

# An efficient synthesis of 2-vinylcyclic 1,3-alkadienes *via* the Cp<sup>\*</sup>Ru(II)-catalyzed intermolecular coupling reactions of alkynes and cyclic allenes†

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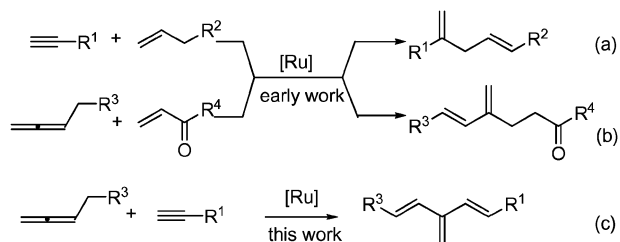
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**2-Vinylcyclic 1,3-alkadienes can be obtained with moderate to good yields *via* the Cp<sup>\*</sup>RuCl(PPh<sub>3</sub>)<sub>2</sub>-catalyzed coupling reaction of alkynes with cyclic allenes.**

2-Vinylcyclic 1,3-alkadienes are a class of important building block because it may participate in a variety of tandem carbon–carbon bond-forming processes, such as sequential Diels–Alder reactions.<sup>1</sup> On the other hand, allenes have shown unique reactivity and stereoselectivity and become an important class of starting materials for modern organic synthesis.<sup>2–4</sup> Recently, different types of intramolecular cyclometallation reactions of allenes with unsaturated compounds<sup>5–7</sup> in the presence of different metallic catalysts have been studied. Trost *et al.* have reported the intermolecular reactions of alkenes with alkynes<sup>8</sup> or allenes with  $\alpha,\beta$ -unsaturated enones<sup>9</sup> for the synthesis of 1,4-dienes and 3-methylene-4-alkenyl ketones, respectively (eqn a and b, Scheme 1). In search of a new type of reaction between allenes and alkynes,<sup>5</sup> herein we wish to report our recent observations on the Cp<sup>\*</sup>RuCl(PPh<sub>3</sub>)<sub>2</sub><sup>10</sup>-catalyzed reaction of cyclic allenes with terminal alkynes, which afforded 2-vinylcyclic 1,3-alkadienes with atom economy<sup>11</sup> (eqn c, Scheme 1).

We used 1,2-nonadiene (**1a**) and prop-2-yn-1-ol (**2a**) as the model substrates to optimize the reaction conditions. The reaction was complicated with RuHCl(CO)(PPh<sub>3</sub>)<sub>3</sub> as the catalyst<sup>12</sup> in toluene (entry 1, Table 1). However, it is pleasing to observe that when a polar solvent such as DMF was used, the reaction afforded 2-(3'-hydroxypropenyl)-1,3-nonadiene (**3a**) highly regioselectivity, albeit in 4%



Scheme 1

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**Table 1** Optimization of the reaction conditions for Ru(II)-catalyzed intermolecular coupling reaction of 1,2-nonadiene (**1a**) with propargyl alcohol (**2a**)<sup>a</sup>

Entry	[Ru]-Cat	Solvent	Temp./ °C	Isolated yield of <b>3a</b> (%)
1	RuHCl(CO)(PPh <sub>3</sub> ) <sub>3</sub>	Toluene	100	Complicated
2	RuHCl(CO)(PPh <sub>3</sub> ) <sub>3</sub>	DMF	100	4
3	Cp <sup>*</sup> RuCl(COD)	Toluene	100	18
4	Cp <sup>*</sup> RuCl(COD)	DMF	100	7
5	Cp <sup>*</sup> RuCl(COD)	<i>i</i> -PrOH	Reflux	14
6	Cp <sup>*</sup> RuCl(COD)	DMA	100	38
7	Cp <sup>*</sup> RuCl(PPh <sub>3</sub> ) <sub>2</sub>	DMA	100	27
8	Cp <sup>*</sup> RuCl(PPh <sub>3</sub> ) <sub>2</sub>	Toluene	100	84
9	[CpRu(MeCN) <sub>3</sub> ]PF <sub>6</sub>	DMF	80	16 <sup>b</sup>

<sup>a</sup> The reaction was conducted using allene (**1a**) (0.25 mmol) and propargyl alcohol (**2a**) (0.3 mmol) in solvent (2 mL). <sup>b</sup> The product is not pure.

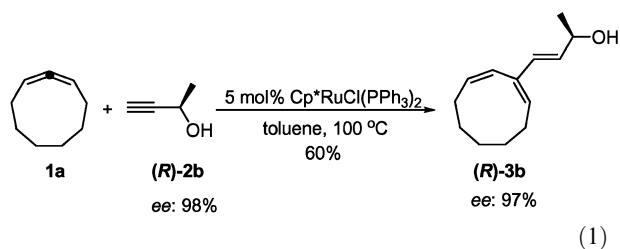
yield (entry 2, Table 1). Then Cp<sup>\*</sup>RuCl(COD)<sup>13</sup> was used as the catalyst, which may effectively catalyze the cyclometallation reaction of alkenes with alkynes.<sup>14</sup> Indeed, we obtained the desired product **3a** with 18% yield (entry 3, Table 1). Other solvents such as DMF, *i*-PrOH and DMA were also tried (entries 4–6, Table 1), however, the yields were not satisfactory. Finally, it was observed that the reaction in DMA with Cp<sup>\*</sup>RuCl(PPh<sub>3</sub>)<sub>2</sub> as the catalyst afforded the product **3a** in 27% yield (entry 7, Table 1). When toluene was used as the solvent, the isolated yield was improved to 84% (entry 8, Table 1). However, the cationic ruthenium catalyst [CpRu(MeCN)<sub>3</sub>]PF<sub>6</sub> failed to catalyze this reaction effectively (entry 9, Table 1).<sup>9</sup> In cases with lower yield of **3a**, the formation of some unidentified products was observed.

With the optimized reaction conditions presented in entry 8 of Table 1, other substituted propargylic alcohols were tested with some typical results being summarized in Table 2. When the 1-alkyl or aryl substituted propargylic alcohols were used as the substrates, the corresponding products (**3b–h**) were formed in 53–76% isolated yields (entries 1–7, Table 2); Furthermore, halogen substituent on the aryl ring can be tolerated, which provides opportunity for further elaboration such as coupling reactions (entries 5 and 6, Table 2).

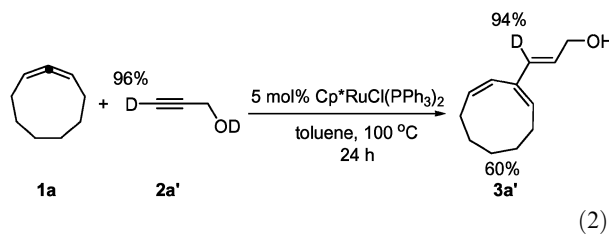
**Table 2** Cp\*RuCl(PPh<sub>3</sub>)<sub>2</sub>-catalyzed intermolecular coupling reaction of 1,2-nonadiene (**1a**) with differently substituted propargyl alcohols

Entry	R	Isolated yield of <b>3</b> (%)
1	Me ( <b>2b</b> )	67 ( <b>3b</b> )
2	Ph ( <b>2c</b> )	66 ( <b>3c</b> )
3	4-MeC <sub>6</sub> H <sub>4</sub> ( <b>2d</b> )	60 ( <b>3d</b> )
4	4-OMeC <sub>6</sub> H <sub>4</sub> ( <b>2e</b> )	53 ( <b>3e</b> )
5	4-ClC <sub>6</sub> H <sub>4</sub> ( <b>2f</b> )	76 ( <b>3f</b> )
6	3-BrC <sub>6</sub> H <sub>4</sub> ( <b>2g</b> )	72 ( <b>3g</b> )
7		61 ( <b>3h</b> )

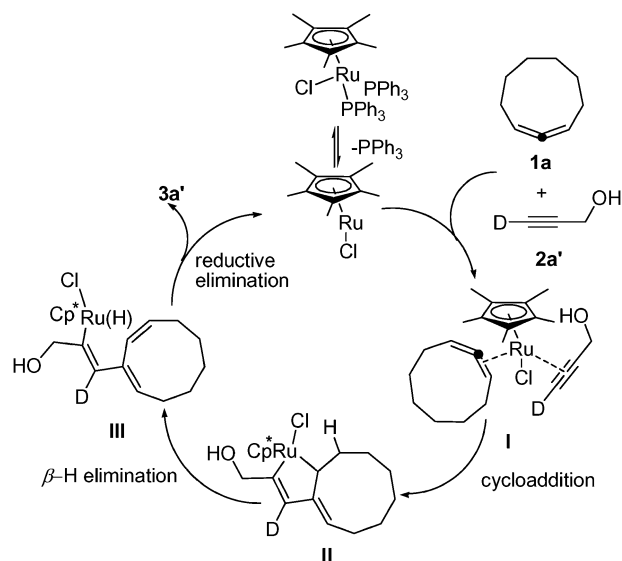
When (*R*)-**2b** was used as the substrate, the desired product (*R*)-**3b** was obtained without obvious loss of the chirality (eqn (1)).



In order to study the mechanism of this reaction, we used the deuterated propargyl alcohol (**2a'**). Its reaction with **1a** in the presence of 5 mol% Cp\*RuCl(PPh<sub>3</sub>)<sub>2</sub> afforded the 3-deuterated 3-(nona-1,3-dien-2-yl)prop-2-enol **3a'** (eqn (2)).



Based on this result, the mechanism involving the vinylidene ruthenium intermediate<sup>15</sup> may be excluded. Thus, a plausible mechanism of this reaction is proposed (Scheme 2).<sup>16</sup> Coordination of allene **1a** and alkyne **2a'** with the [Ru] catalyst afforded the coordination complex **I**, which may undergo cyclometallation reaction to form the metallabicyclic intermediate **II**.<sup>8</sup> The coordination of the hydroxyl group and [Ru] may determine the regioselectivity. Subsequent β-H elimination would yield intermediate **III**, which may undergo reductive elimination to form the final triene product **3a'** and regenerate the catalytically active species.

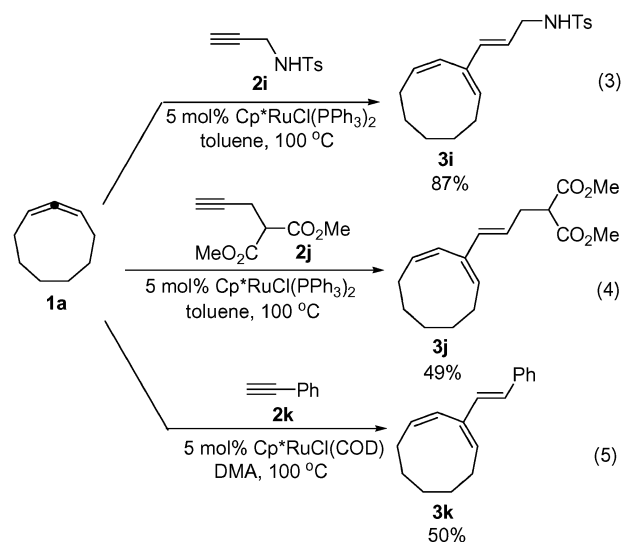


**Scheme 2** Proposed mechanism for the Cp\*Ru(II)-catalyzed coupling reaction of 1,2-nonadiene with **2a'**.

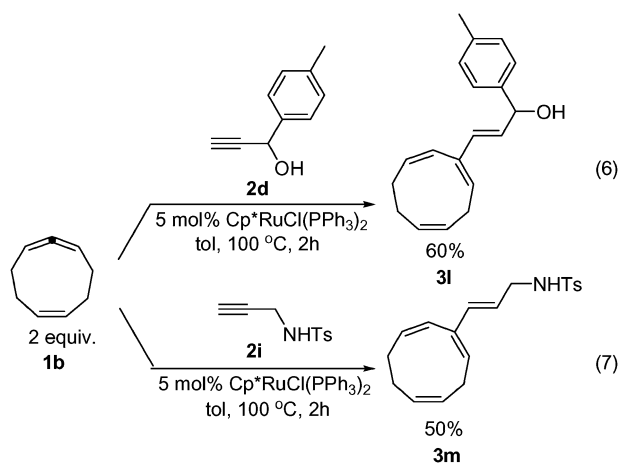
The reaction of propargylic tosyl amide (**2i**) and dimethyl 2-propargylmalonate (**2j**) with 1,2-nonadiene has also been conducted to afford the corresponding products **3i** and **3j** (Scheme 3). The reaction with phenyl acetylene in DMA provided the triene **3k** with 50% isolated yield with Cp\*RuCl(COD) as the catalyst (eqn (5) Scheme 3). Under the catalysis of Cp\*RuCl(PPh<sub>3</sub>)<sub>2</sub> the yield of **3k** is similar (52%), however, its purity is slightly lower.

When 1,2,6-nonatriene **1b** was used, the same type of products were formed in moderate yields (Scheme 4), which indicated that the C–C double bond in **1b** did not participate the reaction.

In summary, the substituted cross-conjugated trienes could be produced *via* the [Cp\*Ru(II)]-catalyzed coupling reactions of cyclic allenes and alkynes. Further studies in this area including the scope of the reaction and the synthetic application of the products are being conducted in our laboratory.



**Scheme 3** Cp\*Ru(II)-catalyzed reaction of other terminal alkynes and cyclic allenes.



**Scheme 4** Cp\*Ru(II)-catalyzed reactions of 1,2,6-nonatriene (**1b**) with alkynes.

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