A Snippet of Grignard Reagent's Histroy

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There are very few reagents in organic chemistry which equal Grignard reagents in the number of transformations they undergo. They react with almost all functional groups that have an electrophilic centre. They are often the best starting compounds to prepare other organomatallic compounds, particularly organocadmium, organocopper and organosilicon compounds. Even after more than 110 years of their discovery the Grignard reagents not only find use in known reactions, but they are also actively researched to find newer applications and to get better insight into the mechanistic pathways of their reactions.

Organomagnesium halides, as every chemist knows, are called Grignard reagents. However, the first organomagnesium halide, phenylmagnesium bromide, was actually prepared by Herman Fleck of Philadelphia in 1890 by reacting diphenylmagnesium with bromine, (eq.1). But he failed to notice the formation of phenylmagnesium bromide, because he was using excess bromine which destroyed it. Hence, he could isolate only bromobenzene, (eq.2). Had he used only one molar equivalent of bromine, perhaps the organomagnesium reagent would bear his name today. (Luck favours the prepared mind: Louis Pastuer).

$$(Ph)_2Mg + Br_2 \longrightarrow PhMgBr + PhBr \quad (1)$$

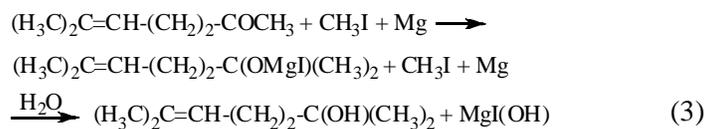$$PhMgBr + Br_2 \longrightarrow PhBr + MgBr_2 \quad (2)$$

Victor Grignard was born at Cherbourg in France on May 6, 1871. He joined in 1894 as an assistant to Phillippe Barbier at Lyon. Barbier was interested in the preparations of tertiary carbinols from organozinc compounds and ketones. As the reaction with organozinc compounds was sluggish, he replaced zinc with more reactive magnesium. In a simple experiment he covered magnesium with an ether solution of methyl iodide and then slowly added methylheptenone. Subsequent hydrolysis gave the carbinol. He formulated the reaction as given in equation (3).

$(H_3C)_2C=CH-(CH_2)_2-COCH_3 + CH_3I + Mg \longrightarrow$

$(H_3C)_2C=CH-(CH_2)_2-C(OMgI)(CH_3)_2 + CH_3I + Mg$

$\xrightarrow{H_2O} (H_3C)_2C=CH-(CH_2)_2-C(OH)(CH_3)_2 + MgI(OH)$ (3)

The reaction was not dependable and yields were not satisfactory. Grignard suggested the possibility of preparing RMgX and then reacting it with the ketone to get the carbinol. As personal initiative was not encouraged the suggestion was ignored by Barbier. Two years later in 1900, when Grignard sought a thesis subject Barbier suggested to him to take up the study of magnesium. As the one-pot reaction did not give satisfactory results, Grignard tried the direct and separate preparation of an organomagnesium halide and then react it with ketone, which, a two-step procedure, turned out successful. When he demonstrated a test-tube preparation to Barbier, he was congratulated for this original discovery. The formation of an organomagnesium halide in the presence of a reactant is known as Barbier procedure, while the two-step reaction is called Grignard reaction. The importance of Grignard's discovery was recognised by the award of Chemistry Nobel Prize in 1912 along with Paul Sabatier.

Grignard succeeded Barbier in 1919 as Chairman and Dean of the Faculty of Science and served on the International Committee of Organic Nomenclature. He received many honours, was regarded highly by students and colleagues, but yet remained modest and humble. He passed away on December 13, 1935.

Henry Gilman (1893–1986, Iowa State University), apart from developing alternate methods for preparing Grignard reagents such as *in situ* entrainment and exchange methods and use of THF in place of ether solvent, discovered a procedure, known as Gilman colour test, to detect Grignard reagents. The test needs two reagents – (1) a 1% solution of Michler's ketone in benzene, and (2) a 1% solution of iodine in glacial acetic acid. The procedure is as follows. The Grignard reagent (1–2 mL solution) is treated with about 2 mL of Michler's ketone solution. The resulting mixture is hydrolysed with water followed by the addition

of a few drops of iodine solution. The formation of immediate green colour (due to the formation of the malachite green dye or its derivative) indicates the Grignard reagent is aromatic, i.e., arylmagnesium halide; but if the green colour formation is delayed by 30 sec or more, the reagent is an alkylmagnesium, (eq. 4).
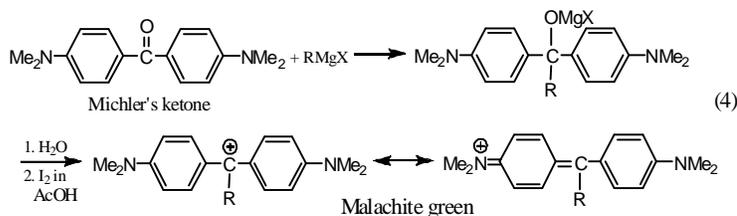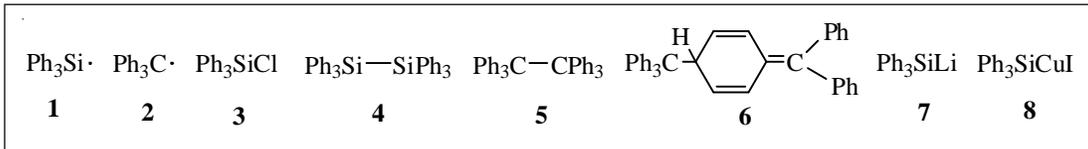

This colour test is also applicable to organolithium reagents and silyllithium compounds (which have Si-Li bond instead of C-Li bond). The first silyllithium compound, triphenyl-silyllithium was made in Gilman's laboratory. There is an interesting anecdote behind this.

Wanting to make triphenylsilyl radical (**1**) similar to Gomberg's triphenylmethyl (trityl) radical (**2**), Gilman asked a graduate student to conduct Wurtz reaction with triphenylchloro-silane (**3**). But instead of the anticipated radical **3,** a high melting solid (m.p. 362 °C) was isolated. It was characterised as hexaphenyl-disilane (**4**). It is an ironical twist in expectations, which often happen in scientific research – while Gomberg expected to get hexaphenyl-ethane (**5**) he got the radical **2** and Gilman wanted to make triphenylsilyl radical (**1**), but he got the dimer **4**. Why Gilman succeeded where Gomberg failed (and *vice versa*) is because the Si-Si bond in **4** is much longer than C-C bond in **5** and the six phenyl groups in **4** do not face the same steric obstruction as they do in **5**. (Ttriphenylmethyl radical **2** does, however, dimerise to **6**, but not **5**).

The formation of hexaphenyldisialne opened up an entirely new silicon chemistry field. The compound **4**, though highly stable, underwent Si-Si bond cleavage with lithium in THF to give reactive triphenylsilyllithium (**7**), which gave positive Gilman colour test. Treatment of **7** with cuprous iodide (CuI) gave the

$$Ph_3Si \cdot \quad Ph_3C \cdot \quad Ph_3SiCl \quad Ph_3Si-SiPh_3 \quad Ph_3C-CPh_3 \quad Ph_3C-\langle\rangle=C\langle{Ph \atop Ph} \quad Ph_3SiLi \quad Ph_3SiCuI$$

$$\mathbf{1} \qquad \mathbf{2} \qquad \mathbf{3} \qquad \mathbf{4} \qquad \mathbf{5} \qquad \mathbf{6} \qquad \mathbf{7} \qquad \mathbf{8}$$

silyl cuprate **8**, which gave negative Gilman colour test. With the discovery of silyllithium reagents, silicon chemistry got a boost.

$$R_3SiCuI \ + \ R^1COCl \longrightarrow R_3SiCOR^1 \qquad (5)$$

Addition of acid chlorides to silyl cuprates such as **8** in THF gave high yields of silyl ketones in a one-pot procedure (eq. 5), compared a multistep process reported by AG Brook.
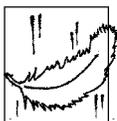
Two Special Numbers

Number 18522: Separate the natural numbers from 1 to 13 into two sets one of which contains 1 and the prime numbers and the other set contains composite numbers as shown below:

$$\{n_i\}=\{1,2,3,5,7,11,13\}\,, \ \{m_i\}=\{4,6,8,9,10,12\}\,.$$

We can see that the number 18522 may be written in two ways as:

$(1^2 + 2^2 + 3^2 + 5^2 + 7^2 + 11^2 + 13^2)\ (4+6+8+9+10+12) = 18522,$
$(1+2+3+5+7+11+13)\ (4^2 + 6^2 + 8^2 + 9^2 + 10^2 + 12^2) = 18522.$

The smallest number which can be written in the above manner using a *contiguous* set of natural numbers is 18522 .

Number 441: The prime factors of 441 are 1, 3 and 7. We have the following result:

$$(1+3+7) + (1^2 + 3^2 + 7^2) + (1^3 + 3^3 + 7^3) = 441 = (1\times3\times7)^2.$$

Observe that the sum $4^2 + 6^2 + 8^2 + 9^2 + 10^2 + 12^2 = 441$ (!).

T V Padmakumar
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