



## Synthesis of *gem*-dihaloenynes and butatrienes from *gem*-dihalovinyl derivatives

Tianhao Meng<sup>a</sup>, Hui-Jun Zhang<sup>b</sup>, Zhenfeng Xi<sup>b,c,\*</sup>

<sup>a</sup> Beijing National Laboratory for Molecular Sciences (BNLMS), Institute of Chemistry, Chinese Academy of Sciences (CAS), Beijing 100190, China

<sup>b</sup> Beijing National Laboratory for Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China

<sup>c</sup> State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry (SIOC), CAS, Shanghai 200032, China

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### ABSTRACT

*gem*-Dihaloenynes were synthesized in high yields from 1,1,4,4-tetrahalo-1,3-butadienes through the Fritsch–Buttenberg–Wiechell (FBW) rearrangement mediated by an organolithium compound. Butatriene derivatives could be obtained efficiently via an organolithium-mediated reaction of *o*-halo-(2,2-dihalovinyl)benzenes.

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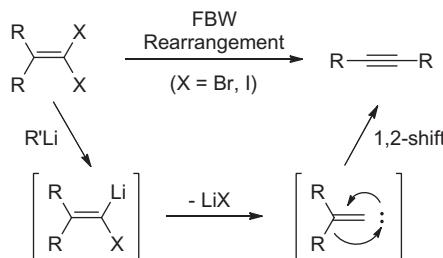
#### Keywords:

Butatriene  
Cumulene  
*gem*-Dihaloolefin  
*gem*-Dihaloynye  
Fritsch–Buttenberg–Wiechell (FBW)  
rearrangement  
*o*-Halo-(2,2-dihalovinyl)benzenes  
1,1,4,4-Tetrahalo 1,3-butadiene

*gem*-Dihalovinyl compounds are useful building blocks in organic synthesis.<sup>1,2</sup> When such a compound is treated with a base such as an organolithium, an alkyne may be generated via the Fritsch–Buttenberg–Wiechell (FBW) rearrangement (Scheme 1).<sup>3,4</sup> On the other hand, butatrienes are interesting compounds both structurally and synthetically.<sup>5,6</sup> The most common synthetic method for butatrienes is via a halolithio carbenoid intermediate generated by a single metal-halo exchange of a *gem*-dihaloalkene with an organolithium reagent.<sup>5</sup> Reductive coupling of the halolithio carbenoid intermediate is usually promoted by a transition metal, such as a copper salt, to afford the corresponding butatriene derivative.<sup>5</sup> In some cases, butatriene derivatives can be also generated via direct dimerization of the carbenoid intermediates.<sup>7</sup> As by-products in these reactions, disubstituted acetylenes might be formed via the FBW rearrangement.

In recent years, we have been interested in the preparation and synthetic applications of polyhalo compounds including *gem*-dihalo vinylic moieties, aiming at utilizing the potential synergistic effect among functional groups on conjugated systems.<sup>8,9</sup> As shown in Scheme 2, we have developed an efficient synthetic method for 1,1,4,4-tetrahalo 1,3-butadienes **1**. Similarly, the

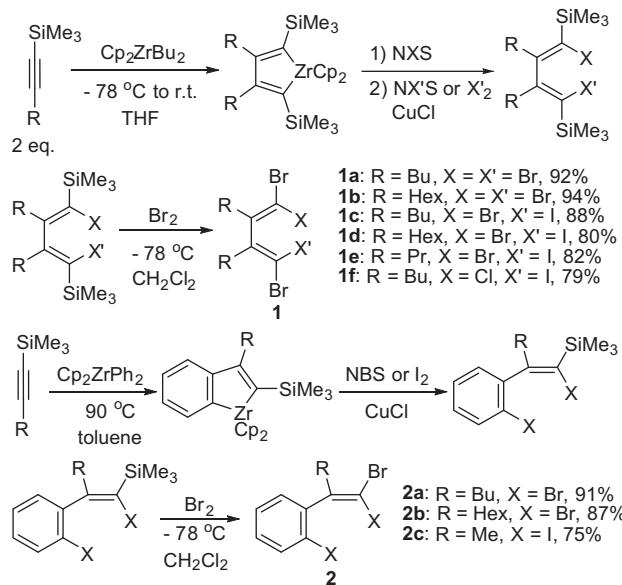
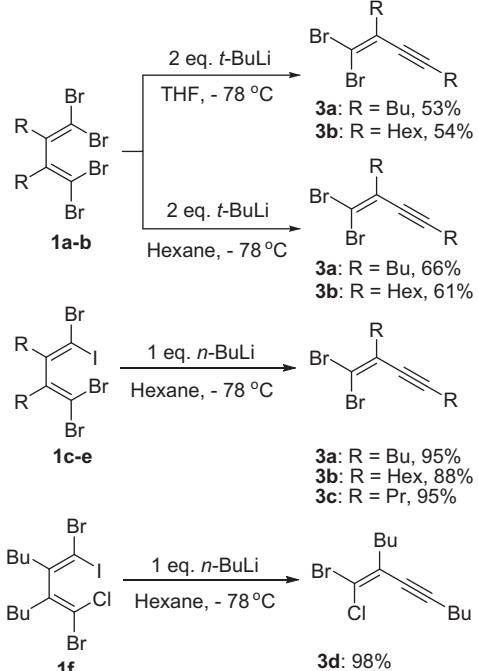
*gem*-dihalovinyl compounds **2**, *o*-halo-(2,2-dihalovinyl)benzenes, can also be readily obtained in high yields. As our continued interest in the synthetic applications of such polyhalo-substituted conjugated systems, we subjected such compounds under the FBW rearrangement conditions. *gem*-Dihaloenynes were generated in high yields via *n*-BuLi-mediated transformation of 1,1,4,4-tetrahalo-1,3-butadienes in hexane. Further applications of *gem*-dihaloenynes were demonstrated. Butatriene derivatives could also be obtained efficiently via an organolithium-mediated reaction of *o*-halo-(2,2-dihalovinyl)benzenes in THF.<sup>5,6</sup> The structure of one butatriene derivative was determined by single-crystal X-ray structural analysis.<sup>5</sup>



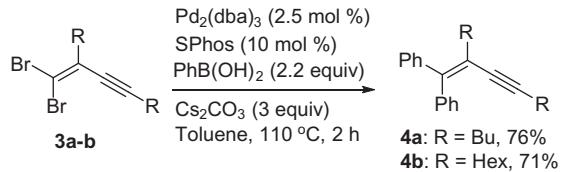
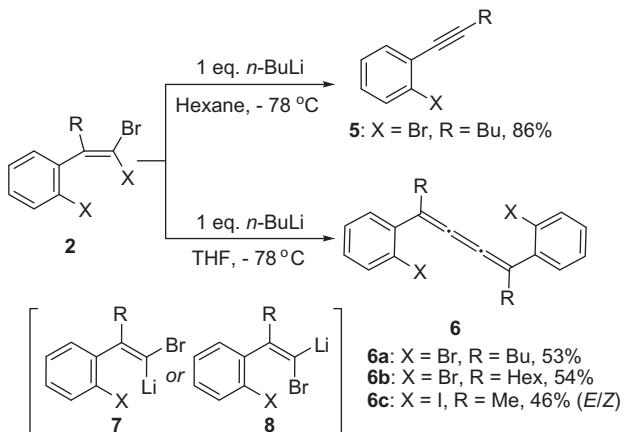
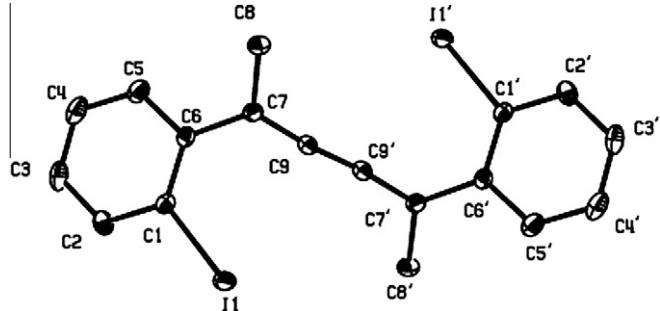
**Scheme 1.** The Fritsch–Buttenberg–Wiechell (FBW) rearrangement.

\* Corresponding author. Tel.: +86 10 6275 9728; fax: +86 10 6275 1708.

E-mail address: zfxi@pku.edu.cn (Z. Xi).

**Scheme 2.** Synthesis of polyhalo-substituted conjugated systems.**Scheme 3.** Synthesis of gem-dihaloenynes 3.

Initially, the 1,1,4,4-tetrabromo-1,3-butadiene **1a–b** was treated with *t*-BuLi in THF (**Scheme 3**). The expected *gem*-dibromoenoyn **3a–b** could be generated, but in moderate yields. When the reaction was carried out in hexane using *t*-BuLi, the *gem*-dibromoenoyn derivatives **3a** and **3b** were obtained in 66% and 61% isolated yields, respectively. The yields increased but were not satisfied. This is probably due to the relatively low reactivity of the C(sp<sup>2</sup>)–Br bond. In fact, when *n*-BuLi was used instead of *t*-BuLi, no lithio–halo exchange was observed under the above reaction condition in THF or in hexane. Therefore, to achieve a higher lithio–halo exchange rate and better yields, the C(sp<sup>2</sup>)–I bond-containing derivatives **1c–e** were synthesized and treated with an

**Scheme 4.** Suzuki–Miyaura coupling of *gem*-dibromoenynes **3**.**Scheme 5.** Synthesis of butatrienes **6**.**Figure 1.** Single-crystal X-ray structure of *E*-**6c** with 30% thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å]: C1–C6 1.406(5), C6–C7 1.485(5), C7–C8 1.505(5), C7–C9 1.328(5), C9–C9' 1.261(7), C1–I1 2.103(3).

organolithium reagent. In these cases, *t*-BuLi was too reactive and the reaction gave a mixture of products. The best condition was realized when *n*-BuLi was applied in hexane solution. As shown in **Scheme 3**, the *gem*-dibromoenoyn **3a–c** could be obtained in excellent isolated yields.<sup>10</sup> To the best of our knowledge, this is the first example of *gem*-dihaloenoyn synthesis via the FBW rearrangement of 1,1,4,4-tetrahalo 1,3-butadienes.<sup>11</sup>

Similarly, as shown in **Scheme 3**, when the Cl, Br, I-mixed polyhalo conjugated butadiene **1f** was treated with *n*-BuLi in hexane, the corresponding *gem*-dihaloenoyn **3d** was generated quantitatively as the sole isomer.

Synthetic application of the *gem*-dihaloenoyn derivatives was preliminarily demonstrated (**Scheme 4**). Thus compounds **3a** and **3b** were subjected to the Suzuki–Miyaura cross-coupling reaction condition, which afforded the diphenyl-substituted enynes **4a** and **4b** in 76% and 71% isolated yields, respectively.<sup>11c</sup>

Butatriene derivatives could be obtained efficiently via an organolithium-mediated reaction of *o*-halo-(2,2-dihalovinyl)benzenes. As given in **Scheme 5**, when the *o*-bromo-(2,2-dibromovinyl)benzene derivative **2a** was treated with *n*-BuLi in hexane, the corre-

sponding FBW rearrangement product, the *o*-bromophenyl acetylene **5** was exclusively formed and obtained in 86% isolated yield. However, when the reaction was carried out in THF, butatriene derivatives **6** mainly as *E*-isomers were obtained as the major products,<sup>12</sup> via direct dimerization of the carbenoid intermediates **7** and/or **8**. The butatriene derivative **6c** was obtained as a mixture of 1:1 *E/Z* isomers. In addition, when the R group was butyl, we also detected trace amount of the Z-form butatriene by the NMR spectra.

Obviously, the solvent polarity and coordination ability seem crucial for these two different transformations. Hexane is found to be the most effective solvent for the FBW rearrangement, while most polar solvents such as THF will afford butatriene derivatives as major products. The structure of *E*-**6c** was confirmed by single-crystal X-ray structural analysis (Fig. 1).<sup>13</sup>

In summary, we developed a convenient synthesis of *gem*-dihaloenyne from 1,1,4,4-tetrahalo-1,3-butadienes through the Fritsch–Buttenberg–Wiechell (FBW) rearrangement. Butatriene derivatives were also obtained efficiently.

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## Supplementary data

Supplementary data (experimental procedures and characterization data for all new compounds and copies of NMR spectra) associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2012.06.060>.

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- Preparation of gem-dibromoenyne 3:* To a stirred solution of 1,1,4,4-mixed-tetrahalo-1,3-butadiene (5 mmol) in dry hexane (20 mL) at –78 °C (acetone/dry ice) was added *n*-BuLi (3.2 mL, 1.6 M in hexane) dropwise. After 5 min the reaction was completed, and the suspended mixture was filtered to remove solid residue, then it was washed with hexane (3 × 10 mL). The combined filtrates were concentrated under reduced pressure to give the pure product of *gem*-dibromoenyne 3 without further purification. Compound **3a**, yellow oil, isolated yield 95% (1.5 g); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.93 (t, *J* = 7.3 Hz, 6H, CH<sub>3</sub>), 1.31–1.59 (m, 8H, CH<sub>2</sub>), 2.29–2.37 (m, 4H, CH<sub>2</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 13.53 (CH<sub>3</sub>) 13.84 (CH<sub>3</sub>), 19.37 (CH<sub>2</sub>), 21.89 (CH<sub>2</sub>), 22.03 (CH<sub>2</sub>), 29.67 (CH<sub>2</sub>), 30.42 (CH<sub>2</sub>), 36.82 (CH<sub>2</sub>), 79.39 (quat. C), 94.47 (quat. C), 98.81 (quat. C), 131.44 (quat. C). HRMS (EI, *m/z*) calcd for [C<sub>12</sub>H<sub>18</sub>Br<sub>2</sub>]<sup>+</sup>: 321.9755; found 321.9750.
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- Typical Procedure for the preparation of butatrienes 6:* In a 50 mL flask, *o*-halo-(2,2-dihalovinyl)benzene **2** (1.0 mmol) was dissolved in dry THF (5 mL) at –78 °C. *n*-BuLi (0.6 mL, 1.6 M in hexane) was added dropwise very slowly and the reaction was stirred at room temperature for 15 min. The solvent of the reaction mixture was evaporated under vacuum and hexane (20 mL) was added. After that, the suspended mixture was filtered to remove solid residue. The filtrate was purified by chromatography to give the butatriene product (eluent: pentane). Compound **6a**, Yellow oil, isolated yield 53% (126 mg); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 0.80 (t, *J* = 7.2 Hz, 6H, CH<sub>3</sub>), 1.31–1.48 (m, 8H, CH<sub>2</sub>), 2.61 (t, *J* = 7.1 Hz, 4H, CH<sub>2</sub>), 7.09–7.59 (m, 8H, CH); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 13.86 (2 CH<sub>3</sub>), 22.25 (2 CH<sub>2</sub>), 30.36 (2 CH<sub>2</sub>), 36.40 (2 CH<sub>2</sub>), 120.63 (2 quat. C), 122.35 (2 quat. C), 127.08 (2 CH), 128.44 (2 CH), 130.03 (2 CH), 133.46 (2 CH), 140.99 (2 quat. C), 158.63 (2 quat. C). HRMS (EI, *m/z*) calcd for [C<sub>24</sub>H<sub>26</sub>Br<sub>2</sub>]<sup>+</sup>: 474.0381, found 474.0389.
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