

Electrophilic alkynylation using hypervalent iodine reagents

Bruno V. M. Teodoro (PG), Luiz F. Silva Jr. (PQ)*

Instituto de Química, Universidade de São Paulo, CP 26077 CEP 05513-970, São Paulo, SP, Brazil

*luizfsjr@iq.usp.br

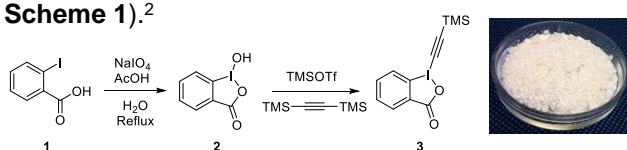
Keywords: Alkynylation, Hypervalent Iodine, Enolate Trapping, Aldehyde

Abstract

We present new methodologies to perform the alkynylation of enones and of aldehydes using hypervalent iodine reagent

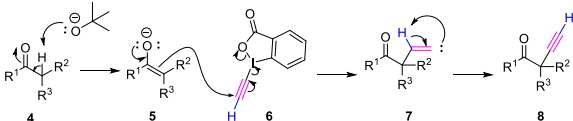
Introduction

Acetylene group has received a great importance in synthetic organic chemistry in recent times due to its reactivity and to be a versatile functional group.¹ Due to its importance, the alkynylation reaction have aroused the interest of several research groups. An alternative of this reaction that is increasingly being explored is the use of electrophilic alkynylating reagents and in this context, Waser introduced a new reagent to perform this reaction, the TMS-EBX (**3**, **Scheme 1**).²



Scheme 1. Preparation of TMS-EBX (**3**)

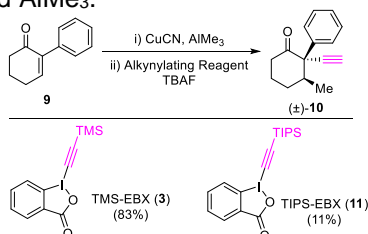
The proposed mechanism for α -alkynylation using TMS-EBX is shown in **Scheme 2**. In the presence of base, the carbonyl compound gives enolate **5**. EBX (**9**) is obtained by reaction of TMS-EBX (**3**) with TBAF. Nucleophilic attack of enolate **5** on the terminal carbon of **6** furnishes carbene **7**. Rearrangement of carbene **7** leads to the alkynylated product **8**.



Scheme 2. Mechanism of α -alkynylation of carbonyl compounds

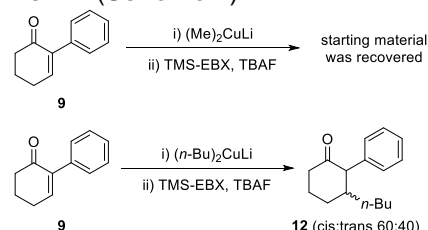
Results and Discussion

After many tests for optimizing the alkynylation reaction by capture enolate trapping, we observed that the best conditions to carry out this reaction uses CuCN and AlMe₃.



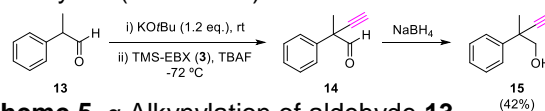
Scheme 3. Alkynylation of enone **9**

A test was performed using TMS-EBX (**3**) and TIPS-EBX (**11**) (**Scheme 3**). The product (\pm)-**10** was obtained in 83% and 11%, respectively. No reaction was observed when using the (Me)₂CuLi reagent, and (*n*-Bu)₂CuLi furnished **12** as a mixture of diastereomer **11** (**Scheme 4**).



Scheme 4. Reactions with others organometallics

In the context of electrophilic alkynylation, it was also tested α -alkynylation of aldehydes due to their synthetic importance and the small number of examples in the literature.^{3,4} The α -alkynylation of aldehyde **13** was carried out using a method previously described for the α -alkynylation of ketones.³ The product **14** was confirmed by GC-MS, but it not was possible to perform the isolation because of their instability during the purification by column chromatography. Therefore, the aldehyde **14** was reduced *in situ* and the alcohol **15** was obtained in 42% yield (**Scheme 5**).



Scheme 5. α -Alkynylation of aldehyde **13**

Conclusions

The alkynylation of enones by enolate trapping is described in this work. From the data obtained, this methodology will be expanded to several enones. Other hypervalent iodine reagents as well other organometallics will be tested. The α -alkynylation of aldehyde **13**, followed by reduction, gave the desired alkynylated product. From this data, this reaction will be optimized and the scope will be expanded.

Acknowledgement

CNPq, FAPESP and CAPES

¹ Brand, J. P. and Waser, J. *Chem. Soc. Rev.* **2012**, *41*, 4165.

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³ Utaka, A.; Cavalcanti, L. N. and Silva, L. F. *Chem. Commun.* **2014**, *50*, 3810.

⁴ Wang, Z.; Li, X. and Huang, Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 14219.