

# Synthetic Methods

## Copper-Catalyzed 1,2-Addition of $\alpha$ -Carbonyl Iodides to Alkynes\*\*

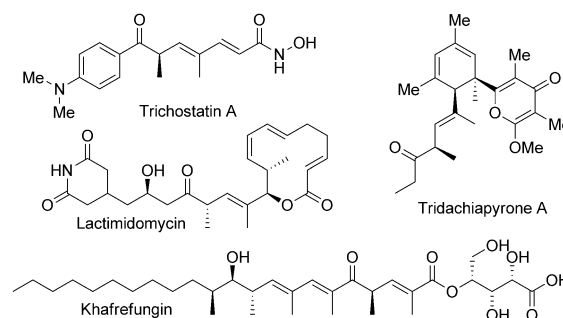
Tao Xu and Xile Hu\*

**Abstract:**  $\beta,\gamma$ -Unsaturated ketones are an important class of organic molecules. Herein, copper catalysis has been developed for the synthesis of  $\beta,\gamma$ -unsaturated ketones through 1,2-addition of  $\alpha$ -carbonyl iodides to alkynes. The reactions exhibit wide substrate scope and high functional group tolerance. The reaction products are versatile synthetic intermediates to complex small molecules. The method was applied for the formal synthesis of ( $\pm$ )-trichostatin A, a histone deacetylase inhibitor.

**$\beta,\gamma$ -Alkenyl ketones** are a recurring motif in natural products and biologically active compounds (Figure 1).<sup>[1]</sup> For example, trichostatin A is a histone deacetylase inhibitor and has potent antitumor activity;<sup>[2]</sup> likewise, lactimidomycin is a promising antitumor agent with a strong antiproliferative effect on tumor cells.<sup>[3]</sup>

$\alpha$ -Alkenylation of carbonyl compounds is a general method for the synthesis of  $\beta,\gamma$ -alkenyl carbonyl compounds.<sup>[4]</sup> Among various  $\alpha$ -alkenylation methods, metal-catalyzed coupling reactions with  $\alpha$ -halo carbonyl compounds are attractive because of the ready accessibility of  $\alpha$ -halo carbonyl derivatives. Fu and Lou reported Ni-catalyzed cross-coupling reactions of  $\alpha$ -bromo ketones with alkenylzirconium reagents (Scheme 1a).<sup>[4a]</sup> Lei and co-workers reported Ni-catalyzed Heck-type cross coupling of  $\alpha$ -bromo esters and amides with styrene derivatives (Scheme 1b).<sup>[4b]</sup> Herein, we report a complementary  $\alpha$ -alkenylation method utilizing  $\alpha$ -bromo ketones and alkynes as reaction partners. In the presence of a Cu catalyst and KI, the reactions yield  $\beta,\gamma$ -alkenyl ketones with a transformable alkenyl iodide functional group (Scheme 1c). The reactions can be considered as 1,2-addition reactions of  $\alpha$ -iodo ketones to alkynes.<sup>[5]</sup> Although several examples of addition reactions of  $\alpha$ -iodo esters and  $\alpha$ -iodo amides to alkenes<sup>[6]</sup> and alkynes<sup>[7]</sup> have been reported, the scope of these reactions is limited.

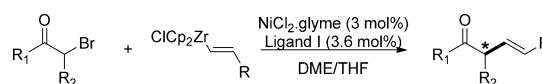
Recently, we found that perfluoroalkyl radicals could be generated from perfluoroalkyl iodides in the presence of  $\text{Cs}_2\text{CO}_3$  and  $\text{FeBr}_2$ .<sup>[8]</sup> The perfluoroalkyl radicals then could add to alkenes and alkynes under Fe catalysis. We hypothesized that  $\alpha$ -ketone radicals might be generated under similar



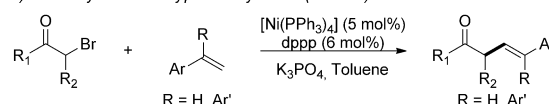
**Figure 1.** Selected complex molecules containing a  $\beta,\gamma$ -alkenyl ketone motif.

### Previous Work:

a) Ni-catalyzed cross-coupling reaction (Ref. 4a)

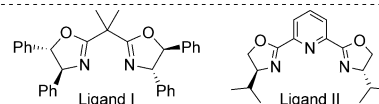
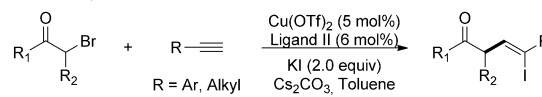


b) Ni-catalyzed Heck-type alkenylation (Ref. 4b)



### This Work:

c) Cu-catalyzed intermolecular addition reaction



**Scheme 1.** Comparison of synthetic methods for the preparation of  $\beta,\gamma$ -alkenyl ketones using  $\alpha$ -bromo carbonyl compounds. DME = dimethoxyethane. dppp = 1,3-bis(diphenylphosphino)propane. Cp = cyclopentadiene.

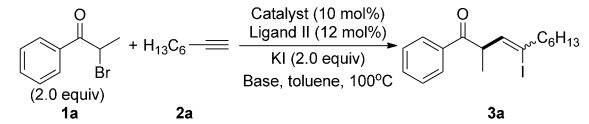
conditions from  $\alpha$ -iodo ketones; addition of these radicals to alkynes would yield  $\beta,\gamma$ -alkenyl iodoketones. To test this hypothesis, the addition of 2-iodopropiophenone, generated in situ from 2-bromopropiophenone (**1a**) and KI, to 1-octyne (**2a**) was examined (Table 1). However, no product was formed using the conditions previously developed for Fe-catalyzed perfluoroalkylation (Table 1, entry 1).<sup>[8]</sup> A screening of catalysts (see Supporting Information) showed that  $\text{Cu}(\text{OTf})_2$  in combination with ligand II could catalyze this reaction in toluene in a 57 % yield (entry 2). Replacement of  $\text{Cu}(\text{OTf})_2$  by other copper salts led to lower yields (entries 3 and 4). Without  $\text{Cu}(\text{OTf})_2$  or ligand, the reaction was less efficient (entries 5,6). Decreasing the loading of  $\text{Cs}_2\text{CO}_3$  to 60 mol % increased the yield to 73 % (entry 7). In

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**Table 1:** Optimization of reaction conditions.<sup>[a]</sup>



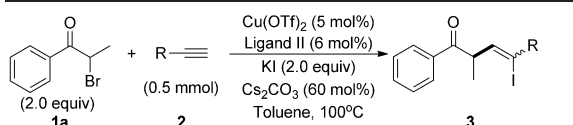
Entry	Catalyst	Base (loading)	Conversion (2a)	Yield (Z/E) <sup>[b]</sup>
1 <sup>[c]</sup>	FeBr <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub> (80%)	25 %	0 (–)
2	Cu(OTf) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub> (150%)	81 %	57 % (6.2)
3	CuI	Cs <sub>2</sub> CO <sub>3</sub> (150%)	95 %	47 % (5.3)
4	Cu(acac) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub> (150%)	74 %	21 % (> 19)
5	–	Cs <sub>2</sub> CO <sub>3</sub> (150%)	56 %	32 % (5.3)
6 <sup>[d]</sup>	Cu(OTf) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub> (150%)	60 %	24 % (3.8)
7	Cu(OTf) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub> (60%)	89 %	73 % (4.0)
8	Cu(OTf) <sub>2</sub>	–	40 %	0 (–)
9	Cu(OTf) <sub>2</sub>	K <sub>2</sub> CO <sub>3</sub> (60%)	85 %	31 % (3.8)
10	Cu(OTf) <sub>2</sub>	<i>t</i> BuONa (60%)	59 %	0 (–)
11	Cu(OTf) <sub>2</sub>	TEA (60%)	72 %	0 (–)
12 <sup>[e]</sup>	Cu(OTf) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub> (60%)	41 %	17 % (3.3)
13 <sup>[f]</sup>	Cu(OTf) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub> (60%)	92 %	76 % (3.3)

[a] The reactions were conducted on a 0.25 mmol scale in toluene (1.0 mL) under N<sub>2</sub>. [b] The yields and the ratios were determined by GC using *n*-decane as the internal standard. [c] The reaction was conducted in dioxane at 60 °C without ligand II. [d] Without ligand II. [e] The reaction was conducted in air. [f] The reaction was conducted on a 0.5 mmol scale with Cu(OTf)<sub>2</sub> (5 mol%) and ligand II (6 mol%) in toluene (1.0 mL).

the absence of Cs<sub>2</sub>CO<sub>3</sub>, no addition product was formed (entry 8). Replacement of Cs<sub>2</sub>CO<sub>3</sub> by K<sub>2</sub>CO<sub>3</sub>, *t*BuONa, or triethylamine (TEA) led to a lower or no yield (entries 9–11). The reaction required a nitrogen atmosphere to proceed; in air the yield was only 17 % (entry 12). Racemic and enantiomerically pure forms of ligand II gave identical yields. The loading of catalyst could be decreased to 5 mol%, to give optimized conditions of: Cu(OTf)<sub>2</sub> as catalyst (5 mol%), ligand II (6 mol%), as substrates 2-bromopropiophenone (2 equiv), KI (2 equiv), and alkyne (1 equiv), and Cs<sub>2</sub>CO<sub>3</sub> (0.6 equiv) as base (Table 1, entry 13).<sup>[9]</sup>

With the optimized conditions in hands, the copper-catalyzed method was first applied for the reactions of 2-bromopropiophenone (**1a**) with various alkynes (Table 2).<sup>[10]</sup> Addition is efficient not only to alkyl alkynes but also to aryl alkynes. Primary (to give products **3a** and **3h–n**), secondary (to give cyclic **3c** or acyclic **3d**) and tertiary (to give **3e**) alkyl alkynes as well as silylacetylenes (to give **3f** and **3g**) were all suitable substrates. The addition to alkyl alkynes is *Z*-isomer selective, with a *Z:E* ratio generally greater than 3:1. The selectivity correlated with the bulkiness of the alkyl substituents, and *Z:E* ratios greater than 50:1 were obtained with silyl and tertiary alkyl alkynes (to give products **3e**, **3f**, **3g**). On the other hand, the addition to aryl alkynes gives an equal mixture of *Z* and *E* isomers (**3b**). The reactions have high functional group tolerance. Ester (**3h**), ketone (**3i**), ether (**3j**, **3k**), amide (**3m**), acetal (**3n**), thioether (**3j**), aryl halide (**3k**), and alkyl halide (**3l**) groups were all compatible. Addition to internal alkynes is not efficient. For example, the reaction of **1a** with 5-decyne gave the product only in 8 % yield.

**Table 2:** Scope of copper-catalyzed 1,2-addition of iodopropiophenone to alkynes.<sup>[a]</sup>

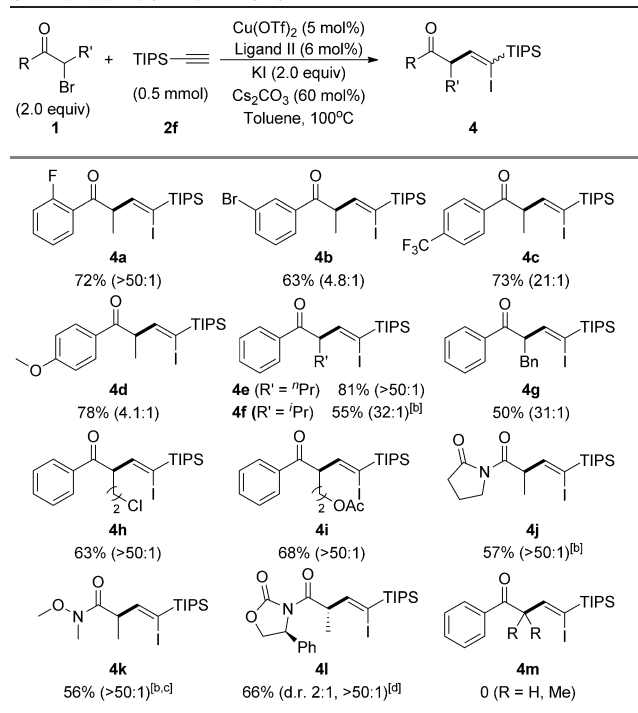


Product	Yield (%)	<i>Z:E</i> Ratio
<b>3a</b>	76%	(3.9:1)
<b>3b</b>	75%	(1.1:1)
<b>3c</b>	73%	(8.7:1)
<b>3d</b>	68%	(4.5:1) <sup>[b]</sup>
<b>3e</b>	64%	(>50:1) <sup>[b,c]</sup>
<b>3f</b>	81%	(>50:1) <sup>[c]</sup>
<b>3g</b>	74%	(>50:1) <sup>[c]</sup>
<b>3h</b>	55%	(3.5:1) <sup>[b]</sup>
<b>3i</b>	57%	(3.4:1)
<b>3j</b>	50%	(3.3:1) <sup>[b]</sup>
<b>3k</b>	55%	(4.0:1)
<b>3l</b>	68%	(3.1:1)
<b>3m</b>	62%	(3.1:1)
<b>3n</b>	61%	(2.4:1)

[a] Reaction conditions: **1a** (2.0 equiv), **2** (0.5 mmol), Cu(OTf)<sub>2</sub> (5 mol%), ligand II (6 mol%), Cs<sub>2</sub>CO<sub>3</sub> (60 mol%), KI (2.0 equiv), toluene (1 mL), 100 °C, 24 h, under N<sub>2</sub>; yields of isolated product were given and *Z:E* ratios are given in parentheses. [b] Cu(OTf)<sub>2</sub> (10 mol%), ligand II (12 mol%). [c] The ratio was measured using <sup>1</sup>H NMR spectroscopy.

The scope of  $\alpha$ -carbonyl ketone reagents in the reaction was then explored using (triisopropylsilyl)acetylene as the reaction partner (Table 3). Aryl ketones with substitution at the *ortho* (**4a**), *meta* (**4b**), or *para* position (**4c**) all reacted to give the corresponding products in high yields and good selectivity. Reagents containing an electron-withdrawing CF<sub>3</sub> group (to give product **4c**) or an electron-donating OMe group (**4d**) were tolerated. The R' functional group is not limited to methyl substituents. Substrates with *n*-propyl (to give **4e**), isopropyl (**4f**), benzyl (**4g**), and functionalized alkyl group (**4h**, **4i**) in this position were all transformed smoothly and with high selectivity. However, when the R' functional group was a proton or a secondary alkyl group (to give product **4m**), the reaction was unsuccessful. The method is not limited to aryl ketones. An amide (**4j**) and a Weinreb amide (**4k**) could also be employed.  $\alpha$ -Alkenylation was successful on a substrate containing an Evans-type auxiliary **4l**, albeit with a low diastereoselectivity.

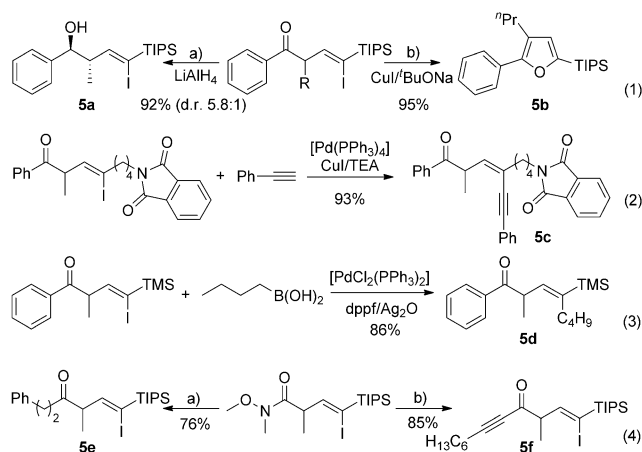
**Table 3:** Scope of copper-catalyzed addition of  $\alpha$ -carbonylbromides to (triisopropylsilyl)acetylene (**2f**).<sup>[a]</sup>



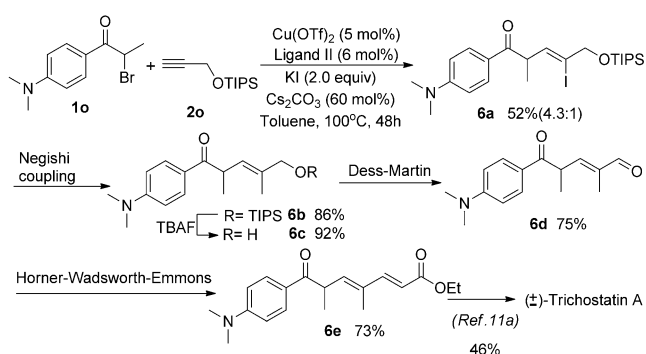
[a] Reaction conditions: **1** (2.0 equiv), **2f** (0.5 mmol),  $\text{Cu}(\text{OTf})_2$  (5 mol%), ligand II (6 mol%),  $\text{Cs}_2\text{CO}_3$  (60 mol%), KI (2.0 equiv), toluene (1 mL), 100°C, 24 h, under  $\text{N}_2$ ; yields of isolated product were given and the *Z/E* ratios (given in parentheses) were measured using  $^1\text{H}$  NMR spectroscopy. [b] Reaction time was 48 h. [c]  $\text{Cu}(\text{OTf})_2$  (10 mol%), ligand II (12 mol%), **1k** (3.0 equiv), KI (3.0 equiv). [d]  $\text{Cu}(\text{OTf})_2$  (10 mol%), ligand II (12 mol%). Bn = benzyl. d.r. = diastereomeric ratio.

The Cu-catalyzed  $\alpha$ -alkenylation method produces  $\beta,\gamma$ -unsaturated ketones with an alkenyl iodide group. These compounds are versatile synthetic intermediates. For example, reduction of the ketone group by  $\text{LiAlH}_4$  gave a homoallylic alcohol **5a** in a high yield and moderate regioselectivity [Scheme 2, Eq. (1a)]. With CuI as catalyst and *t*BuONa as base, the vinyl iodide ketone was easily converted into a substituted furan **5b** [Eq. (1b)]. As expected, the vinyl iodide group was amenable to cross-coupling reactions, such as Sonogashira coupling to form product **5c** [Eq. (2)] and Suzuki coupling giving **5d** [Eq. (3)]. Importantly, products containing the Weinreb amide group could be transformed to give alkyl (**5e**) and alkynyl ketones (**5f**) [Scheme 2, Eq. (4)]. Thus, even though alkyl and alkynyl ketones are not suitable substrates for the direct alkenylation reaction, their equivalent alkenylation can be achieved using Weinreb amides as starting reagents.

To further illustrate the utility of the Cu-catalyzed  $\alpha$ -alkenylation reaction, the method was applied for the formal synthesis of ( $\pm$ )-trichostatin A (Scheme 3).<sup>[11]</sup> The addition reaction of substrate **1o** to the TIPS-protected propynol **2o** (TIPS = triisopropylsilyl) gave the product **6a** in a 52% yield and with a *Z/E* ratio of 4.3:1. Pd-catalyzed Negishi coupling of **6a** with  $\text{MeZnCl}$  installed the methyl group at the  $\gamma$  position, giving product **6b** in an 86% yield. Desilylation gave the



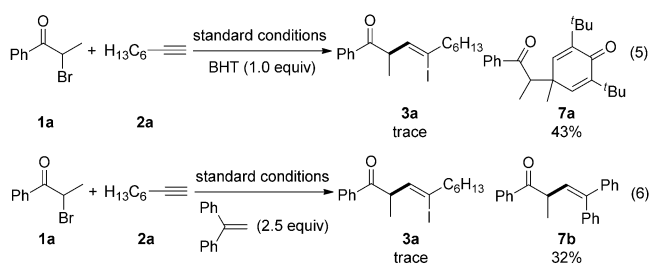
**Scheme 2.** Further functionalization of  $\beta,\gamma$ -unsaturated ketones. dppf = 1,1'-bis(diphenylphosphino)ferrocene. TEA = triethylamine.



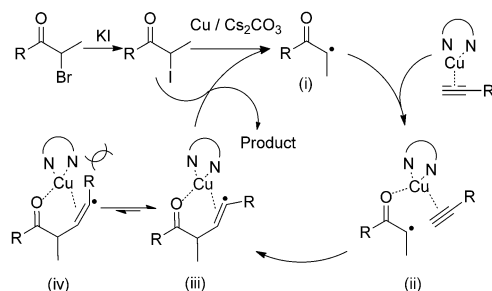
**Scheme 3.** Formal total synthesis of ( $\pm$ )-trichostatin A. TBAF = tetrabutylammonium fluoride.

alcohol **6c** in a 92% yield, which was oxidized with the Dess-Martin reagent to the aldehyde **6d** in a 75% yield. Horner-Wadsworth-Emmons reaction of **6d** produced the diene ester **6e** in a 73% yield; intermediate **6e** was previously transformed to ( $\pm$ )-trichostatin in a one-step reaction.<sup>[11a]</sup>

To give some insight into the mechanism of the addition reaction, several experiments using radical probes were performed. In the presence of 2,2,6,6-tetramethylpiperidinoxy (TEMPO; 1 equiv), most of the reactants remained and no addition product was formed; however, alkylated TEMPO was not detected probably as a result of the steric hindrance of this bulky alkyl group (see Table S2 in the Supporting Information for the detailed outcome of the reaction). To further verify the possibility of a radical process, the addition reaction was conducted in the presence of additional radical probes including 2,6-di-*tert*-butyl-4-methylphenol (BHT, 1.0 equiv) and 1,1-diphenylethylene (DPE, 2.5 equiv).<sup>[6a]</sup> Indeed, the reaction was inhibited by both BHT and DPE. In the presence of BHT, the alkyl radical was trapped as **7a** in 43% yield [Scheme 4, Eq. (5)]; in the presence of DPE, the alkyl radical was trapped by the olefin to give **7b** in 32% yield respectively [Eq. (6)].<sup>[12]</sup> These results suggest that the  $\alpha$ -carbonyl alkyl radical is produced in the addition reaction. A radical mechanism is also consistent with previous work showing that in the presence of a metal salt,



**Scheme 4.** Reactions in the presence of radical probes. BHT = 2,6-di-*tert*-butyl-4-methylphenol.



**Scheme 5.** Hypothetical catalytic cycle.

$\text{Cs}_2\text{CO}_3$  is able to generate the alkyl radical from activated alkyl halides at an elevated temperature.<sup>[8]</sup>

The mechanism of the  $\alpha$ -alkenylation reaction is subject to further study, so only a hypothetical catalytic cycle is proposed here based on the above results (Scheme 5). The reaction starts from the in situ generation of an  $\alpha$ -iodo ketone from the reaction of the  $\alpha$ -bromo ketone with KI. Consistent with this, the reaction of **1a** with **2a** in the absence of KI under otherwise standard conditions gave the vinyl bromide product in only 11 % yield. Activation of  $\alpha$ -iodo ketone by  $\text{Cs}_2\text{CO}_3$ , possibly with the involvement of the copper catalyst, leads to an  $\alpha$ -ketone radical (i). Coordination of both the  $\alpha$ -ketone radical and alkyne to Cu gives intermediate (ii). Intramolecular addition of  $\alpha$ -ketone radical to the alkyne then gives  $\gamma$ -ketone vinyl radical (iii, iv) which reacts with a second molecule of  $\alpha$ -iodo ketone to yield the addition product and regenerate the  $\alpha$ -ketone radical (intermediate iii or iv to form i). The *Z/E* selectivity of the reaction likely depends on the relative stability of intermediates (iii) and (iv).

In summary, Cu-catalyzed 1,2-addition of  $\alpha$ -iodo ketones to alkynes has been developed as an efficient method for  $\alpha$ -alkenylation of ketones. The method employs readily available reagents and has broad scope and high functional-group tolerance. The resulting  $\beta,\gamma$ -alkenyl iodo ketones prove to be versatile synthetic intermediates. The synthetic utility of the method was further demonstrated in the formal synthesis of ( $\pm$ )-trichostatin A.

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**Keywords:** 1,2-addition reactions · alkynes · copper · ketones · olefination

- [1] a) S. M. Mandala, R. A. Thornton, M. Rosenbach, J. Milligan, M. Garcia-Calvo, H. G. Bull, M. B. Kurtz, *J. Biol. Chem.* **1997**, 272, 32709; b) T. Kolter, K. Sandhoff, *Angew. Chem. Int. Ed.* **1999**, 38, 1532; *Angew. Chem.* **1999**, 111, 1632; c) T. Wakabayashi, K. Mori, S. Kobayashi, *J. Am. Chem. Soc.* **2001**, 123, 1372; d) M. B. Ksebati, F. J. Schmitz, *J. Org. Chem.* **1985**, 50, 5637.
- [2] a) M. Yoshida, M. Kijama, M. Akita, T. Beppu, *J. Biol. Chem.* **1990**, 265, 17174; b) M. S. Finnin, J. R. Donigian, A. Cohen, V. M. Richon, R. A. Rifkind, P. A. Marks, R. Breslow, N. P. Pavletich, *Nature* **1999**, 401, 188; c) N. Tsuji, M. Kobayashi, K. Nagashima, Y. Wakisaka, K. Koizumi, *J. Antibiot.* **1976**, 29, 1; d) N. Mishra, D. R. Brown, I. M. Olorenshaw, G. M. Kammer, *Proc. Natl. Acad. Sci. USA* **2001**, 98, 2628; e) K. T. Andrews, A. Walduck, M. J. Kelso, D. P. Fairlie, A. Saul, P. G. Parsons, *Int. J. Parasitol.* **2000**, 30, 761.
- [3] a) K. Sugawara, Y. Nishiyama, S. Toda, N. Komiyama, M. Hatori, T. Moriyama, Y. Sawada, H. Kamei, M. Konishi, O. Toshikazu, *J. Antibiot.* **1992**, 45, 1433; b) K. Nakae, Y. Yoshimoto, T. Sawa, T. Y. Homma, Y. M. Hamada, T. Takeuchi, M. Imoto, *J. Antibiot.* **2000**, 53, 1130; c) E. J. Woo, C. M. Starks, C., Jr. Carney, R. Arslanian, L. Cadapan, S. Zavala, P. Licari, *J. Antibiot.* **2002**, 55, 141.
- [4] a) S. Lou, G. C. Fu, *J. Am. Chem. Soc.* **2010**, 132, 5010; b) C. Liu, S. Tang, D. Liu, J. Yuan, L. Zheng, L. Meng, A. Lei, *Angew. Chem. Int. Ed.* **2012**, 51, 3638; *Angew. Chem.* **2012**, 124, 3698; c) K. Takami, H. Yorimitsu, K. Oshima, *Org. Lett.* **2004**, 6, 4555; d) Q. Liu, H. Yi, J. Liu, Y. Yang, X. Zhang, Z. Zeng, A. Lei, *Chem. Eur. J.* **2013**, 19, 5120; e) H. Jiang, C. Huang, J. Guo, C. Zeng, Y. Zhang, S. Yu, *Chem. Eur. J.* **2012**, 18, 15158; f) A. M. Taylor, R. A. Altman, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, 131, 9900; g) G. K. Friestad, Y. Wu, *Org. Lett.* **2009**, 11, 819; h) J. Huang, E. Bunel, M. M. Fail, *Org. Lett.* **2007**, 9, 4343; i) F. Luo, T. Lu, C. Xue, *Tetrahedron Lett.* **2003**, 44, 7249; j) S. Watanabe, T. Ikeda, T. Kataoka, G. Tanabe, O. Muraoka, *Org. Lett.* **2003**, 5, 565; k) B. P. Branchaud, W. D. Detlefsen, *Tetrahedron Lett.* **1991**, 32, 6273; l) H. C. Brown, B. T. Cho, W. S. Park, *J. Org. Chem.* **1986**, 51, 3398; m) A. Pelter, C. R. Harrison, D. Kirkpatrick, *Tetrahedron Lett.* **1973**, 14, 4491.
- [5] For selected reviews on the addition reaction, see: a) X. Zeng, *Chem. Rev.* **2013**, 113, 6864; b) U. Wille, *Chem. Rev.* **2013**, 113, 813; c) J. F. Bower, I. S. Kim, R. L. Patman, M. J. Krische, *Angew. Chem. Int. Ed.* **2009**, 48, 34; *Angew. Chem.* **2009**, 121, 36; d) I. Beletskaya, C. Moberg, *Chem. Rev.* **1999**, 99, 3435.
- [6] a) J.-H. Fan, W.-T. Wei, M.-B. Zhou, R.-J. Song, J.-H. Li, *Angew. Chem. Int. Ed.* **2014**, 53, 6650; *Angew. Chem.* **2014**, 126, 6768; b) F. Mo, G. Dong, *Science* **2014**, 345, 68; c) X. Fang, K. Liu, C. Li, *J. Am. Chem. Soc.* **2010**, 132, 2274; d) H. Miyabe, R. Asada, A. Toyoda, Y. Takemoto, *Angew. Chem. Int. Ed.* **2006**, 45, 5863; *Angew. Chem.* **2006**, 118, 5995; e) J. Wang, C. Li, *J. Org. Chem.* **2002**, 67, 1271; f) M. J. Joung, J. H. Ahn, D. W. Lee, N. M. Yoon, *J. Org. Chem.* **1998**, 63, 2755; g) E. Lee, C. H. Yoon, T. H. Lee, *J. Am. Chem. Soc.* **1992**, 114, 10981; h) M. Mori, Y. Kubo, Y. Ban, *Tetrahedron* **1988**, 44, 4321; i) M. Mori, N. Kanda, Y. Ban, *J. Chem. Soc. Chem. Commun.* **1986**, 1375.
- [7] a) H. Miyabe, R. Asada, Y. Takamoto, *Beilstein J. Org. Chem.* **2013**, 9, 1148; b) Z. Liu, J. Wang, Y. Zhao, B. Zhou, *Adv. Synth. Catal.* **2009**, 351, 371; c) Y. Tang, C. Li, *Org. Lett.* **2004**, 6, 3229; d) S. D. Mawson, R. T. Weavers, *Tetrahedron* **1995**, 51, 11257; e) Y. Ichinose, S. Matsunaga, K. Fugami, K. Oshima, K. Utimoto, *Tetrahedron Lett.* **1989**, 30, 3155.
- [8] T. Xu, C. W. Cheung, X. Hu, *Angew. Chem. Int. Ed.* **2014**, 53, 4910; *Angew. Chem.* **2014**, 126, 5010.
- [9] No enantioselectivity was detected in the product.
- [10] The reactions with 2-iodopropiophenone (without KI) or 2-chloropropiophenone (with KI) gave the product **3a** in 76 % and 45 % yields, respectively, with similar *Z/E* selectivity.

- [11] a) I. Fleming, J. Iqbal, *Tetrahedron* **1983**, 39, 841; b) C. C. Cosner, V. B. R. Iska, A. Chatterjee, J. T. Markiewicz, S. J. Corden, J. Lofstedt, T. Ankner, J. Richer, T. Hulett, D. J. Schauer, O. Wiest, P. Helquist, *Eur. J. Org. Chem.* **2013**, 162; c) C. C. Cosner, P. Helquist, *Org. Lett.* **2011**, 13, 3564; d) J. T. Markiewicz, D. J. Schauer, J. Lofstedt, S. J. Corden, O. Wiest, P. Helquist, *J. Org. Chem.* **2010**, 75, 2061; e) A. Chatterjee, J. Richer, T. Hulett, V. B. R. Iska, O. Wiest, P. Helquist, *Org. Lett.* **2010**, 12, 832; f) S. Zhang, W. Duan, W. Wang, *Adv. Synth. Catal.* **2006**, 348, 1228; g) S. Hosokawa, T. Ogura, H. Togashi, K. Tatsuta, *Tetrahedron Lett.* **2005**, 46, 333; h) F. L. Cells, I. Antipode, *Tetrahedron* **1988**, 44, 6013.
- [12] Compound **7a** was formed in only 2 % GC yield in the reaction in the absence of the copper–ligand catalyst.