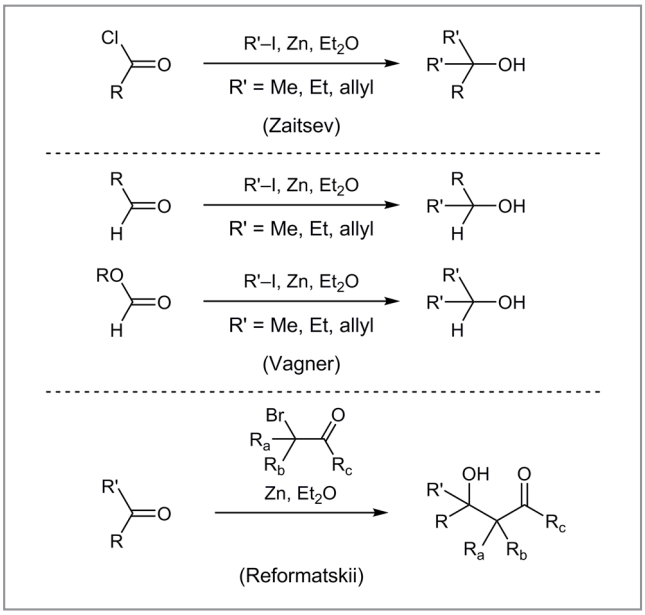
# Philippe Barbier (1848–1922) and Victor Grignard (1871–1935): Pioneers of Organomagnesium Chemistry

There are few synthetic organic chemists who have not used the Grignard synthesis of alcohols, named for Victor Grignard of the Université de Lyon, at some point in their careers.

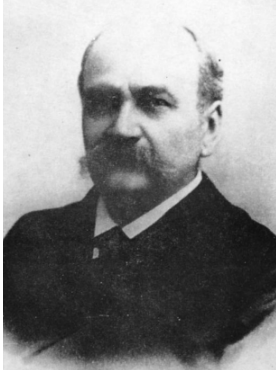
Building on earlier work in organozinc chemistry by Russian chemists, especially Zaitsev and his students[1] (Scheme 1), Barbier and Grignard developed organomagnesium nucleophiles that were much easier to use in synthesis. Henry Gilman, who will be the subject of a later Name Reaction Bio, studied the Grignard reaction extensively, and from there expanded his work with organometallic reagents of other metals.




**Scheme 1**

Philippe Antoine François Barbier (1848–1922), who is considered by many to be the father of organometallic chemistry, is something of a mystery man because just prior to his death he destroyed almost all the records of his life and career.

Barbier was born in Luzy (France) but little else is known about him (including his personal life) until he began his career. His death notice in the *Comptes Rendus* was reproduced in the *Journal Officielle de la République Française*;[2] it states that he was a student of (Pierre Eugène) Marcelin Berthelot (1827–1907) at the Collège de France, and it was here that he published his first work, on the conversion of terpineol into cymene (Scheme 2),[3] and his first work on the pyrolysis of aromatic compounds (in this case, fluorene). In his early career, he continued studying these pyrolysis reactions[4] (Scheme 2). He earned his Dr. ès sciences from the École supérieure de Pharmacie de Paris in 1876 for a thesis on pyrolysis of aromatic hydrocarbons.[5] He immediately became préparateur at the École before moving to Besançon as Director of the Agricultural Station, and Chargé de cours in chemistry in the faculty of sciences during the 1879–1880 academic year. In 1880, he moved to Lyon as Professor of Chemistry and became Professor of General Chemistry in 1884.

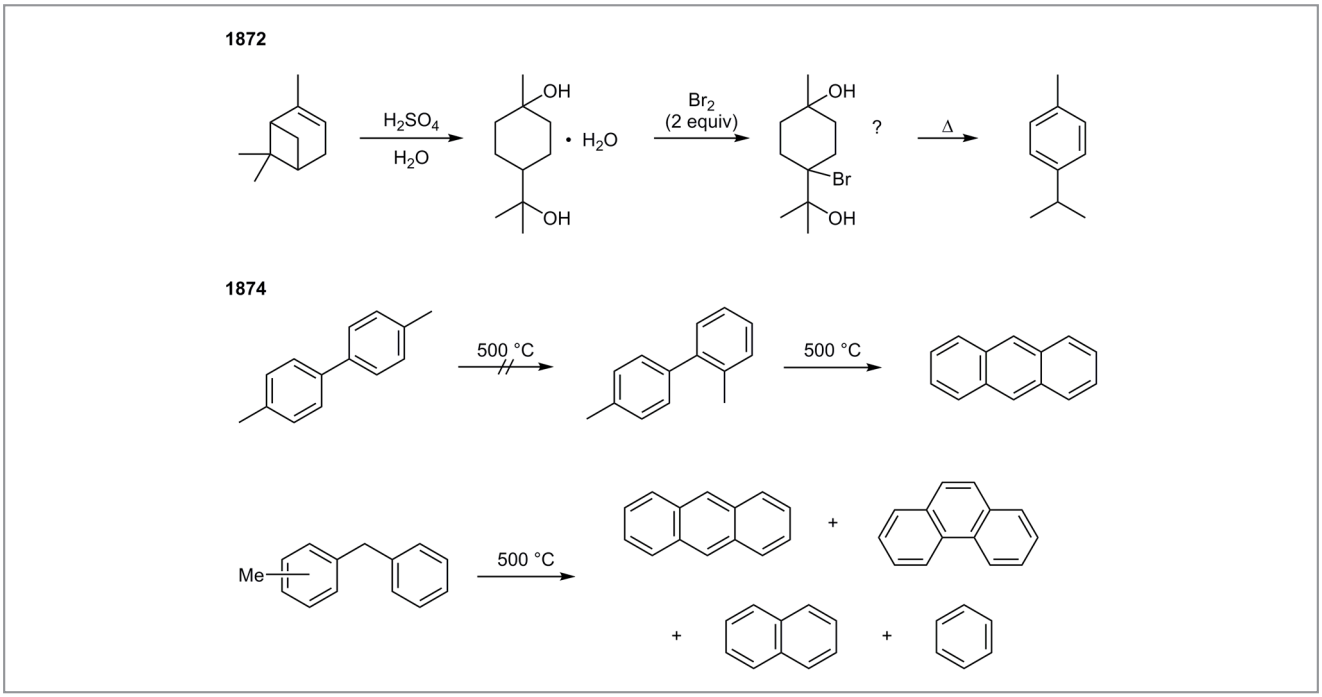


*Philippe Barbier*

There have been no detailed obituaries or biographies of Barbier, something his student, Victor Grignard, felt was unjust. Grignard had planned to complete a biography of his mentor but was unable to find the time to hunt down the material. His son, Roger Grignard gave the most comprehensive biography of Barbier in his celebration of the centenary of the birth of his father.[7]

Barbier had the reputation of being a man of few words and was considered short, abrupt, and acerbic. He was the head of the physical science department and was known for frightening beginners away. However, once he warmed up to a person he was not shy about giving praise where appropriate.

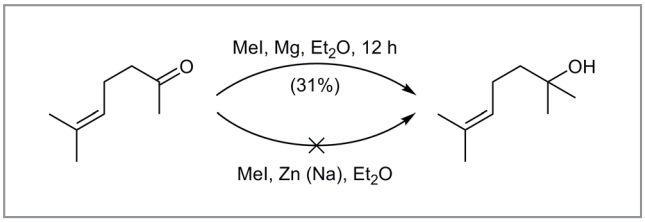
Although his work on pyrolysis reactions was quite important in clearing up the chemistry of coal tar, he is best remembered for the Barbier reaction,[6] which was the first study of organomagnesium nucleophiles (Scheme 3). In the single paper describing this reaction, he also indicates that he has used the reaction to make several other compounds; unfortunately, these syntheses never appeared in print. In this exothermic reaction, an alkyl halide is added to a mixture of a carbonyl compound, magnesium metal and ether. Barbier lost interest in pursuing this reaction when he found the yields to be mediocre and frequently irreproducible, and he passed it on to Victor Grignard as his doctoral problem. Barbier's pub-




Scheme 2

lications in the 20th century concern mineralogical chemistry and the isolation and structure elucidation of new terpenoid compounds.

Victor Grignard was born in the city of Cherbourg in France, the son of a sailmaker.[7] He attended public schools before earning a scholarship to the École Normale Spécial at Cluny in 1889, a school that specialized in training future secondary school teachers before it closed. The closure of the École Normale gave him the opportunity to join the University of Lyon where his interest in the sciences began. He initially preferred the field of mathematics but struggled in his classes and even failed his first attempt at the final examinations. His academic career was temporarily put on hold in 1892 when, at the age of 21, he fulfilled his military service obligation, rising to the rank of corporal before being demobilized. He returned to Lyon in 1894 to earn his Bachelor of Mathematical Sciences after passing his examinations the second time around.

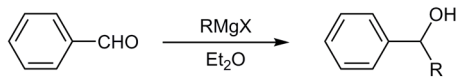



Scheme 3

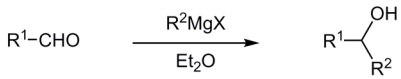
*Victor Grignard*

A friend persuaded Grignard to foster his interest in chemistry, encouraging him to accept a junior laboratory assistant position at the university. Chemistry was a subject in which he excelled, and he found himself liking it so much that he accepted a position as préparateur. This led him to be introduced to Philippe Barbier, under whose direction he was awarded his Dr. ès Sciences degree in 1901.[8] The alcohols synthesized by Grignard as part of his dissertation at Lyon are gathered in Scheme 4. As is evident, he explored the use of magnesium as a replacement for zinc in most of the alcohol syntheses previously reported by Zaitsev and Wagner.[1a–l] He found that in general, his yields were superior to the older reaction. The one exception was in the formation of allyl carbinols, where the allylzinc halide was a superior nucleophile.

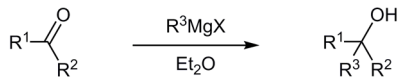
Grignard published his doctoral work under his name alone, which suggests that Barbier was not especially in-



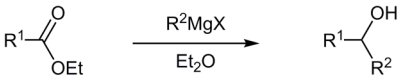

R = *n*-Pr, *i*-Pr (51%), *i*-Bu, $CH_2CH_2CHMe_2$ (56%)




$R^1 = R^2 = Me$ (67%)
$R^1 = R^2 = i\text{-Bu}$ (55%)
$R^1 = MeCH{=}CH$, $R^2 = Me$
$R^1 = MeCH{=}C(Me)$, $R^2 = Me$ (65%)
$R^1 = MeCH{=}CH$, $R^2 = Me_2CHCH_2CH_2$ (45%)
$R^1 = Me_2C{=}CHCH_2CH_2CH(Me)CH_2$, $R^2 = Et$ (65–70%)
$R^1$ = 2-furyl, $R^2 = CH_2CH_2CHMe_2$ (43%)

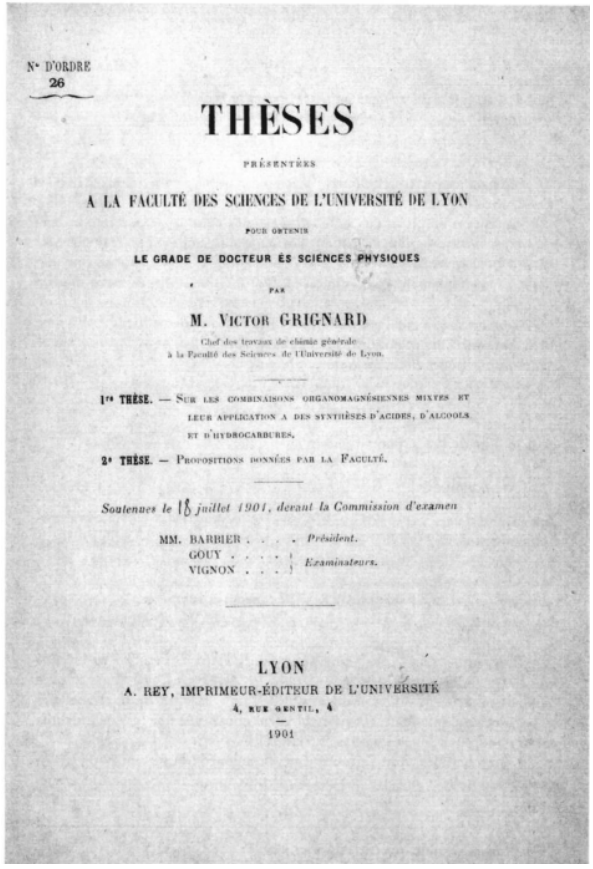



$R^1 = R^2 = R^3 = Me$ (70%)
$R^1 = R^2 = Me$, $R^3 = CH_2CH_2CHMe_2$
$R^1 = R^3 = Me$, $R^2 = Ph$ (65%)
$R^1 = R^2 = Me$, $R^3 = PhCH_2$ (33%)
$R^1 = R^2 = Me$, $R^3$ = 1-naphthyl




$R^1 = H$, $R^2 = Et$ (73%)
$R^1 = H$, $R^2 = i\text{-Bu}$ (78%)
$R^1 = R^2 = Me$ (82%)
$R^1 = Me$, $R^2 = CH_2CH_2CHMe_2$ (45%)

**Scheme 4**



N° D'ORDRE
26

THÈSES

PRÉSENTÉES

A LA FACULTÉ DES SCIENCES DE L'UNIVERSITÉ DE LYON

POUR OBTENIR

LE GRADE DE DOCTEUR ÈS SCIENCES PHYSIQUES

PAR

M. VICTOR GRIGNARD

Chef des travaux de chimie générale
à la Faculté des Sciences de l'Université de Lyon.

1re THÈSE. — SUR LES COMBINAISONS ORGANOMAGNÉSIENNES MIXTES ET LEUR APPLICATION A DES SYNTHÈSES D'ACIDES, D'ALCOOLS ET D'HYDROCARBURES.

2e THÈSE. — PROPOSITIONS DONNÉES PAR LA FACULTÉ.

*Soutenues le 18 juillet 1901, devant la Commission d'examen*

MM. BARBIER . . . . *Président.*
GOUY . . . . } *Examinateurs.*
VIGNON . . . }

LYON
A. REY, IMPRIMEUR-ÉDITEUR DE L'UNIVERSITÉ
4, RUE GENTIL, 4
1901

*Title page to Grignard's doctoral work*

terested in it at the time. Still, there is some evidence that the attention paid to his junior colleague after the early publications of his reaction[9] gradually irked Barbier. Nevertheless, Grignard continued to work with his mentor, even after he had left Lyon.[10]

Grignard left Lyon for Nancy in 1909; there he became professor of organic chemistry in 1910. He married the widowed Augustine Marie Boulan that same year. In 1912, he shared the Nobel Prize in Chemistry with Paul Sabatier. He was made a Chevalier of the Légion d'honneur the same year, rising to Officier (1920) and Commandeur (1933).

Following his service in World War I, Grignard returned to his family and his academic work at the University of Nancy, but the university had been badly damaged during the war, and it was so difficult to find professors capable of teaching the courses, that it was closed until it could be rebuilt; Grignard returned to the Université de Lyon and his 'Venerable Mentor', Barbier. He spent the rest of his career there.

*Corporal Victor Grignard. Note the Médaille Légion d'Honneur on his uniform.*

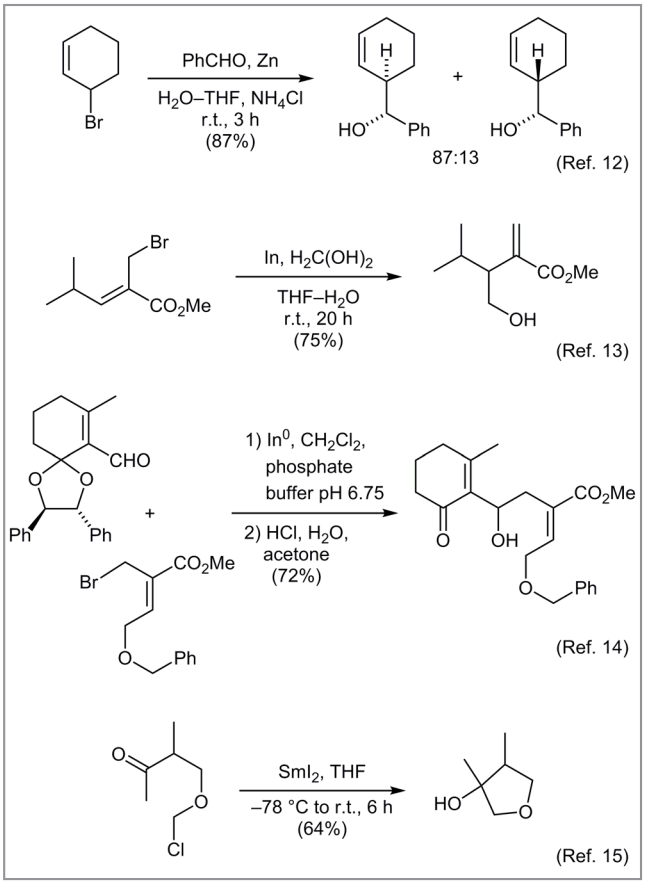
Being a Nobel laureate did not protect Grignard from being drafted into the French army at his former rank when World War I broke out; as a corporal, he was placed on sentry duty. After months of routine guard duty, Grignard was brought to the attention of the General Staff because he continued to wear his Médaille Légion d'Honneur medal after being ordered by his immediate superior to desist.

When the army looked more closely at the background of this corporal, they realized what a resource they had wasted: a world-class chemist had talents that were much better suited elsewhere. He was first assigned the task of increasing the production of explosives: when the production of TNT became inadequate, the French army turned to chemical warfare. He was seconded to the discovery and production of antidotes to chemical weapons, and then to the production of new chemical weapons.

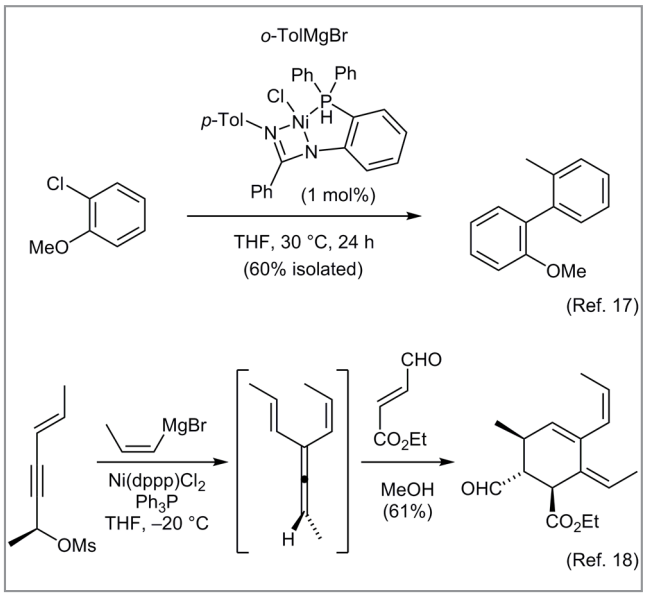
The Nobel Prize in Chemistry for 1912 was not devoid of controversy. Neither Barbier, nor Sabatier's collaborator Jean-Baptiste Senderens, received the prize, despite their contributions being essentially of equal importance with those of the laureates. This omission was an injustice noted by Grignard himself,[11] who wrote to his friend Meunier on November 13, 1912 (just days after his Nobel was announced) "…to tell the truth, and between us, I would even have preferred to wait a little longer, to see the prize shared between Sabatier and Senderens and then share it myself with Barbier at a later time, But what can I do against such a verdict if not congratulate myself for it! You will be very kind to give me as much information as you can on the state of health and on the state of mind of Barbier. I wonder how he will take it. But if he feels frustrated, I do not think he can blame me for it." There is evidence that the decision of the Nobel Committee may have played a major part in Barbier's decision to destroy his personal records.

The field of organomagnesium chemistry has continued to flourish and to expand to other metals since the work of these pioneering chemists. The Barbier reaction, which had been so difficult to carry out reproducibly, is still used, but the magnesium has been replaced by less reactive metals, including zinc,[12] indium[13,14] and samarium[15] that lead to organometallic intermediates that react very slowly or not at all with water, thus permitting their use in aqueous or mixed aqueous solvents (Scheme 5).

The commercial availability of solutions of Grignard reagents, including difficult-to-form allylic Grignard reagents, has made the Grignard reaction much more convenient to carry out. It has also made it possible to use the Grignard reagent as a participant in cross-coupling reactions, such as the Corriu–Kumada cross-coupling for the synthesis of diaryls.[16] Recent examples[17,18] are given in Scheme 6.




Scheme 5




Scheme 6

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(11) This extract from the letter (in French) is cited in: T. Urbański *Chem. Brit.* **1976**, *12*, 191–192. The French original reads: "…vrai dire et entre nous, j'aurais préféré, quitte à attendre encore un peu, voir partager le prix entre Sabatier et Senderens et le partager ensuite—moi-même avec Barbier, Mais que puis-je contre un tel verdict sinon m'en féliciter! Tu sera bien aimable de me donner ausitôtque tu le pourras quelques renseignements sur l'état de la santé et sur l'état d'esprit de M. Barbier, Je me demande comment il va prendre la chose. Mais s'il se considère comme frustré, je ne pense pas qu'il puisse m'en rendre responsable…"

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