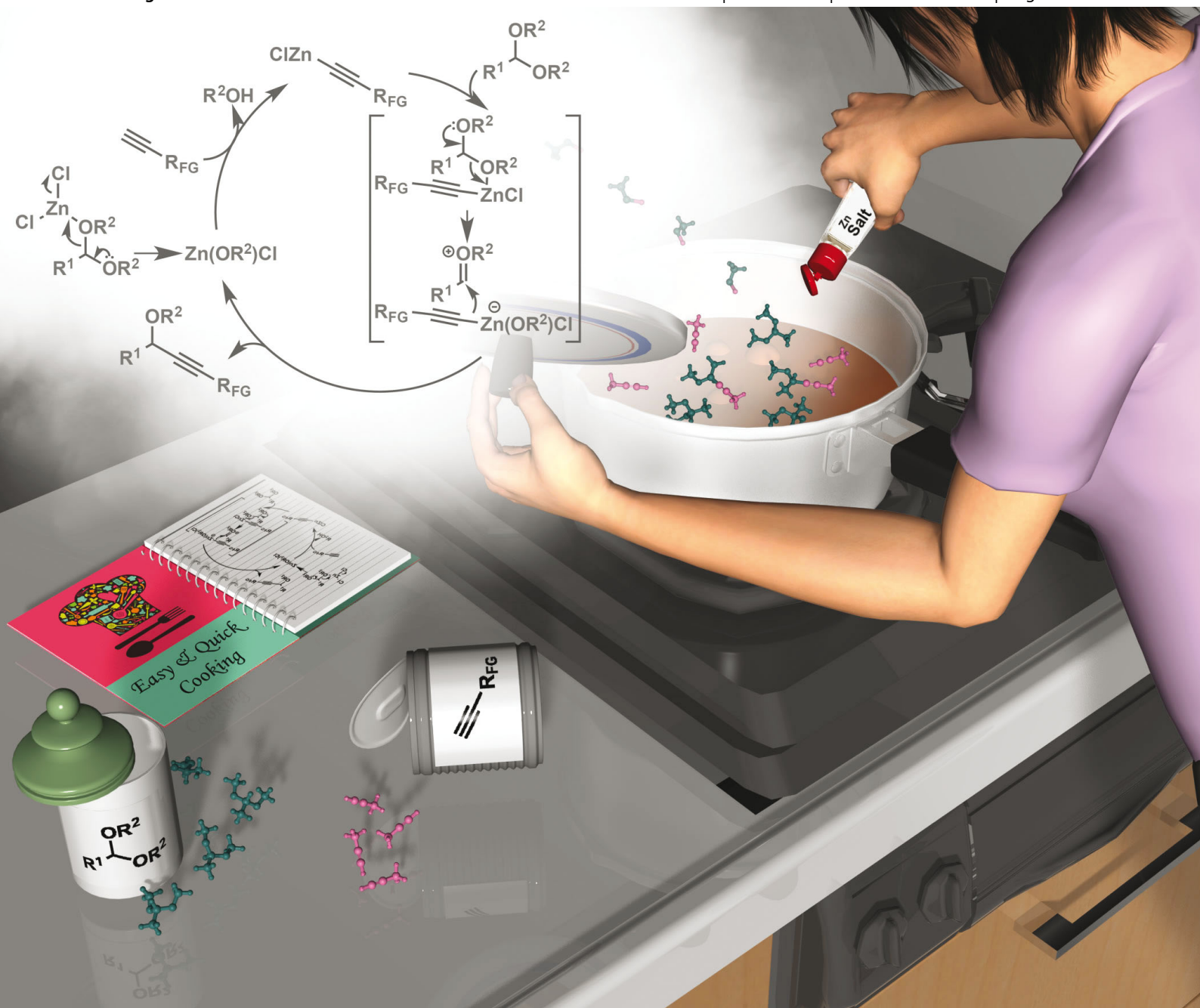


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## COMMUNICATION

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Zn(II) chloride-catalyzed direct coupling of various alkynes with acetals:  
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# Zn(II) chloride-catalyzed direct coupling of various alkynes with acetals: facile and inexpensive access to functionalized propargyl ethers†

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The coupling of acetals with various alkynes was achieved using only 1 mol% of inexpensive and mild Lewis acid ZnCl<sub>2</sub>, which furnished propargyl ethers. The coupling was catalyzed by Zn(OMe)Cl, which was generated *in situ* to form an alkynylzinc species. This protocol was allowed to expand to a one-pot subsequent reaction with allylchlorosilane to obtain a 1,4-enyne product.

Alkynylation is a fundamental and valuable method<sup>1</sup> for the preparation of bioactive compounds<sup>2</sup> and charge transport materials.<sup>3</sup> The employment of alkynyl metal agents such as alkynyllithiums,<sup>4</sup> -silanes,<sup>5</sup> -stannanes,<sup>6</sup> and -boranes<sup>7</sup> makes for versatile methods, but these cannot avoid the annoying preparation of, and the incompatibility that results from, various functional groups. To overcome these issues, the direct use of terminal alkynes has been the focus from an environmental point of view.<sup>8</sup>

Our group has reported the direct synthesis of alkynylstannanes from various terminal alkynes and Bu<sub>3</sub>SnOMe as catalyzed by ZnBr<sub>2</sub>, in which Zn(OMe)Br is generated by transmetalation between Bu<sub>3</sub>SnOMe and ZnBr<sub>2</sub> and plays a key role in producing an active alkynylzinc species *in situ* (Scheme 1a).<sup>9</sup> We expected the reaction between dimethyl acetals and ZnBr<sub>2</sub> to generate oxonium cations along with Zn(OMe)Br,<sup>10</sup> which may be an alternative formation of Zn(OMe)Br. This idea prompted us to develop the reaction between terminal alkynes and acetals in the presence of ZnBr<sub>2</sub> wherein the generated alkynyl zinc from Zn(OMe)Br was

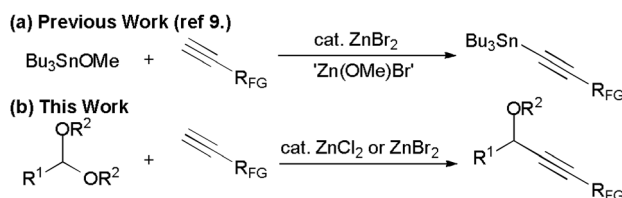
expected to promote the coupling (Scheme 1b). Some examples of coupling between acetals and alkynes have been recently reported, but these generated a cation of metals like Au<sup>+</sup> for the activation of alkynes<sup>11</sup> or more than one equimolar amount of base for alkynyl metal generation.<sup>12</sup> Fortunately, direct coupling could be promoted by using only a catalytic amount of inexpensive ZnBr<sub>2</sub> or ZnCl<sub>2</sub> to furnish propargyl ethers, and it was a surprise that a weak Lewis acid such as ZnCl<sub>2</sub> worked with no additives.

An investigation into the reaction conditions was commenced. Benzaldehyde dimethyl acetal (**1a**) did not react with 1-decyne (**2a**) without a catalyst under toluene refluxing conditions (Table 1, entry 1). The addition of 10 mol% of ZnBr<sub>2</sub> provided the coupling product **3aa** in an 81% yield (entry 2). A higher yield was realized when ZnCl<sub>2</sub> was utilized (entry 3). The reaction was completed in 12 h using only 1 mol% loading of ZnCl<sub>2</sub>-Et<sub>2</sub>O, furnishing **3aa** quantitatively (entry 4). ZnI<sub>2</sub> and Zn(OTf)<sub>2</sub> gave moderate yields,

Table 1 Screening of catalysts<sup>a</sup>

Entry	Catalyst	Yield <sup>b</sup> (%)
1	None	0
2	ZnBr <sub>2</sub>	81
3	ZnCl <sub>2</sub>	90
4 <sup>c</sup>	ZnCl <sub>2</sub> -Et <sub>2</sub> O	99 (86)
5	ZnI <sub>2</sub>	76
6	Zn(OTf) <sub>2</sub>	50
7	Zn(OAc) <sub>2</sub> ·2H <sub>2</sub> O	0
8	InCl <sub>3</sub>	55
9	CuCl <sub>2</sub>	65
10	BiCl <sub>3</sub>	40
11	AlCl <sub>3</sub>	0
12	TiCl <sub>4</sub>	0
13	BF <sub>3</sub> ·OEt <sub>2</sub>	5
14	SnCl <sub>4</sub>	0
15	SnCl <sub>4</sub> + ZnCl <sub>2</sub>	0

<sup>a</sup> Reaction conditions: **1a** (2.0 mmol), **2a** (1.0 mmol), and a catalyst (0.10 mmol) were refluxed in toluene (1 mL) for 24 h. <sup>b</sup> <sup>1</sup>H NMR yield. The value in parentheses indicates the isolated yield. <sup>c</sup> Catalyst (0.01 mmol), 12 h.



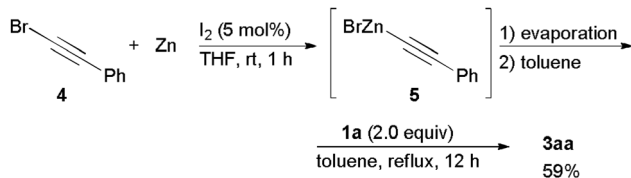
Scheme 1 Comparison of previous work with this work.

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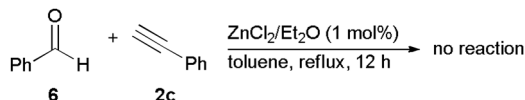
† Electronic supplementary information (ESI) available. See DOI: 10.1039/c3cc46570e







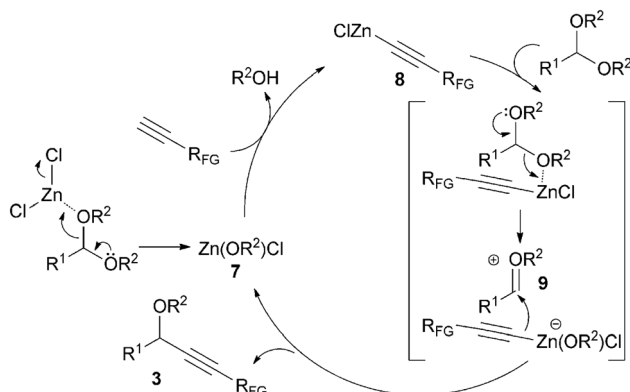
**Scheme 3** Reaction of alkynylzinc **5** with acetal **1a**.



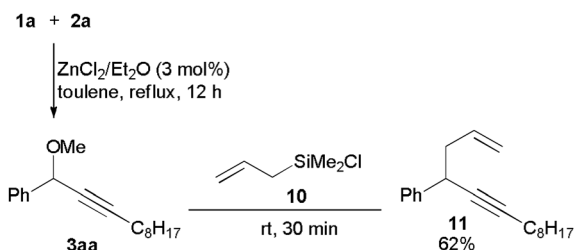
**Scheme 4** Reaction of aldehyde **6** with alkyne **2c**.

We investigated whether this protocol would allow the alkynylation of aldehydes, because the catalytic alkynylation of aldehydes with terminal alkynes has been reported.<sup>15</sup> The fact that there was no reaction of alkyne **2c** with benzaldehyde (**6**) (Scheme 4) implies that the active species, Zn(OMe)Cl, generated from dimethyl acetals is essential for the catalytic coupling reaction.

A plausible reaction mechanism is shown in Scheme 5. ZnCl<sub>2</sub> activates the acetal to give zinc species **7**, which interacts with an alkyne and leads to the formation of alkynylzinc **8**. The alkynylzinc **8** reacts with acetal **1** via an oxonium cation **9** and a zincate complex to afford the desired product **3** along with the regeneration of **7**. The kinetic study of the coupling was carried out by GC (see ESI<sup>†</sup>) and showed that the reaction was dependent on the first order of each component ( $v = k[1a][2a][\text{catalyst}]$ ;  $k$ ;  $4.06 \times 10^{-2} \text{ mol}^{-2} \text{ L}^2 \text{ s}^{-1}$ ,  $T = 130 \text{ }^\circ\text{C}$ ). The result and implication of



**Scheme 5** Plausible reaction mechanism.



**Scheme 6** One-pot allylation of the product **3aa**.

containing an alkynylzinc as shown in Scheme 3 might indicate that the interaction between an acetal and alkynylzinc **8** is the rate-limiting step.

The produced propargyl ether **3aa** was found to subsequently react with allylchlorosilane **10** in a one-pot treatment, where the allylation was completed in 30 min at room temperature, yielding 1,5-enyne **11** (Scheme 6). The isolated **3aa** did not react with **10** in the absence of ZnCl<sub>2</sub>, which apparently suggested the catalytic role of ZnCl<sub>2</sub> in the substitution of the OMe moiety to the allyl one.

In conclusion, we developed an alkynylation of acetals with various alkynes including alkyls that can be catalyzed by inexpensive ZnCl<sub>2</sub>. This reaction needs no expensive metal catalyst, such as gold,<sup>11</sup> nor does it need additives.<sup>12</sup> The product, propargyl ether, was functionalized without isolation, which shows that this reaction is clean enough to effectively undergo further transformation.

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