

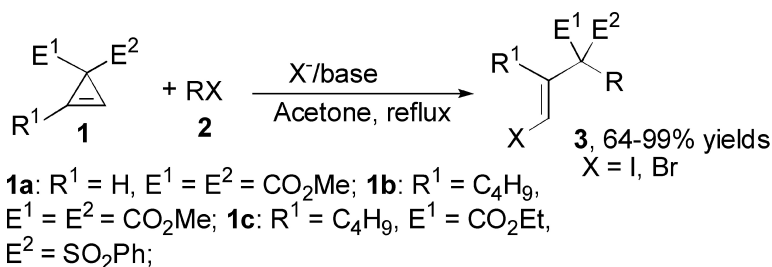
Communication

## An X (X = I, Br)-Triggered Ring-Opening Coupling Reaction of Cyclopropenes with Organic Halides

Shengming Ma, Junliang Zhang, Yangjun Cai, and Lianghua Lu

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## An X<sup>-</sup> (X = I, Br)-Triggered Ring-Opening Coupling Reaction of Cyclopropenes with Organic Halides

Shengming Ma,<sup>\*,†,‡</sup> Junliang Zhang,<sup>†</sup> Yangjun Cai,<sup>‡</sup> and Lianghua Lu<sup>†</sup>

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, P.R. China, and Department of Chemistry, Zhejiang University, Hangzhou 310027, Zhejiang, P. R. China

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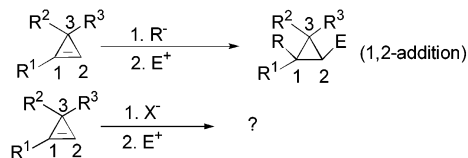
Alkenyl halides are important building blocks because of their diverse synthetic importance.<sup>1,2</sup> Thus, the efficient formation of alkenyl halides in a stereoselective fashion is an important continuing goal in organic synthesis.<sup>3</sup>

Cyclopropenes, highly strained but readily accessible carbocyclic molecules, have been shown to possess unique reactivity in organic synthesis.<sup>4</sup> In past years, many sequential addition reactions of organometallic reagents such as organic lithium,<sup>5</sup> Grignard,<sup>6</sup> cuprate,<sup>7</sup> and zinc<sup>6b,8</sup> reagents (RMX) with cyclopropenes and electrophiles (E<sup>+</sup>), leading efficiently to polysubstituted cyclopropanes, have been developed, in which the R group is uniquely<sup>9</sup> directed toward the sterically more hindered 1-position, with the E group being subsequently introduced to the 2-position (Scheme 1). However, to the best of our knowledge, the sequential addition of halides such as I<sup>-</sup> and Br<sup>-</sup> to cyclopropenes and the coupling with electrophiles has not been reported. Herein we report a novel I<sup>-</sup> or Br<sup>-</sup>-catalyzed ring-opening coupling reaction of cyclopropenes with organic halides to give polyfunctionalized (*E*)-alk-1-enyl halides with excellent regioselectivity and stereoselectivity.

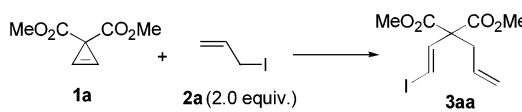
Initially, we tested the coupling reaction of 3,3-bis(methoxycarbonyl)cycloprop-1-ene (**1a**)<sup>10</sup> with allyl iodide (**2a**) in the presence of different alkali metal iodide and additives (Table 1). After some trial and error, we were pleased to find that the reaction of **1a** with **2a** (2.0 equiv) in acetone under reflux for 2.5 h in the presence of a catalytic amount of NaI (10 mol %) and 50 mol % of Na<sub>2</sub>CO<sub>3</sub> (conditions A) occurred smoothly to give a ring-opening coupling product **3aa** in 69% yield with excellent stereoselectivity (entry 5, Table 1). A higher yield (77%) of **3aa** was observed when 4 equiv of **2a** was applied (entry 6, Table 1). The yield was lower when the amount of the base was reduced (entries 3–5, Table 1). The coupling reaction also afforded **3aa** in somewhat lower yields, either under the catalysis of other salt–base combination such as LiI/Li<sub>2</sub>CO<sub>3</sub>, KI/K<sub>2</sub>CO<sub>3</sub>, and CsI/Cs<sub>2</sub>CO<sub>3</sub> (entries 1, 12, and 13, Table 1) or in other solvents such as THF, CH<sub>3</sub>CN, DMA, and DMF (entries 8–11, Table 1).

This transformation is general, and some typical results are listed in Table 2 and Scheme 2. The following details are noteworthy: (1) Besides allylic iodides **2a**, **f–h**, benzyl iodide (**2b**),  $\alpha$ -iodoacetophenone (**2c**),  $\alpha$ -iodoacetate (**2d**), and propargylic iodide (**2e**) could be used as the organic halides to give a variety of polyfunctionalized (*E*)-alk-1-enyl iodides **3** under conditions A in good to excellent yields (entries 1–8, Table 2). (2) Organic bromides such as benzyl bromide (**2i**) and *trans*-cinnamyl bromide (**2j**) could also be used as reactants to give the corresponding alk-1-enyl bromides **3** under conditions B (10–20 mol % of LiBr and 50 mol % of Li<sub>2</sub>CO<sub>3</sub>) in good yields (entries 8 and 9, Table 2). (3) The regioselectivity<sup>11</sup> is opposite to that reported in refs 5–8; i.e., the X<sup>-</sup> attacks the less

### Scheme 1



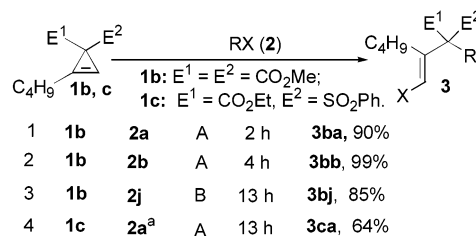
**Table 1.** Coupling Reaction of **1a** with **2a** under Different Reaction Conditions



entry	MI <sup>a</sup>	additive <sup>b</sup>	solvent	temp (°C)	time (h)	yield of <b>3aa</b> (%)
1	LiI	Li <sub>2</sub> CO <sub>3</sub>	acetone	reflux	2.5	60
2	NaI	no	acetone	reflux	2.5	60
3	NaI	Na <sub>2</sub> CO <sub>3</sub> <sup>c</sup>	acetone	reflux	2	57
4	NaI	Na <sub>2</sub> CO <sub>3</sub> <sup>d</sup>	acetone	reflux	2.5	67
5	NaI	Na <sub>2</sub> CO <sub>3</sub>	acetone	reflux	2.5	69
6	NaI	Na <sub>2</sub> CO <sub>3</sub>	acetone	reflux	1	77 <sup>e</sup>
7	NaI	Na <sub>2</sub> SO <sub>3</sub> <sup>f</sup>	acetone	reflux	2.5	64
8	NaI	Na <sub>2</sub> CO <sub>3</sub>	THF	reflux	2.5	31
9	NaI	Na <sub>2</sub> CO <sub>3</sub>	DMA	70	2.5	41
10	NaI	Na <sub>2</sub> CO <sub>3</sub>	DMF	70	2.5	13
11	NaI	Na <sub>2</sub> CO <sub>3</sub>	CH <sub>3</sub> CN	70	2.5	27
12	KI	K <sub>2</sub> CO <sub>3</sub>	acetone	reflux	3	60
13	CsI	Cs <sub>2</sub> CO <sub>3</sub>	acetone	reflux	4	63

<sup>a</sup> 10 mol % was used. <sup>b</sup> Unless otherwise specified, 50 mol % was used. <sup>c</sup> 10 mol % was used. <sup>d</sup> 25 mol % was used. <sup>e</sup> 4 equiv of **2a** was used. <sup>f</sup> 20 mol % was used.

### Scheme 2



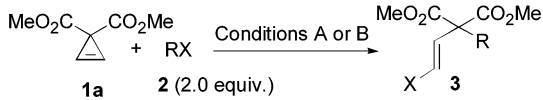
<sup>a</sup> 20 mol % of NaI and 4 equiv of **2a** were used.

hindered 2-position (Scheme 2). (4) The stereochemistry was established by the X-ray diffractational study of **3ah**,<sup>12</sup> the coupling constant of two olefinic protons in **3**, and the NOESY analysis of **3bb** (Figure 1).

The synthetic utilities of the ring-opening coupling products **3** were demonstrated by transformations of the representative product **3aa** (Scheme 3). Treatment of **3aa** with phenylboronic acid gave a Suzuki–Miyaura<sup>13</sup> coupling product (**4aa**) in 72% yield. Phenylacetylene underwent the Sonogashira<sup>14</sup> coupling reaction with **3aa**

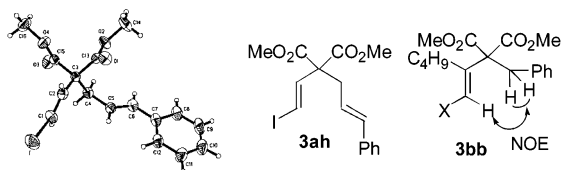
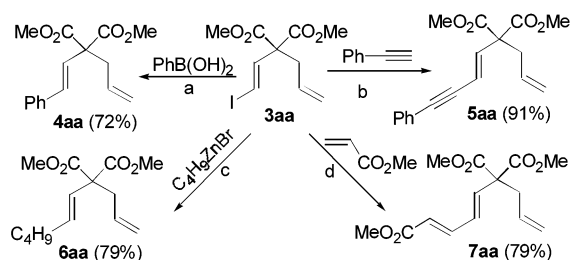
<sup>†</sup> Chinese Academy of Sciences.

<sup>‡</sup> Zhejiang University.

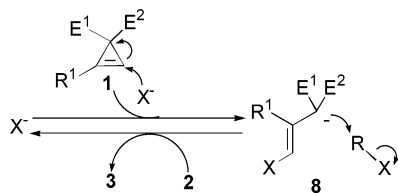
**Table 2.** Ring-Opening Coupling Reaction of Cyclopropenes **1** with Organic Halides **2** under Conditions A or B


Entry	<b>2</b> RX	Cond. <sup>a</sup>	Time (h)	Isolated Yield of <b>3</b> (%)
1	Bnl ( <b>2b</b> )	A	2	81 ( <b>3ab</b> )
2	PhCOCH <sub>2</sub> I ( <b>2c</b> )	A	2	80 ( <b>3ac</b> )
3	EtO <sub>2</sub> CCH <sub>2</sub> I ( <b>2d</b> )	A	1.5	65 ( <b>3ad</b> )
4	C <sub>5</sub> H <sub>11</sub> —CH <sub>2</sub> I ( <b>2e</b> )	A	2	82 ( <b>3ae</b> )
5	CH <sub>2</sub> =C(CH <sub>3</sub> )CH <sub>2</sub> I ( <b>2f</b> )	A	2.5	71 ( <b>3af</b> )
6	MeO <sub>2</sub> C—CH=CH—CH <sub>2</sub> I ( <b>2g</b> )	A	2.5	79 ( <b>3ag</b> )
7	Ph—CH=CH—CH <sub>2</sub> I ( <b>2h</b> )	A	1.25	92 ( <b>3ah</b> )
8	BnBr ( <b>2i</b> )	B	1.5	67 ( <b>3ai</b> )
9	Ph—CH=CH—Br ( <b>2j</b> )	B <sup>b</sup>	1	64 ( <b>3aj</b> )

<sup>a</sup> Conditions A: NaI (10 mol %), Na<sub>2</sub>CO<sub>3</sub> (50 mol %), acetone, reflux. Conditions B: LiBr (10 mol %), Li<sub>2</sub>CO<sub>3</sub> (50 mol %), acetone, reflux. <sup>b</sup> 20 mol % of LiBr was used.

**Figure 1.** Stereochemistry of **3ah** and **3bb**.**Scheme 3<sup>a</sup>**

<sup>a</sup> Reagents and conditions: (a) Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol %), Na<sub>2</sub>CO<sub>3</sub>, toluene/H<sub>2</sub>O, reflux, 5 h; (b) PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (5 mol %), CuI (10 mol %), K<sub>2</sub>CO<sub>3</sub> (2 equiv), CH<sub>3</sub>CN, room temperature, 6 h; (c) Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol %), THF, room temperature, 1 h; (d) Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol %), K<sub>2</sub>CO<sub>3</sub> (2.0 equiv), CH<sub>3</sub>CN, 70 °C, 24 h.

**Scheme 4**

to afford a stereodefined conjugated enyne (**5aa**) in an excellent yield. The Negishi<sup>15</sup> coupling reaction of **3aa** with butylzinc bromide gave **6aa** in 79% yield. Moreover, **3aa** could also undergo Heck<sup>16</sup> reaction with methyl acrylate to provide 2,4,8-trienoate **7aa** in 79% yield.

The plausible mechanism for this transformation is depicted in Scheme 4. The soft nucleophile X<sup>-</sup> (I<sup>-</sup> and Br<sup>-</sup>) attacked regioselectively the 2-position of cyclopropenes **1** to give a stereodefined

carbanion **8**, which would react with RX **2** to give (*E*)-alk-1-enyl halides **3** and regenerate X<sup>-</sup>.

In conclusion, we have developed a novel X<sup>-</sup> (X = I, Br)-triggered ring-opening coupling reaction of cyclopropenes with organic halides, providing an efficient, highly regio- and stereo-selective route to a series of polyfunctionalized (*E*)-alk-1-enyl halides. This reaction may open up the X<sup>-</sup>-catalyzed reaction of cyclopropenes with other kinds of electrophiles. Further studies to determine the reaction scope and synthetic applications of this reaction are now being carried out in this laboratory.

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**Supporting Information Available:** Experimental procedures and characterization data of all new compounds (PDF, CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

**References**

- (1) For very recent synthetic transformations of alkenyl halides, see: (a) Nordmann, G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 4978. (b) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001.
- (2) Alkenyl halides are reactive under transition-metal catalysts; for reviews, see: (a) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2002; Vol. 1. (b) Tsuji, J. *Transition Metal Reagents and Catalysts Innovations in Organic Synthesis*; John Wiley & Sons: Chichester, 2000. (c) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46.
- (3) For reviews, see: (a) Urch, C. J. In *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon: Oxford, 1995; Vol. 2, pp 606–619. (b) Kelly, S. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon: Oxford, 1991; Vol. 1, pp 807–808.
- (4) For reviews, see: (a) Binger, P.; Büch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77. (b) Jennings, P. W.; Johnson, L. L. *Chem. Rev.* **1994**, *94*, 2241. (c) Baird, M. S. Cyclopropenes: Transformations. In *Houben-Weyl*; Thieme: Stuttgart, Germany, 1997; Vol. E17d/2, p 2781. (d) Nakamura, M.; Isobe, H.; Nakamura, E. *Chem. Rev.* **2003**, *103*, 1295.
- (5) Kubota, K.; Mori, S.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **1998**, *120*, 13334.
- (6) (a) Liao, L.; Fox, J. M. *J. Am. Chem. Soc.* **2002**, *124*, 14322. (b) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **2000**, *122*, 978 and references therein.
- (7) (a) Nakamura, E.; Isaka, M.; Matsuzawa, S. *J. Am. Chem. Soc.* **1988**, *110*, 1297. (b) Isaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **1990**, *112*, 7428.
- (8) Nakamura, M.; Arai, M.; Nakamura, E. *J. Am. Chem. Soc.* **1995**, *117*, 1179.
- (9) For an exceptional example of ligand effect on regioselective allylzincation of 1-trimethylsilyl (Ge,Sn)-cyclopropenone acetals, see: Nakamura, M.; Inoue, T.; Sato, A.; Nakamura, E. *Org. Lett.* **2000**, *2*, 2193.
- (10) Wheeler, T. N.; Ray, J. *J. Org. Chem.* **1987**, *52*, 4875.
- (11) The regioselectivity is more than 97:3, as determined by the <sup>1</sup>H NMR analysis of the crude mixture.
- (12) X-ray data for compound **3ah**: C<sub>16</sub>H<sub>17</sub>O<sub>4</sub>S, M<sub>w</sub> = 400.20, orthorhombic, space group *Pbca*, Mo K $\alpha$ , final *R* indices [*I* > 2 $\sigma$ (*I*)], *R*<sub>1</sub> = 0.0422, *wR*<sub>2</sub> = 0.1055, *a* = 17.5719(16) Å, *b* = 8.3749(7) Å, *c* = 23.260(2) Å,  $\alpha$  = 90°,  $\beta$  = 90°,  $\gamma$  = 90°, *V* = 3423.0(5) Å<sup>3</sup>, *T* = 293(2) K, *Z* = 8, reflections collected/unique: 19496/4093 (*R*<sub>int</sub> = 0.0872), number of observations [*I* > 2 $\sigma$ (*I*)] 2416, parameters 259. Supplementary crystallographic data has been deposited at the Cambridge Crystallographic Data Center, CCDC 217324.
- (13) For a recent review, see: Suzuki, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2002; Vol. 1, p 249.
- (14) For a recent review, see: Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2002; Vol. 1, p 493.
- (15) For a recent review, see: Negishi, E. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2002; Vol. 1, p 229.
- (16) For reviews, see: (a) Heck, R. F. *Org. React.* **1982**, *27*, 345. (b) Larhed, M.; Hallberg, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2002; Vol. 1, p 1133.

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