## Organic & Biomolecular Chemistry

## PAPER

Cite this: DOI: 10.1039/c4ob01404a

# Selective oxygenation of alkynes: a direct approach to diketones and vinyl acetate†

Xiao-Feng Xia,\* Zhen Gu, Wentao Liu, Ningning Wang, Haijun Wang, Yongmei Xia, Haiyan Gao and Xiang Liu

Arylalkynes can be converted into  $\alpha$ -diketones with the use of a copper catalyst, and also be transformed into vinyl acetates under metal-free conditions, both in the presence of Phl(OAc)<sub>2</sub> as an 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 could be all easily embedded into the alkynes.

www.rsc.org/obc

Received 7th July 2014,

Accepted 9th October 2014

DOI: 10.1039/c4ob01404a

## Introduction

Alkyne chemistry can be dated back to the early nineteenth century. From that time, the transformation of alkynes has been a fundamental method that has been widely used in organic synthesis.1 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 obtain 1,2diketones from alkynes.<sup>5</sup> However, these reactions still suffer from some drawbacks such as harsh conditions, a 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 crosscoupling reactions or halogen-metal exchange reactions.<sup>6</sup> Consequently, much attention has been paid to preparing vinyl halides from different starting materials.<sup>7</sup> For instance, the Jiang group recently reported a silver-catalyzed difunctionali-

#### (a) Jiang's work:

$$R \longrightarrow \frac{\text{cat. Ag}}{\text{NXS, Ac_2O, 120 °C}} \qquad R \longrightarrow \frac{H}{\text{OAc}} \chi \quad (Z)$$

(b) Yanada's work:

$$Ar \longrightarrow Ar \qquad \xrightarrow{NXS, AcOH} \qquad Ar \longrightarrow X (Z)$$

(c) Our work:



Scheme 1 Previous work of halogenation of alkynes.

zation of terminal alkynes to obtain 1-halo-1-alkenes (Scheme 1a).<sup>7b</sup> Very recently, the Yanada group reported NISmediated halogenation of alkynes, but only non-terminal alkynes can be used (Scheme 1b).<sup>7c</sup> Our group has been committed to the research on functionalization of alkynes.<sup>8</sup> As a part of this continuing project, herein we found that arylalkynes can be oxidized to 1,2-diketones in the presence of PhI-(OAc)<sub>2</sub> using copper as a catalyst, and when TBAI (tetrabutylammonium iodide) was used instead of a copper catalyst, (*E*)-vinyl halides were prepared in similar reaction systems.

Published on 09 October 2014. Downloaded by The University of Texas at El Paso (UTEP) on 08/11/2014 19:33:30.

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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 1002379 for **3e**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ob01404a

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



Entry	Catalyst	Oxidant	Solvent	Yield <sup>b</sup>
L	20% Cu(OAc) <sub>2</sub>	2.0 eq. $PhI(OAc)_2$	HFIP	10% <b>2a</b>
2	$10\% \text{ Cu(OAc)}_{2}^{2} + 5\% \text{ Pd(OAc)}_{2}$	2.0 eq. PhI( $OAc$ ) <sub>2</sub>	HFIP	15% <b>2a</b>
3	$20\% \text{ Cu}(\text{OTf})_2$	2.0 eq. PhI( $OAc$ ) <sub>2</sub>	HFIP	20% <b>2a</b>
1	$20\% \text{ Cu}(\text{OTf})_2$	3.0 eq. PhI( $OAc$ ) <sub>2</sub>	HFIP	30% <b>2a</b>
5 <sup>c</sup>	$20\% \text{ Cu}(\text{OTf})_2$	3.0 eq. PhI( $OAc$ ) <sub>2</sub>	HFIP	35% <b>2a</b>
5	$10\% \operatorname{Cu}(\operatorname{OTf})_2$	3.0 eq. PhI( $OAc$ ) <sub>2</sub>	HOAc-HFIP(1:2)	90% 2a
7	5% Cu( $OTf$ ) <sub>2</sub>	3.0 eq. PhI( $OAc$ ) <sub>2</sub>	HOAc-HFIP(1:2)	74% 2 <b>a</b>
3	$10\% \operatorname{Cu}(\operatorname{OTf})_2$	3.0 eq. PhI( $OAc$ ) <sub>2</sub>	HOAc-HFIP(2:1)	40% 2a
)	$10\% \text{ Cu}(\text{OTf})_2$	3.0 eq. PhI( $OAc)_2$	HOAc	0
10	$10\% \text{ Cu}(\text{OTf})_2$	2.0 eq. PhI( $OAc$ ) <sub>2</sub>	HOAc-HFIP(1:2)	81% <b>2a</b>
1	10% [Cu(OTf)] <sub>2</sub> ·Ph	3.0 eq. PhI( $OAc$ ) <sub>2</sub>	HOAc-HFIP(1:2)	50% 2a
12	$10\% Cu(OAc)_2^{2}$	3.0 eq. PhI( $OAc$ ) <sub>2</sub>	HOAc-HFIP(1:2)	10% 2a
13	$10\% \text{ Cu}(\text{OTf})_2$		HOAc-HFIP(1:2)	0
4		3.0 eq. $PhI(OAc)_2$	HOAc-HFIP(1:2)	0
15	20% TBAI	2.2 eq. PhI( $OAc$ ) <sub>2</sub>	HOAc-HFIP(2:1)	15% <b>3a</b>
16	_	1.2 eq. TBAI, 2.4 eq. PhI(OAc) <sub>2</sub>	HOAc-HFIP(2:1)	90% 3a
17	_	1.2 eq. TBAI, 3.0 eq. $PhI(OAc)_2$	HOAc-HFIP(2:1)	60% <b>3a</b>
18	_	1.2 eq. TBAI, 1.2 eq. $PhI(OAc)_2$	HOAc-HFIP(2:1)	72% <b>3a</b>
19	_	2.2 eq. TBAI, 2.4 eq. $PhI(OAc)_2^2$	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 12 h in air. <sup>*b*</sup> Isolated yield. <sup>*c*</sup> 5 eq. HOAc was used. HFIP = hexafluoroisopropanol; TBAI = tetrabutylammonium iodide.

### **Results and discussion**

The results from the optimization studies are summarized in Table 1. Our investigation began with the oxidation of 1,2diphenylethyne 1a catalyzed by  $Cu(OAc)_2$  using PhI(OAc)<sub>2</sub> as an 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 Cu(OTf)<sub>2</sub> displayed high catalytic activity (entries 1-4). When 5 equivalents of HOAc was used as an additive, the yield of 2a was increased to 35% (entry 5). So we chose HOAc as a co-solvent, and when a volume ratio of HOAc: HFIP in 1:2 was used, the yield of 2a could reach 90%. However, when the volume ratio of HOAc: HFIP was 2:1, the yield decreased to 40%. Only when HOAc was used as a solvent, no reaction occurred (entry 9), which meant that HFIP played an important role in the reaction. In our opinion, HFIP can increase the solubility of PhI(OAc)<sub>2</sub> in our system, and can increase the rate of product formation. When 10% [Cu-(OTf)]<sub>2</sub>·Ph was tried in our system, a 50% yield was obtained (entry 11). In addition, in the absence of the copper catalyst or  $PhI(OAc)_2$ , no product was detected (entries 13 and 14). When TBAI was used instead of the copper catalyst, vinyl iodide 3a was obtained. The yield of 3a could increase to 90%, when 1.2 equivalents of TBAI was used (entry 16). The amounts of TBAI and  $PhI(OAc)_2$  were also screened, and there were no better results, with 1.2 equivalents of TBAI and 2.4 equivalents of  $PhI(OAc)_2$  being optimal (entries 17–19).

With the optimized conditions in hand (Table 1, entry 6), the oxidation of arylalkynes was firstly investigated. As shown



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

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. The *ortho*-substituted substrate gave a lower yield (2e). In addition, the heterocyclederived thiophene substrate can be also tolerated in the reaction (2h). It is worth mentioning that 1-phenylpropane-1,2dione and 1-phenylbutane-1,2-dione can be synthesized under these conditions (2i and 2j).

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Scheme 3 Control experiment.



Scheme 4 Proposed mechanism.

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 reports,<sup>9</sup> we propose a possible reaction pathway as shown in Scheme 4. The  $Cu(II)(OTf)_2$  is oxidized to the active Cu(III)(OAc)<sub>2</sub>(OTf) using the oxidant PhI(OAc)<sub>2</sub> which then coordinates and inserts alkynes forming the intermediate species iv. Release of A from iv by a S<sub>N</sub>2-type reductive elimination leads to Cu(I)OTf, which is oxidized back to the active Cu(m) species ii by PhI(OAc)<sub>2</sub>. 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 using the oxidant  $PhI(OAc)_2$ .

Next, we went on to study the halogenation of alkynes. Scheme 5 reveals that the electronic properties 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 the E-isomer is the major product in most cases (3a-3i).<sup>10</sup> To confirm further the structural assignment of products under the present oxidative conditions, the structure of the product 3e was unambiguously assigned by X-ray crystallography (see the ESI,† Fig. 1).<sup>11</sup> The heterocycle-derived thiophene substrate was also compatible, and the desired product was isolated in 61% yield (3h). When the 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



Scheme 5 Halogenation of arylalkynes.



Fig. 1 The X-ray structure of 3e.

substrates, alkynyl halides, such as alkynyl bromide and alkynyl iodide, can also react with TBAI or TBAC to obtain vinyl dihalides in moderate to good yields (**3n**–**3q**). Aliphatic terminal alkynes cannot give any products in this reaction.

According to the above results and the Taniguchi reported mechanism,<sup>12</sup> we proposed a plausible reaction pathway (Scheme 6). Firstly, AcOI was generated by the reaction between PhI(OAc)<sub>2</sub> and the iodide ion,<sup>13</sup> which can work as a strong electrophile against alkynes to give iodonium ion intermediate **C**. Then, the nucleophile HOAc attacks the positive charge density of intermediate **C** from behind 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 obtained as the minor product (**Path b**).<sup>14</sup>



Scheme 6 Proposed mechanism for the formation of vinyl iodide.



Scheme 7 Illustrative synthetic transformations.

Further synthetic transformations of the haloenol acetate 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 Sonogashira reaction with a 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 a subunit in many bioactive natural products and pharmaceutically important substances.<sup>15</sup>

### Conclusions

In conclusion, we have developed convenient and expedient methods for the synthesis of  $\alpha$ -diketones and  $\beta$ -haloenol acetates from arylalkynes using PhI(OAc)<sub>2</sub> as an oxidant. In contrast to previous reports, the (*E*)- $\beta$ -haloenol acetates were obtained regio- and stereo-specifically as the major products in moderate to good yields. In addition, the (*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 <sup>1</sup>H NMR spectra were recorded on 400 MHz in CDCl<sub>3</sub> and *d*-DMSO, <sup>13</sup>C NMR spectra were recorded on 100 MHz in CDCl<sub>3</sub> and *d*-DMSO. IR spectra were recorded on an FT-IR spectrometer, and only major peaks are reported in cm<sup>-1</sup>.

Melting points were determined on a microscopic apparatus and were uncorrected. All new products were further characterized by HRMS (high resolution mass spectra), and high resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF-Q instrument equipped with an ESI<sup>†</sup> source; copies of their <sup>1</sup>H NMR and <sup>13</sup>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) were added Cu(OTf)<sub>2</sub> (10.9 mg, 10 mol%) and PhI(OAc)<sub>2</sub> (289 mg, 3 equiv.). The reaction mixture was then stirred for 12 h at room temperature in air. The resulting mixture was quenched with saturated  $Na_2S_2O_3$  and extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over  $Na_2SO_4$  and concentrated. The purification of the crude product by flash column chromatography afforded the product 2 (petroleum ether-ethyl acetate as an 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) were added *n*-Bu<sub>4</sub>NI (132.8 mg, 1.2 equiv.) and PhI(OAc)<sub>2</sub> (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 saturated  $Na_2S_2O_3$  and extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over  $Na_2SO_4$  and concentrated. The purification of the crude product by flash column chromatography afforded the product **3** (petroleum ether–ethyl acetate as an eluent (30:1)).

#### Acknowledgements

We thank the National Science Foundation NSF 21402066, the Fundamental Research Funds for the Central Universities (JUSRP11419) and Natural Science Foundation of Jiangsu Province (SBK201222312 and BK20140139) for financial support. Financial support from MOE&SAFEA for the 111 project (B13025) is also gratefully acknowledged.

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