) } Ph_2C\text{=}O} \quad Ph_2CHOH \ + \ Ph_2\underset{\underset{\displaystyle CH_2CH\text{=}CH_2}{|}}{C}OH \qquad (13)$$
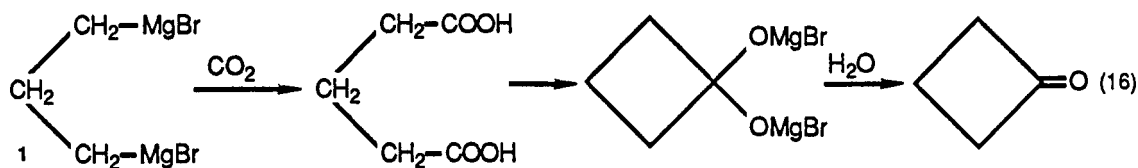
This abnormal reactivity of **1** is caused by the strong hydridic activation of the β-hydrogen from the carbanionic centers on both sides; even pure **1** in THF solution slowly decomposes by elimination of magnesium hydride (half life about 100 days) (eq. 14); the reaction is catalyzed by additional magnesium bromide.

$$\textbf{1} \quad BrMg\text{-}CH_2CHCH_2\text{-}MgBr \longrightarrow BrMg\text{-}CH_2CH\text{=}CH_2 \ + \ HMgBr \qquad (14)$$
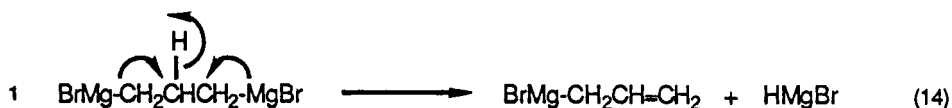
1,3-Di-Grignard reagents without this complicating β-hydrogen behave quite normal towards carbonyl compounds and give 1,5-diols as illustrated for **2** in eq. 15 (3).

$$\textbf{2} \quad \underset{CH_3}{\overset{CH_3}{>}}\!C\!\underset{CH_2\text{-}MgBr}{\overset{CH_2\text{-}MgBr}{<}} \ + \ 2 \ O\!=\!\bigcirc \longrightarrow \text{(diol structure)} \qquad (15)$$

When hard electrophiles such as metal salts or CO_2 are reacted with **1**, the β-hydride elimination is not important. Thus, an excess of CO_2 reacts with **1** to give glutaric acid (eq. 3a); more interestingly, slow addition of gaseous CO_2 leads to the formation of 40 % cyclobutanon in one of the most attractive syntheses of this simple compound (27) (eq.16).

$$\text{(structure)} \xrightarrow{CO_2} \text{(structure)} \longrightarrow \text{(structure)} \xrightarrow{H_2O} \text{(structure)}\!=\!O \qquad (16)$$

Sometimes, complications may arise from intramolecular complexation after reaction of the first organometallic function, as illustrated for **3** in eq.17 (28). With ketones, the reaction stops at the stage of **21** even in the presence of an excess of the ketone; only under the influence of magnesium bromide, the chelate ring is opened and further reaction to **22** (and finally to the isochromane **23**) is facilitated.

3   **21**   (17)

22   **23**
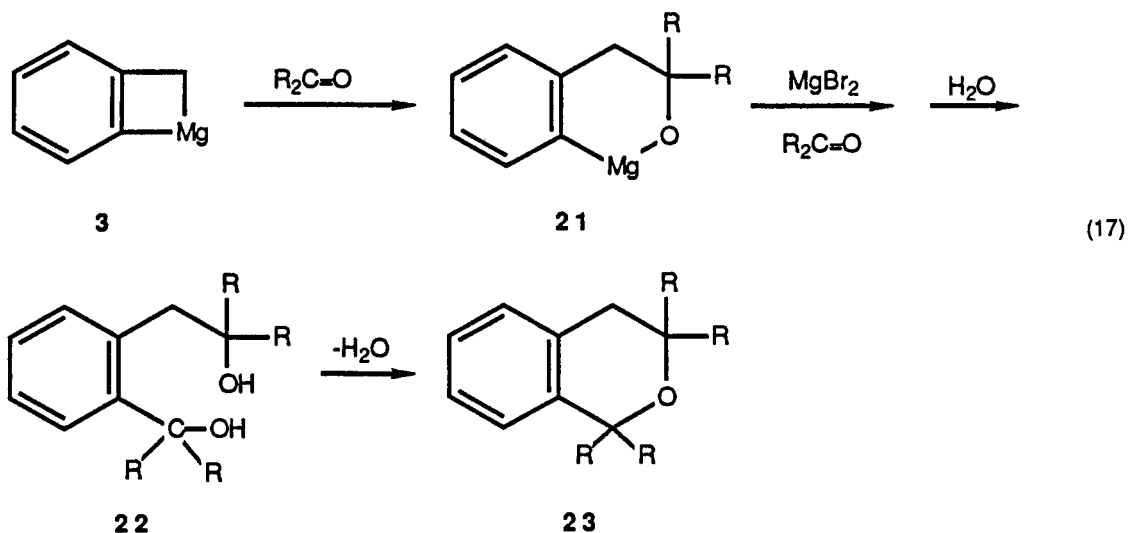
As another example of synthetic applications, the conversion of **4** and of its dilithium analogue to $1H$-cyclobuta[de]naphthalene (**12**, $ML_n = CH_2$) by Shechter et al. (16) has already been pointed out (eq. 6).

CONCLUSION

Short di-Grignard reagents and their analogues with one to three carbon atoms between the organometallic functions have become available with reasonable ease. They, and the transition metal derivatives accessible through them, have shown sufficient promise to warrant further exploration of their synthetic and catalytic potential.

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