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ARTICLE TYPE

## Selective Oxygenation of Alkynes: A Direct Approach to Diketones and Vinyl Acetate†

Xiao-Feng Xia,<sup>\*a</sup> Zhen Gu,<sup>a</sup> Wentao Liu,<sup>a</sup> Ningning Wang,<sup>a</sup> Haijun Wang,<sup>a</sup> Yongmei Xia,<sup>a</sup> Haiyan Gao,<sup>a</sup> Xiang Liu,<sup>a</sup>

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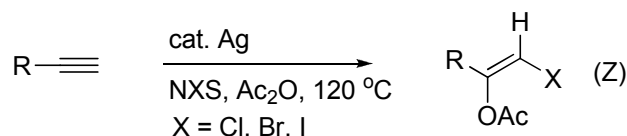
Arylalkynes can convert into  $\alpha$ -diketones by the use of copper catalyst, and also transform into vinyl acetates under metal-free conditions both in the presence of  $\text{PhI}(\text{OAc})_2$  as oxidant at room temperature. A series of substituted  $\alpha$ -diketones were prepared in moderate to good yields. A variety of vinyl halides could be regio- and stereo-selectively synthesized under mild conditions, and I, Br and Cl can be all easily embedded into the alkynes.

### Introduction

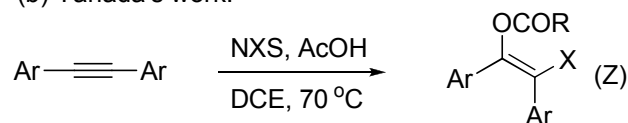
Alkyne chemistry can be dated back to the early nineteenth century. From that time, the transformation of alkynes is a fundamental method that has been widely used in organic synthesis.<sup>[1]</sup> Various catalytic systems were developed to synthesize useful compounds from alkynes. Among these, the Pd-catalyzed Wacker-type oxidation to generate 1,2-diketones is one of the most important industrial processes.<sup>[2]</sup> 1,2-Diketones are known as one of the most important skeletons in biologically active molecules<sup>[3]</sup> and are very useful building blocks which can easily be transformed into a variety of other chemicals, especially heterocyclic compounds.<sup>[4]</sup> This fact has stimulated a growing interest in the development of a large number of new oxidants and catalytic systems to get 1,2-diketones from alkynes.<sup>[5]</sup> However, these reactions are still suffering from some drawbacks such as harsh conditions, narrow substrate scope, and chemo-selectivity. Thus, developing a mild and efficient protocol for catalytic oxidation of alkynes is still highly desirable.

Vinyl halides (1-halo-1-alkenes), especially vinyl bromides and iodides, represent one kind of organic synthetic blocks, which play important roles in the construction of polysubstituted alkenes through transition-metal-catalyzed cross-coupling reactions or halogen-metal exchange reactions.<sup>[6]</sup> Consequently, much attention has been paid to prepare vinyl halides from different starting materials.<sup>[7]</sup> For instance, Jiang group recently reported a silver-catalyzed difunctionalization of terminal alkynes to get 1-halo-1-alkenes (Scheme 1-a).<sup>[7b]</sup> Very recently, Yanada group reported NIS-mediated halogenation of alkynes, but only non-terminal alkynes can be used (Scheme 1-b).<sup>[7c]</sup> Our group has been committed to the research of functionalization of alkynes,<sup>[8]</sup> as part of this continuing project, herein we found that arylalkynes can be oxidized to 1,2-diketones in the presence of  $\text{PhI}(\text{OAc})_2$  using copper as catalyst, and when TBAI (tetrabutylammonium iodide) was instead of copper catalyst, (E)-vinyl halides were prepared in similar reaction systems.

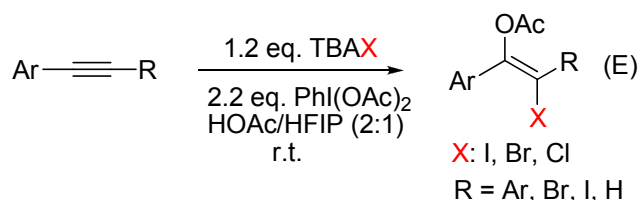
(a) Jiang's work:



(b) Yanada's work:



(c) Our work:



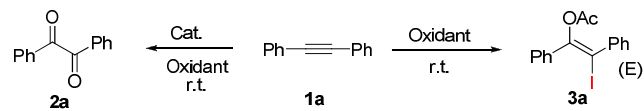
Scheme 1. Previous work of halogenation of alkynes

### Results and discussion

The results from the optimization studies are summarized in Table 1. Our investigation began with the oxidation of 1,2-diphenylethyne **1a** catalyzed by  $\text{Cu}(\text{OAc})_2$  using  $\text{PhI}(\text{OAc})_2$  as oxidant in HFIP (Hexafluoroisopropanol) at room temperature. To our delight, the target 1,2-diketones **2a** was obtained (Table 1, entry 1). Consequently, a series of other catalytic systems were evaluated, wherein  $\text{Cu}(\text{OTf})_2$  displayed high catalytic activity (entries 1-4). When 5 equivalents of HOAc was used as additive, the yield of **2a** was increased to 35% (entry 5). So we choose

HOAc as co-solvent, when volume ratio of HOAc : HFIP in 1:2 was used, the yield of **2a** can reach to 90%. However, when the volume ratio of HOAc : HFIP was 2:1, the yield decreased to 40%. Only HOAc was used as solvent, no reaction occurred (entry 9), which meant that HFIP plays an important role in the reaction. In our opinion, HFIP can increase the solubility of  $\text{PhI}(\text{OAc})_2$  in our system, and can increase the rate of product formation. When 10%  $[\text{Cu}(\text{OTf})_2]\cdot\text{Ph}$  was tried in our system, a 50% yield was got (entry 11). In addition, in the absence of copper catalyst or  $\text{PhI}(\text{OAc})_2$ , no product was detected (entries 13 and 14). When TBAI was instead of copper catalyst, vinyl iodide **3a** was obtained. The yield of **3a** can increase to 90%, when 1.2 equivalents of TBAI was used (entry 16). The amounts of TBAI and  $\text{PhI}(\text{OAc})_2$  were also screened, and there is no better results, with 1.2 equivalents of TBAI and 2.4 equivalents of  $\text{PhI}(\text{OAc})_2$  being optimal (entries 17-19).

Table 1. Optimization of reaction conditions for the difunctionalization of 1,2-diphenylethyne<sup>a</sup>



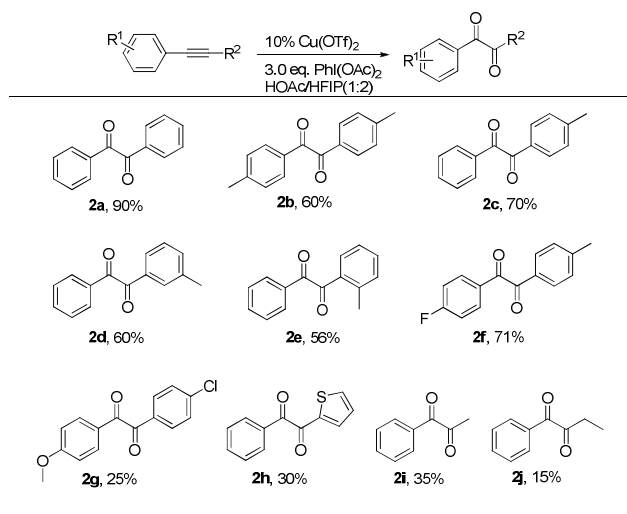
Entry	Catalyst	Oxidant	Solvent	Yield <sup>b</sup>
1	20% $\text{Cu}(\text{OAc})_2$	2.0 eq. $\text{PhI}(\text{OAc})_2$	HFIP	10% <b>2a</b>
2	10% $\text{Cu}(\text{OAc})_2$ + 5% $\text{Pd}(\text{OAc})_2$	2.0 eq. $\text{PhI}(\text{OAc})_2$	HFIP	15% <b>2a</b>
3	20% $\text{Cu}(\text{OTf})_2$	2.0 eq. $\text{PhI}(\text{OAc})_2$	HFIP	20% <b>2a</b>
4	20% $\text{Cu}(\text{OTf})_2$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HFIP	30% <b>2a</b>
5 <sup>c</sup>	20% $\text{Cu}(\text{OTf})_2$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HFIP	35% <b>2a</b>
6	10% $\text{Cu}(\text{OTf})_2$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(1:2)	90% <b>2a</b>
7	5% $\text{Cu}(\text{OTf})_2$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(1:2)	74% <b>2a</b>
8	10% $\text{Cu}(\text{OTf})_2$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(2:1)	40% <b>2a</b>
9	10% $\text{Cu}(\text{OTf})_2$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc	0
10	10% $\text{Cu}(\text{OTf})_2$	2.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(1:2)	81% <b>2a</b>
11	10% $[\text{Cu}(\text{OTf})_2]\cdot\text{Ph}$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(1:2)	50% <b>2a</b>
12	10% $\text{Cu}(\text{OAc})_2$	3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(1:2)	10% <b>2a</b>
13	10% $\text{Cu}(\text{OTf})_2$	-	HOAc/HFIP(1:2)	0
14	-	3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(1:2)	0
15	20% TBAI	2.2 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(2:1)	15% <b>3a</b>
16	-	1.2 eq. TBAI, 2.4 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(2:1)	90% <b>3a</b>
17	-	1.2 eq. TBAI, 3.0 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(2:1)	60% <b>3a</b>
18	-	1.2 eq. TBAI, 1.2 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(2:1)	72% <b>3a</b>
19	-	2.2 eq. TBAI, 2.4 eq. $\text{PhI}(\text{OAc})_2$	HOAc/HFIP(2:1)	80% <b>3a</b>

<sup>a</sup> Reaction conditions: **1a** (0.3 mmol), solvent (2.0 mL), at room temperature for 12h in air. <sup>b</sup> Isolated yield. <sup>c</sup> 5eq. HOAc was used. HFIP = hexafluoroisopropanol; TBAI = tetrabutylammonium iodide.

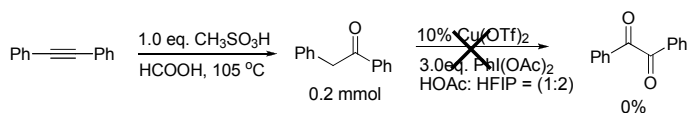
With the optimized conditions in hand (Table 1, entry 6), the oxidation of arylalkynes was firstly investigated. As shown in Scheme 2, a variety of diarylalkynes can easily convert to the corresponding 1,2-diketones in moderate to good yields. Several

useful functional groups were tolerated, including chloro, fluoro and ether substituents. Ortho-substituted substrate gave a lower yield (**2e**). In addition, heterocycle-derived thiophene substrate can be also tolerated in the reaction (**2h**). It is worth mentioning that 1-phenylpropane-1,2-dione and 1-phenylbutane-1,2-dione can be synthesized in this condition (**2i** and **2j**).

To study the reaction pathway, one possible intermediate, deoxybenzoin, was independently synthesized and tested under the standard conditions, and no product was detected, which meant that the deoxybenzoin was not the intermediate in this reaction (Scheme 3). On the basis of this result and previous report<sup>[9]</sup>, we propose a possible reaction pathway as shown in Scheme 4. The  $\text{Cu}(\text{II})(\text{OTf})_2$  is oxidized to the active  $\text{Cu}(\text{III})(\text{OAc})_2(\text{OTf})$  by the oxidant  $\text{PhI}(\text{OAc})_2$  which then coordinates and inserts alkynes forming the intermediate species **iv**. Release of **A** from **iv** by a  $\text{S}_{\text{N}}2$ -type reductive elimination leads to  $\text{Cu}(\text{I})\text{OTf}$ , which is oxidized back to the active  $\text{Cu}(\text{III})$  species **ii** by  $\text{PhI}(\text{OAc})_2$ . The reaction of the intermediate **A** with acetic acid will then lead to the product **2a**. The intermediate **A** can also react with water to give the intermediate **B**, which can convert into the product **2a** under the oxidant of  $\text{PhI}(\text{OAc})_2$ .



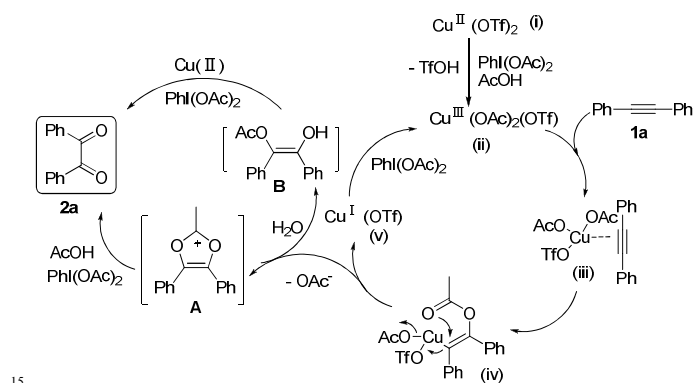
Scheme 2. Copper-catalyzed synthesis of 1,2-diketones.



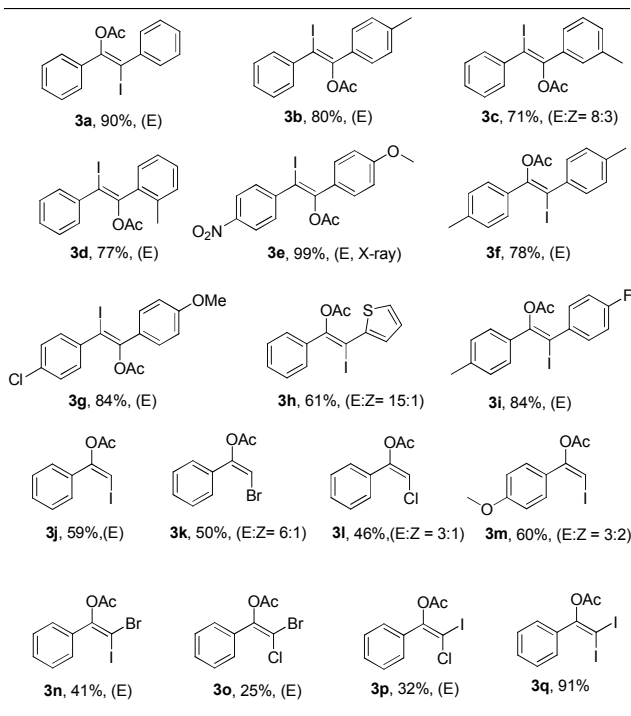
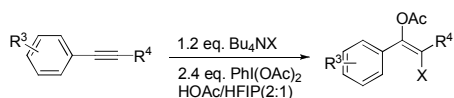
Scheme 3. Control experiment.

Next, we went on to study the halogenation of alkynes. Scheme 5 reveals that the electronic property of alkyne substitutions did not show obvious influences on the reaction efficiency. A series of substituents such as nitro, chloro, fluoro and ether can be tolerated in the reaction. A series of vinyl iodides can be obtained in good to excellent yields. It is noteworthy that only E-isomer is the major products in most cases (**3a-3i**).<sup>[10]</sup> To confirm further the structural assignment of products in the present oxidative conditions, the structure of the product **3e** was unambiguously assigned by X-ray crystallography (see the Supporting

Information, Figure 1).<sup>[11]</sup> Heterocycle-derived thiophene substrate was also compatible, and the desired product was isolated in 61% yield (**3h**). When alkylated alkyne such as prop-1-ynylbenzene was used in this system, an unseparated mixture was obtained. Terminal arylalkynes can be also involved in this reaction (**3j-3m**). TBAB (tetrabutylammonium bromide) and TBAC (tetrabutylammonium chloride) could afford the corresponding  $\beta$ -haloenol acetates in moderate to good yields as well (**3k** and **3l**). As the challenging substrates, alkynyl halides, such as alkynyl bromide and alkynyl iodide, can also react with TBAI or TBAC to get vinyl dihalides in moderate to good yields (**3n-3q**). Aliphatic terminal alkynes can not give any products in this reaction.

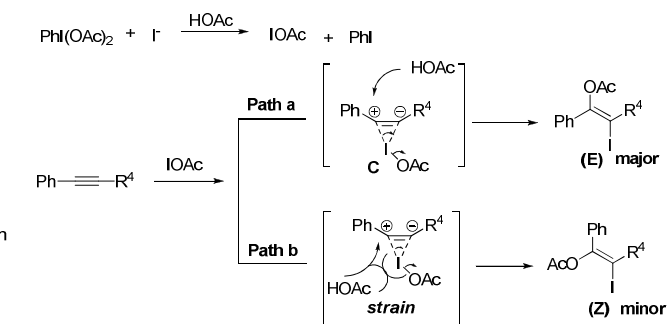


Scheme 4. Proposed mechanism



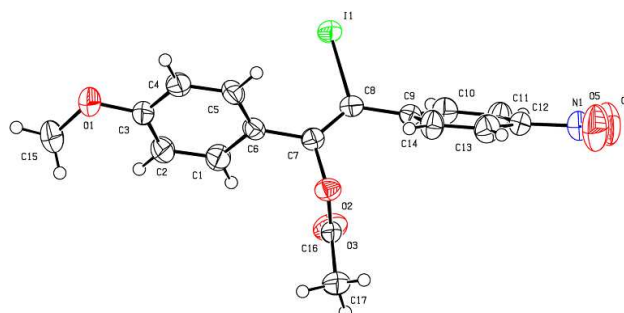
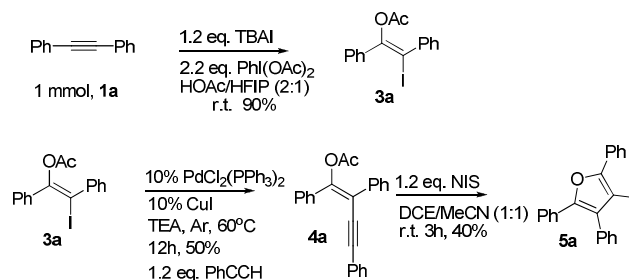
Scheme 5. Halogenation of arylalkynes.

20 According to the above results and Taniguchi reported mechanism,<sup>[12]</sup> we proposed a plausible reaction pathway (Scheme 6). Firstly, AcOI was generated by the reaction between  $\text{PhI}(\text{OAc})_2$  and iodide ion,<sup>[13]</sup> which can work as a strong electrophile against alkynes to give iodonium ion intermediate **C**.  
25 Then, nucleophile HOAc attacks the positive charge density of intermediate **C** from the back of it to give the E-isomer as the major product (**Path a**). When HOAc attacks from the front of intermediate **C**, due to the steric hindrance, the Z-isomer was got as the minor product (**Path b**).<sup>[14]</sup>



Scheme 6. Proposed mechanism for the formation of vinyl iodide

Further synthetic transformations of the haloenol acetates products were investigated with **3a** as a model substrate (Scheme 7). Take **3a** as an example to increase molecular complexity *via* palladium- and copper-catalyzed a Sonogashira reaction with terminal alkyne affording the corresponding **4a** in 50% yield. **4a** can undergo a NIS inducing electrophilic cyclization to generate 3-iodo-2,4,5-triphenylfuran **5a**, which is frequently found as subunit in many bioactive natural products and pharmaceutically  
40 important substances.<sup>[15]</sup>

Figure 1. The X-ray structure of **3e**.

Scheme 7. Illustrative Synthetic Transformations

## Conclusions

In conclusion, we have developed convenient and expedient methods for the synthesis of  $\alpha$ -diketones and  $\beta$ -haloenol acetates from arylalkynes using  $\text{PhI}(\text{OAc})_2$  as oxidant. In contrast to previous reported, the (E)- $\beta$ -haloenol acetates were obtained regio- and stereo-specifically as the major products in moderate to good yields. In addition, (E)- $\beta$ -haloenol acetate was briefly transformed to the polysubstituted furans in two steps.

## Experimental

### General information

Column chromatography was carried out on silica gel. Unless noted  $^1\text{H}$  NMR spectra were recorded on 400 MHz in  $\text{CDCl}_3$  and  $d$ -DMSO,  $^{13}\text{C}$  NMR spectra were recorded on 100 MHz in  $\text{CDCl}_3$  and  $d$ -DMSO. IR spectra were recorded on an FT-IR spectrometer and only major peaks are reported in  $\text{cm}^{-1}$ . Melting points were determined on a microscopic apparatus and were uncorrected. All new products were further characterized by HRMS (high resolution mass spectra), high resolution mass spectrometry (HRMS) spectra was obtained on a microTOF-Q instrument equipped with an ESI source; copies of their  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra are provided. Commercially available reagents and solvents were used without further purification.

#### Typical procedure for the synthesis of product 2.

To a solution of 1,2-diphenylethyne (**1a**, 0.3 mmol, 53.4 mg) in HOAc/HFIP (V:V = 1:2, 2.0 mL) was added  $\text{Cu}(\text{OTf})_2$  (10.9 mg, 10 mol%),  $\text{PhI}(\text{OAc})_2$  (289 mg, 3 equiv.). The reaction mixture was then stirred for 12 h at room temperature in air. The resulting mixture was quenched with saturation  $\text{Na}_2\text{S}_2\text{O}_3$  and extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. Purification of the crude product by flash column chromatography afforded the product **2** (petroleum ether/ethyl acetate as eluent (30:1)).

#### Typical procedure for the synthesis of product 3.

To a solution of 1,2-diphenylethyne (**1a**, 0.3 mmol, 53.4 mg) in HOAc/HFIP (V:V = 2:1, 2.0 mL) was added  $n\text{-Bu}_4\text{NI}$  (132.8 mg, 1.2 equiv.),  $\text{PhI}(\text{OAc})_2$  (231 mg, 2.4 equiv.). The reaction mixture was then stirred for 12 h at room temperature in air. The resulting mixture was quenched with saturation  $\text{Na}_2\text{S}_2\text{O}_3$  and extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. Purification of the crude product by flash column chromatography afforded the product **3** (petroleum ether/ethyl acetate as eluent (30:1)).

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## Notes and references

<sup>50</sup> *The Key Laboratory of Food Colloids and Biotechnology, Ministry of Education, School of Chemical and Material Engineering, Jiangnan University, Wuxi, Jiangsu, 214122, China. E-mail: xiaxf@jiangnan.edu.cn. Fax: +86-510-85917763*

†*Electronic Supplementary Information (ESI) available: [Experimental*

*procedures and analysis data for new compounds, CCDC reference numbers CCDC 1002379 (3e)]. See DOI: 10.1039/b000000x/*

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- 5 11 CCDC 1002379 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).
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- 14 When  $\text{R}^4$  was hydrogen atom, mixtures of *anti* and *syn* addition products were obtained and E-isomer was the major product.
- 15 When  $\text{R}^4$  was Br or I, due to steric hindrance of halogen atom, only E-isomer was product.
- When  $\text{R}^4$  was phenyl, the bridging by iodine must be weaker and, consequently, the interaction between the carbon and iodine atoms decreases and then, this atom will have a higher positive charge density than with less hindered alkynes. Under these conditions, OAc may interact with the iodine atom because of the greater positive charge density yielding a *syn* addition. At same time, OAc can also attack to give an *anti* addition.
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