Ovidius University Annals of Chemistry Volume 21, Number 1, pp.20-22, 2010

Iron Catalysis in C(sp)-C(sp^2) Bond Forming Reactions

Gabriel TOMA

Kyoto University, Yoshida , Sakyo-ku, Kyoto, Japan

Abstract Although iron was known and widely used by people for hundreds of years, Grignard reagents also used for about a century, binding together these two concepts still took a long time and surprisingly it did not become a hot topic in chemistry until this decade. This paper is presenting several developments in iron catalysis done mainly during the past 5 years and where Grignard reagents are used as nucleophilic reagents and related papers. It is focused on Sonogashira type reaction, but it also presents other important and interesting reactions that gathered the attention of scientists worldwide during the past few years. We are also trying to explain why it is so.

Keywords: Sonogashira reaction, iron catalysis, cross-coupling, Grignard reagents

1. Introduction

Considering the availability of iron it is amazing that we had to wait until this decade to see iron's true colors in homogeneous catalysis. Recent reviews describe iron catalysis progresses in iron catalysis [1], a comparison between metals used recently in Sonogashira reaction [2] and respectively applications of Sonogashira reaction in organic synthesis [3]. In this paper we wish to discuss what led to the discovery of the iron-catalyzed Sonogashira cross-coupling reaction and also of other reactions that involve Grignard alkynyl reagents and iron catalysts.

2. Experimental

A. Transitional Metal-free Sonogashira-type Cross-coupling reaction

One of the toughest competitors of iron is the water/PEG/NaOH/microwave methodology [4].

Although microwave methodologies are nowadays not suitable for the large scale synthesis of organic compounds, they are to be considered as a representative tool in testing the necessity of transitional metals in catalysis and in obtaining new compounds. The reaction described by N.E.Leadbeater et. al. shows a moderate reactivity for several bromo- and iodo- aryls. The reaction scale can show completely different results and the reactivity of bromides is significantly lower than the one for iodides. Still, the method is interesting despite the elevated temperature required for the reaction (170^o C) (Reaction 1).

B. Iron-copper Sonogashira-type cross-coupling reaction

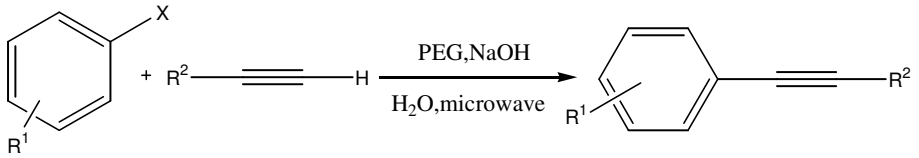
The combination between iron and copper is reported to be efficient in the Sonogashira-type cross-coupling reaction [5] and [6]. In the work of Hong Liu et al. [5] the reaction undergoes in moderate yield only in the presence of copper and shows no yield only in the presence of iron (Reaction 2). In the work of Pierre Vogel et al.[6] it slightly reacts just in the presence of copper, showing no yield just in the presence of iron (Reaction 3). Both reactions show a good versatility, but how copper and iron work together as well as whether this is the true reason that the reaction performs as written by the authors cannot be entirely justified in our opinion.

C. Copper free Iron-catalyzed Sonogashira-type cross-coupling reaction

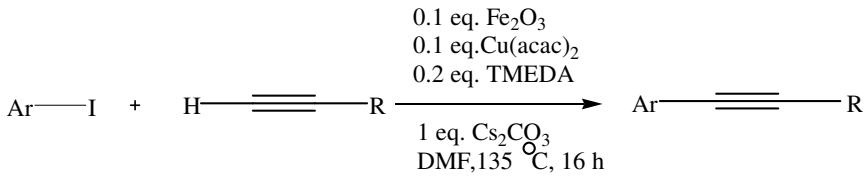
Although first time the iron catalyzed Sonogashira-type was presented by Toma G. et al. at the J.A.C. in Osaka (March 2007), showing that ligand free, salt free iron catalyzed Sonogashira reaction is possible, followed by a paper published

ISSN-1223-7221

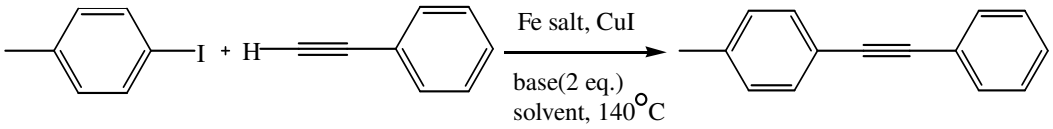
later[7] (Reaction 4); the first paper that presented this reaction with iron was done by C.Bolm et al.[8] It does not require Grignard reagents, but it takes days to complete (Reaction 5).



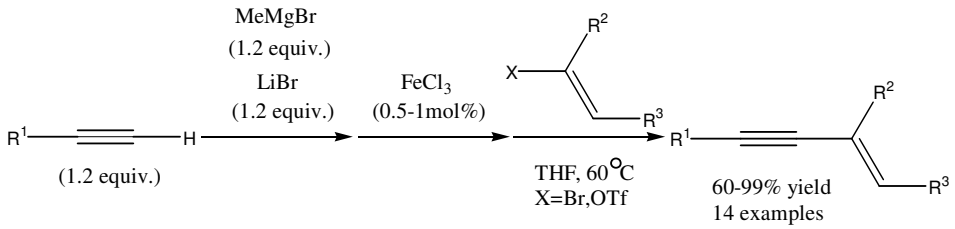
Reaction 1



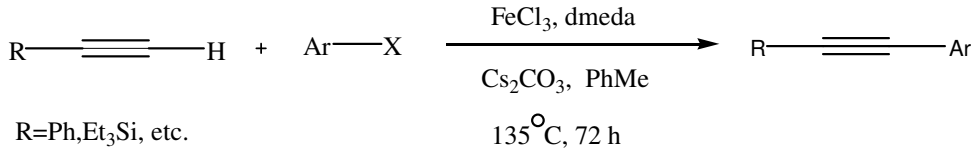
Reaction 2



Reaction 3



Reaction 4



Reaction 5

3. Results and discussions

C-C bond forming reactions using iron became more and more popular during the past few years. The reasons for this may be the increasing of the price of palladium due to the limited amounts of this metal existing on our planet and also the increasing in the level of experimental laboratory techniques that allow metals that are not easy to handle (like iron, cobalt etc.) to be used through new Schlenck tube developments.

Although there are several hypotheses regarding the mechanism of this type of reactions, recent developments [9] show that reactions for which preparation of Grignard reagents was necessary can be done without previous preparation of Grignard reagents by using magnesium and reacting substances along with the iron catalyst.

Generally it is believed that low valent iron species are formed during the reaction and in case of iron chloride(III) for example iron(I) species are formed while in the case of iron chloride(II), iron(0) species are formed through the reaction pathway.

4. Conclusions

Iron-catalyzed methodologies are becoming one of the most attractive targets of organic chemists. Further understanding of the iron-catalyzed Sonogashira reaction and applications of the reactions are expected to be published in the near future.

5. References

* E-mail address: tomagabi@yahoo.com

[1]. H. Plenio, Angew. Chem. Int. Ed., **47**, 6954-6956 (2008).
[2]. R. Chinchilla and C. Njera, Chem.Rev. **107**, 874-922 (2007)
[3]. N. Leadbeater, M.Marco and B.J.Tominack, Org. Lett. **5**,3919-3922 (2003)
[4]. H. Huang, H.Jiang, K.Chen and H.Liu, J. Org. Chem. **73**, 9061-9064 (2008)
[5]. C.M. Rao Volla and P. Vogel, Tetrahedron Letters **49**, 5961-5964 (2008)
[6]. T. Hatakeyama, Y. Yoshimoto G. Toma and M. Nakamura, Org. Lett. **10**, 5341-5344 (2008).
[7]. M. Carril, A. Correa and C. Bolm, Angew. Chem. Int. Ed. **47,** 4862-4865 (2008).
[8]. A. Furstner, Angew. Chem. Int. Ed. Highlights (2009).
[9]. W. M. Czaplik, M. Mayer and A. Jacobi Angew. Chem. Int. Ed. **48,** 607-610 (2009).