

# Gallium(III) halide promoted synthesis of 1,3,5-triaryl-1,5-dihalo-1,4-pentadienes<sup>☆</sup>

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**Abstract**—Aryl substituted alkynes undergo smooth coupling with aldehydes in the presence of gallium(III) halides under extremely mild conditions to afford the corresponding 1,3,5-triaryl-1,5-dihalo-1,4-pentadienes in good yields with *E,Z*-selectivity. Similarly 1,3,5-triaryl-1,5-dichloro-1,4-pentadienes are also obtained with niobium(V) chloride.  
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The coupling of alkynes to aldehydes is an important reaction in organic synthesis for generating carbon–carbon multiple bonds.<sup>1</sup> The addition of alkynylmetal reagents to aldehydes to produce propargyl alcohols has been extensively studied using various metal reagents.<sup>2</sup> The reaction between alkynes and aldehydes to generate  $\alpha,\beta$ -unsaturated ketones has also been reported using Lewis acids such as  $\text{SbF}_5$ ,  $\text{Yb}(\text{OTf})_3$  and  $\text{In}(\text{OTf})_3$  to promote this reaction.<sup>3,4</sup> Recently,  $\text{TiCl}_4$  and  $\text{BX}_3$  have been utilized for the 2:1 coupling of aryl substituted alkynes and aryl aldehydes to afford 1,5-dihalo-1,4-pentadienes.<sup>5</sup> The use of corrosive reagents such as titanium or boron halides limits their use especially in large scale synthesis. Therefore, the development of simple and convenient procedures for the preparation of 1,3,5-triaryl-1,5-dihalo-1,4-pentadienes continues to be a challenging endeavour. Owing to their unique catalytic properties, gallium halides have recently been widely used for a variety of organic transformations.<sup>6,7</sup> In particular, gallium(III) compounds are considered as effective Lewis acids to activate alkynes under extremely mild conditions.<sup>8</sup> However, there have been no reports on the use of gallium(III) halides for the preparation of synthetically useful dihalo-1,4-pentadienes.

In this letter, we disclose a mild and efficient methodology for the preparation of triaryl-1,5-dihalo-1,4-pentadienes from alkynes and aldehydes using gallium(III) halides as novel promoters. Initially, we attempted the condensation of phenylacetylene with benzaldehyde in the presence of gallium(III) chloride. The reaction went to completion within 2.0 h and the product was obtained in 87% yield (Scheme 1).

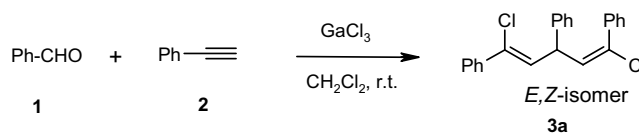
Encouraged by this result, we turned our attention to other aromatic aldehydes. *p*-Chloro-, *p*-methyl-, *p*-cyano- and *m*-phenoxybenzaldehydes underwent smooth coupling with phenylacetylene to afford the corresponding 1,5-dichloro-1,4-pentadienes (entries b–e, Table 1). Like gallium trichloride, gallium tribromide and gallium triiodide gave the respective bromo- and iodo-adducts under similar conditions (entries f–h, Table 1, Scheme 2).

In most of the cases, the reactions were found to be highly stereoselective affording exclusively *E,Z*-isomers in high yields except for the reactions of *p*-chloro- and *p*-cyanobenzaldehyde (entries b and d, Table 1)

**Keywords:** Gallium(III) compounds; Aldehydes; Alkynes; 1,4-Pentadienes.

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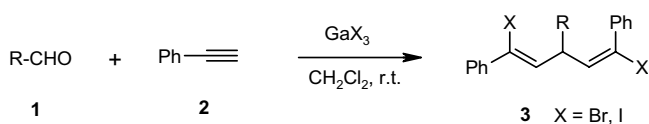
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Scheme 1.

**Table 1.** Gallium trihalide-promoted stereoselective synthesis of triaryl 1,5-dihalo-1,4-pentadienes

Entry	Aldehyde <b>1</b>	Alkyne <b>2</b>	Product <sup>a</sup> <b>3</b>	Time (h)	Yield (%) <sup>b</sup>
	R-CHO				
a	R = C <sub>6</sub> H <sub>5</sub>		<b>3a</b> : R = C <sub>6</sub> H <sub>5</sub> , X = Cl	2.0	87
b	R = 4-ClC <sub>6</sub> H <sub>4</sub>		<b>3b</b> : R = 4-ClC <sub>6</sub> H <sub>4</sub> , X = Cl	2.0	85 <sup>c</sup>
c	R = 4-MeC <sub>6</sub> H <sub>4</sub>		<b>3c</b> : R = 4-MeC <sub>6</sub> H <sub>4</sub> , X = Cl	1.5	89
d	R = 4-NCC <sub>6</sub> H <sub>4</sub>		<b>3d</b> : R = 4-NCC <sub>6</sub> H <sub>4</sub> , X = Cl	2.0	60 <sup>c</sup>
e	R = 3-PhOC <sub>6</sub> H <sub>4</sub>		<b>3e</b> : R = 3-PhOC <sub>6</sub> H <sub>4</sub> , X = Cl	1.5	50
f	R = C <sub>6</sub> H <sub>5</sub>		<b>3f</b> : R = C <sub>6</sub> H <sub>5</sub> , X = Br	0.5	86
g	R = C <sub>6</sub> H <sub>5</sub>		<b>3g</b> : R = C <sub>6</sub> H <sub>5</sub> , X = I	1.5	85
h	R = C <sub>6</sub> H <sub>5</sub>		<b>3h</b> : R = 4-NCC <sub>6</sub> H <sub>4</sub> , X = Br	2.0	87
i	R = C <sub>2</sub> H <sub>5</sub>		<b>3i</b> : R = C <sub>2</sub> H <sub>5</sub> , X = Cl	1.5	80
j	R = <i>n</i> -C <sub>5</sub> H <sub>11</sub>		<b>3j</b> : R = <i>n</i> -C <sub>5</sub> H <sub>11</sub> , X = Br	1.5	80
k	R = <i>n</i> -C <sub>5</sub> H <sub>11</sub>		<b>3k</b> : R = <i>n</i> -C <sub>5</sub> H <sub>11</sub> , X = I	2.0	78
	R-CHO				
l	R = C <sub>6</sub> H <sub>5</sub>		<b>3l</b> : R = C <sub>6</sub> H <sub>5</sub> , X = Cl	2.0	91
m	R = 4-FC <sub>6</sub> H <sub>4</sub>		<b>3m</b> : R = 4-FC <sub>6</sub> H <sub>4</sub> , X = Cl	2.5	90
n	R = 4-ClC <sub>6</sub> H <sub>4</sub>		<b>3n</b> : R = 4-ClC <sub>6</sub> H <sub>4</sub> , X = Cl	1.0	89

<sup>a</sup> All products were characterized by <sup>1</sup>H NMR and IR spectra and mass spectrometry.<sup>b</sup> Yield refers to the isolated pure products after column chromatography.<sup>c</sup> *E,Z,Z*-isomers obtained after column chromatography.**Scheme 2.**

which produced a minor amount of the *Z,Z*-isomers in 7% and 4% yields, respectively. The *E,Z*-isomers were assigned on the basis of the chemical shift values of the protons in the <sup>1</sup>H NMR spectra of the products and also by comparison with reported spectroscopic data.<sup>5</sup> The stereochemistry of the product **3k** was also established by NOE experiments which clearly showed the presence of the *E,Z*-isomers. Aliphatic aldehydes

such as propanal and *n*-hexanal also afforded similar adducts under identical reaction conditions (entries i–k, Table 1). Furthermore, treatment of *p*-tolylacetylene with aromatic aldehydes in the presence of gallium trichloride gave the corresponding 1,5-dichloro-1,4-pentadienes in high yields (entries l–n, Table 1). In all cases, the reactions proceeded rapidly at room temperature with high efficiency.<sup>9</sup> In the absence of gallium trihalide, no reaction was observed. Alkyl-substituted alkynes such as *n*-hexyne and *n*-octyne failed to produce the desired products under similar conditions. As solvent, dichloromethane appeared to give the best results. Among various Lewis acids such as InCl<sub>3</sub>, InBr<sub>3</sub>, InI<sub>3</sub>, CeCl<sub>3</sub>·7H<sub>2</sub>O, YCl<sub>3</sub> and BiCl<sub>3</sub> tested, gallium trihalides were found to be the most effective for this conversion. Niobium(V) chloride (20 mol%) also worked well to

afford the corresponding 1,5-dichloro-1,4-pentadienes. The scope and generality of this process is illustrated with respect to various aldehydes and the results are presented in Table 1.

In summary, we have described a simple, convenient and efficient protocol for the preparation of 1,3,5-triaryl-1,5-dihalo-1,4-pentadienes from aryl-substituted alkynes and aldehydes using gallium trihalides as reagents. This method offers several significant advantages such as high conversions, easy handling, the highly active nature of the gallium compounds, cleaner reaction profiles and short reaction times, which makes it a useful and attractive process for the rapid preparation of substituted 1,4-pentadienes in a single-step.

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- A mixture of aldehyde (1 mmol), phenyl or tolyl acetylene (2.5 mmol), gallium trihalide (0.65 mmol) in dichloromethane (10 mL) was stirred at room temperature for the appropriate time (see Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water and extracted with dichloromethane (2 × 10 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated in vacuo and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 0.5:9.5) to afford the pure 1,5-dihalo-1,4-pentadienes. Spectroscopic data for selected products: (3g): Liquid, IR (KBr):  $\nu_{\max}$ : 3061, 3028, 2928, 2856, 1901, 1667, 1603, 1490, 1447, 1406, 1331, 1217, 1179, 1092, 1014, 982, 824, 768, 693, 530 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.42–7.18 (m, 15H), 6.70 (d, *J* = 9.4 Hz, 1H), 6.05 (d, *J* = 9.1 Hz, 1H), 4.54 (t, *J* = 10.1 Hz, 1H). EIMS: *m/z* (%): 548 (M<sup>+</sup>, 8), 421 (5), 391 (10), 319 (20), 294 (70), 215 (15), 192 (72), 154 (70), 127 (12), 69 (82), 55 (100). HRMS calcd for C<sub>23</sub>H<sub>18</sub>I<sub>2</sub>: 548.9576. Found: 548.9582. (3h): Liquid, IR (KBr):  $\nu_{\max}$ : 3025, 2927, 2229, 1911, 1682, 1605, 1496, 1444, 1220, 1073, 1023, 841, 761, 698, 561 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.61 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.38–7.30 (m, 12H), 6.36 (d, *J* = 9.1 Hz, 1H), 6.28 (d, *J* = 8.9 Hz, 1H), 4.82 (t, *J* = 9.8 Hz, 1H). EIMS: *m/z* (%): 479 (M<sup>+</sup>, 5), 414 (10), 320 (100), 240 (10), 216 (25), 102 (10). HRMS calcd for C<sub>24</sub>H<sub>17</sub>NBr<sub>2</sub>: 476.9727. Found: 476.9733. (3i): Liquid, IR (KBr):  $\nu_{\max}$ : 3028, 2923, 2857, 1693, 1607, 1508, 1450, 1244, 1182, 1113, 1024, 872, 815, 774, 699, 631 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.49–7.42 (m, 4H), 7.35–7.08 (m, 9H), 6.26 (d, *J* = 9.3 Hz, 1H), 6.12 (d, *J* = 9.1 Hz, 1H), 4.85 (t, *J* = 10.1 Hz, 1H), 2.36 (s, 3H), 2.33 (s, 3H). EIMS: *m/z* (%): 393 (M<sup>+</sup>, 5), 360 (100), 321 (28), 241 (10), 229 (30), 205 (32), 165 (15), 139 (20), 119 (35), 91 (40). HRMS calcd for C<sub>25</sub>H<sub>22</sub>Cl<sub>2</sub>: 392.1098. Found: 392.1093.