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# gem-DIMETALLIC COMPOUNDS. A "WITTIG" REACTION OF METHYLENE MAGNESIUM HALIDES. A SIMPLE METHOD TO OBTAIN METHYLENIC OLEFINS FROM ALDEHYDES AND KETONES.

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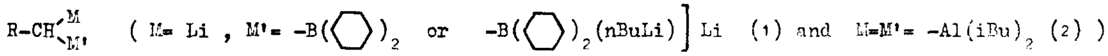
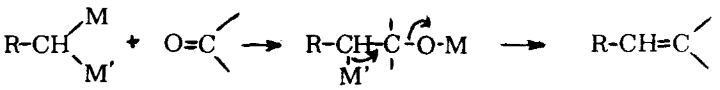
Recently we reported that gem-organometallic compounds of general formula:



$R\text{-}CH{<}^{M}_{M'}$ ( M= Li , M'= $-B(⬡)_2$ or $\left.-B(⬡)_2(nBuLi)\right]$ Li (1) and M=M'= $-Al(iBu)_2$ (2) )

react with aldehydes and ketones to give olefins very probably according to an addition-elimination sequence (3) :



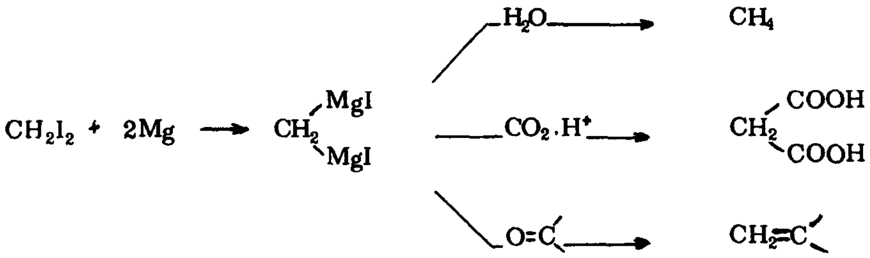
The results of this investigation led us to assume that a "Wittig like" olefination reaction of the above type could be obtained by using other gem-organometallic compounds containing at least one carbon metal bond capable of addition to a carbonyl group.

We wish, now, to report a simple new method of methylenation of aldehydes and ketones with a methylene magnesium halide.

Methylene magnesium bromide and iodide have been prepared previously from the corresponding methylene halides and magnesium (4). The reactivity of these compounds toward carbonyls has been reported to be exceptionally low (4).

We have now found that treatment of methylene iodide with magnesium amalgam (or, less conveniently, magnesium turnings) at room temperature in ether-benzene 1:1 affords in ca. 60% yield, stable 0,2 Molar solutions of methylene magnesium iodide which reacts with water to give methane and with aldehydes and ketones affording the product of substitution of the carbonyl group by a methylene in good yields.

The gem-dimetallic nature of this Grignard reagent has been confirmed by carbonatation which led to malonic acid in substantial yield:



For preparative purposes, it is convenient to prepare the reagent in situ. The reaction is simply carried out by adding, slowly, an ether solution containing equimolecular amounts of methylene bromide or iodide and the carbonyl compound to an excess of magnesium turnings covered by a small quantity of ether. A few minutes at reflux temperature completes the process. The use of magnesium amalgam affords, in general, better and more reproducible results than magnesium turnings. With this modification average yields of 70% are typical. A choice of experimental results is summarized in table I.

TABLE I

Olefins from the reaction of methylene halides and magnesium with carbonyls compounds.

| Carbonyl compound | Olefin obtained | Yield % |
|---|---|---|
| Dodecanal | 1-Tridecene | 65,[a] 60[b] |
| Benzaldehyde | Styrene | 70[a] |
| p-Chlorobenzaldehyde | p-Chlorostyrene | 80[a] |
| 6-Undecanone | 1,1-Di-n-amyl-ethylene | 30[b] |
| Cyclohexanone | Methylencyclohexane | 68[a], 63[e] |
| Benzophenone | 1,1-Diphenylethylene | 40[a], 30[b] |
| 5α-Cholestan-3-one | 3-Methylene-5α-cholestane | 67[a],35[b],22[d],52[e] |
| Cholest-4-en-3-one | 3-Methylene-cholest-4-ene | 70[a],33[b] |
| Pregn-5-en-3β-ol-20-one | Pregn- 5 -en-3β-ol-20-methylene | 80[a,c] |
| Androst-5-en-3β-ol-17-one | Androst-5-en-3β-ol-17-methylene | 45[a,c] |

[a] With magnesium amalgam. [b] With magnesium turnings. [c] Three moles of $CH_2I_2$ and six moles of Mg were employed per mole of carbonyl compound. [d] Magnesium amalgam, tetrahydrofuran as solvent. [e] $CH_2Br_2$ instead of $CH_2I_2$.

Product identification was carried out either by direct comparison with authentic material or by proton n.m.r., ultraviolet, infrared and mass spectra and elemental analysis.

The solvent seems to influence the reaction markedly, e.g. the use of tetrahydrofuran or dimetoxyethane instead of ethyl ether greatly reduces the yields. In this case other products are formed wich are currently under investigation in our laboratory.

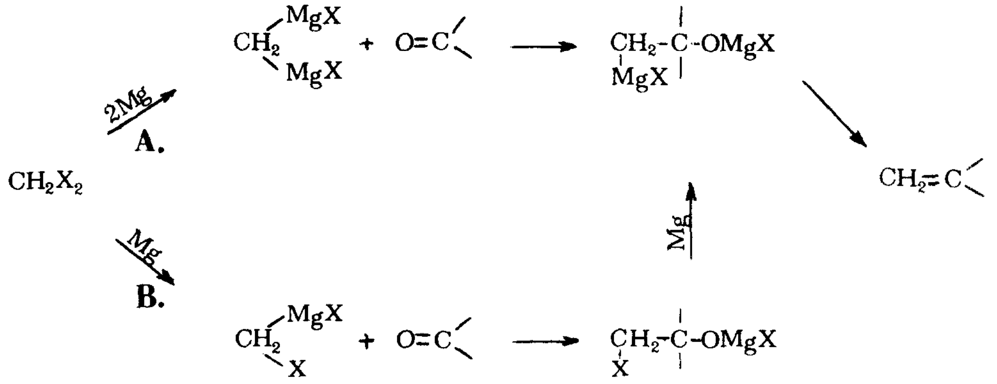
In a typical experimental procedure a solution of 0,25 mole of the carbonyl compound ( for instance cyclohexanone) and 0,26 mole of methylene bromide or iodide in 100 ml of ether was added dropwise over 2 hours to a stirred suspension of magnesium amalgam ( 0,5 g atom of magnesium in 400 g of mercury (5) ) in 100 ml of ether under argon. After 30 minutes reflux, the usual work up of the reaction mixture followed by chromatographic purification or distillation led finally to the olefins.

Use of a large excess of methylene halide should be avoided as the resulting olefin may, in this case, be contaminated with other products probably arising from an attack on the olefinic double bond by a carbenoidic species, perhaps $X\text{-}CH_2\text{-}MgX$.

Thus, in the case of 5α-cholestan-3-one a certain, variable, amount of the corresponding 3-spyrocyclopropane is detected when working with a large excess of methylene iodide and magnesium turnings.

As shown in table I, the reaction has already been applied to a number of different carbonyl compounds varying from simple alkyl derivatives to steroids. α,β- unsaturated ketones in certain cases react normally ( e.g. cholest-4-en-3-one ); others, however, show anomalous ( i.e. 1:4 ) addition of the reagent and these require further investigation.

Hydroxyl groups seem to be compatible with the reaction, provided that an additional mole of methylene halide and two g-atoms of magnesium for hydroxyl group are employed. The behavior of other characteristic groups towards the reagent is at present under investigation in our laboratory.



X= Br or I

The formation of methylene compounds from the carbonyl derivatives may be logically explained as resulting from the addition of the methylene magnesium halide to the carbonyl function followed by elimination (6) (route A).

In the case of the reagent prepared in situ an alternative sequence involving the attack of a α -halomethyl-Grignard reagent followed by the magnesium induced elimination of halohydrin derivative can be considered (route B) .

Work is in progress in our laboratory in order to study all synthetic possibilities of this and related gem-dimagnesium compounds and to further investigate this interesting and promising field.

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## REFERENCES

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2. G.Cainelli,F.Bertini,P.Grasselli,G.Zubiani, Tetrahedron Letters 1581 (1967)
3. In this scheme should be included, at least formally, the α-metallated PO-compounds which are known to olefinate carbonyls. cfr. for instance:
   L. Horner,H.Hoffmann,W.Klink,H.Ertel and V.G.Toscano Ber 95 581 (1962)
   E.G.Corey and G.T.Kwiatowsk J.Am.Chem.Soc. 88 5652 (1966)
4. cfr. for instance: D.A.Fidler,J.R.Jones,S.L.Clark,H.Stange J.Am.Chem.Soc.77 6634 (1955)
5. The concentration of the magnesium amalgam does not appear to be critical. We have prepared a suitable material simply by stirring for a few hours under argon 200-400 g of mercury with the necessary quantity ( not more than a half g atom per 400 g of Hg ) of magnesium turnings.
6. This route parallels closely that proposed for the hydroxyl assisted methylenation of 17β-acetoxy-11β-hydroxyester-5(10)-en-3-one with a reagent obtained by refluxing a large excess of zinc-copper couple with methylene iodide in ether solution cfr.:
   P.Turnbull,K.Syhora,J.H.Fried, J.Am.Chem.Soc. 88 4764 (1966)