

## An Olefination via Ruthenium-Catalyzed Decarbonylative Addition of Aldehydes to Terminal Alkynes

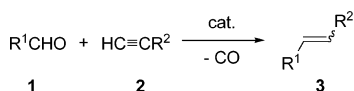
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The generation of C=C double bonds, a principal functionality in organic chemistry, is one of the most important reactions in synthesis.<sup>1</sup> Various olefination methodologies have been developed throughout the history of organic chemistry.<sup>1</sup> The well-known Wittig reaction provides access to C=C bonds with higher efficiency and better regio- and stereoselectivities over the classical elimination reactions (E1, E2, E1cB).<sup>1,2</sup> Other olefination reactions between nucleophiles and aldehydes include the Horner–Wadsworth–Emmons reaction,<sup>3</sup> the Peterson olefination,<sup>4</sup> the Julia–Lythgoe olefination,<sup>5</sup> and the Tebbe olefination.<sup>6</sup> However, such reactions generally involve highly reactive carbanions and suffer from lower atom economy.<sup>7</sup> The recently developed olefin metathesis reaction provides an alternative for olefin synthesis that overcomes some of the limitations of the earlier methods.<sup>8</sup> These reactions are particularly useful in the synthesis of cyclic alkenes (to avoid homoalkene exchange).<sup>8d</sup> However, the development of catalytic, more atom-economical, and highly regioselective methods for intermolecular olefination reactions remains an ongoing synthetic challenge. Herein, we report a novel method for synthesizing C=C bonds by decarbonylative addition of aldehydes to alkynes (Scheme 1).

### Scheme 1. Catalytic Decarbonylative Aldehyde–Alkyne Addition



Transition-metal-catalyzed decarbonylation reactions of aldehydes are an attractive subject that has been studied for decades.<sup>9</sup> However, very limited research has focused on decarbonylative addition reactions, which utilize the decarbonylative intermediate for addition to an unsaturated system.<sup>10</sup> During our studies of C–H activation of aldehydes, we observed that when an alkyne is added, an alkene (corresponding to a decarbonylative addition) is generated. Subsequently, various conditions concerning the catalysts and the additives were examined to optimize the formation of this decarbonylative addition product (Table 1). Water was found to be beneficial to the reaction (entries 1 and 2). With the use of [Ru(COD)Cl<sub>2</sub>]<sub>n</sub> together with 4 μL of water, the product was generated in 35% yield (entry 3). The addition of various ligands reduced the yield (entries 4–8). Complex hydrates were found to be an alternative to added water: the addition of 30 mol % CuCl<sub>2</sub>·2H<sub>2</sub>O increased the product yield to 48% (entry 9).<sup>11</sup> We speculated that chloride ion might serve as a weak coordinating ligand that could facilitate the reaction by stabilizing the catalyst. Indeed, in the presence of 5 equiv of LiCl, the product could still be generated in 16% yield without adding water or CuCl<sub>2</sub>·2H<sub>2</sub>O (entry 10). The use of cationic ruthenium catalysts or the combination of [Ru(COD)Cl<sub>2</sub>]<sub>n</sub> with AgOTf reduced the product yield.<sup>11</sup> A combination of the catalyst, CuCl<sub>2</sub>·2H<sub>2</sub>O, and LiCl was examined:<sup>11</sup> an 83% yield of the desired product was achieved with 10 mol % catalyst together with CuCl<sub>2</sub>·2H<sub>2</sub>O and LiCl (entry 12).

Table 1. Decarbonylative Addition under Various Conditions<sup>a</sup>

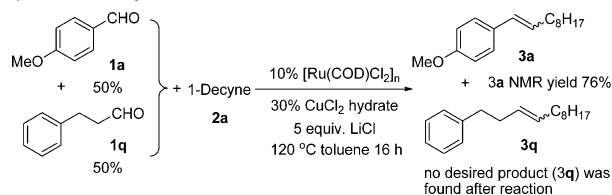
entry	% catalyst	% additive or ligand	% NMR yield <sup>b</sup>
1	5% RuCl <sub>3</sub>		NR
2	5% RuCl <sub>3</sub> ·3H <sub>2</sub> O		19
3	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	4 μL of H <sub>2</sub> O	35
4	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	10% dppp + 4 μL of H <sub>2</sub> O	22
5	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	10% dppe + 4 μL of H <sub>2</sub> O	11
6	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	10% Ph <sub>3</sub> P + 4 μL of H <sub>2</sub> O	23
7	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	10% ((F <sub>3</sub> C) <sub>2</sub> CH) <sub>3</sub> P + 4 μL of H <sub>2</sub> O	11
8	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	50% 1,5 -COD + 4 μL of H <sub>2</sub> O	6
9	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate	48
10	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	5 equiv of LiCl	16
11	5% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	59
12	10% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	83
13	10% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	65 <sup>c</sup>
14	10% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	48 <sup>d</sup>
15	10% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	NR <sup>e</sup>
16	10% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	72 <sup>f</sup>
17	10% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	70 <sup>g</sup>
18	10% [Ru(COD)Cl <sub>2</sub> ] <sub>n</sub>	30% CuCl <sub>2</sub> hydrate + 5 equiv of LiCl	50 <sup>h</sup>

<sup>a</sup> Conditions: **1a** (0.2 mmol), **2a** (0.8 mmol), toluene (1 mL), 120 °C, 16 h under argon, unless otherwise noted. <sup>b</sup> Determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. <sup>c</sup> In anisole. <sup>d</sup> In diglyme. <sup>e</sup> In water. <sup>f</sup> At 130 °C. <sup>g</sup> At 110 °C. <sup>h</sup> In air.

The reaction temperature and solvents were also examined (entries 13–17). The yield was reduced to 50% when the reaction was conducted under air (entry 18).<sup>11</sup> Although a small amount of water was beneficial for the reaction, no product was generated when the reaction was conducted in water (entry 15). When D<sub>2</sub>O instead of H<sub>2</sub>O was added,<sup>11</sup> no deuterated product was detected and a similar yield (32%) was obtained. We reasoned that water is not involved in the catalytic cycle and that a trace amount of water can help the chloride ion disperse in the reaction system and coordinate to the metal catalyst, whereas too much water would quench the reaction.

With the optimized reaction conditions in hand, different substrates were investigated using this reaction (Table 2). Aliphatic aldehydes failed to react under the current catalytic system, which provides an

### Scheme 2. One-Pot Competing Reaction between Aromatic and Aliphatic Aldehydes<sup>a</sup>



<sup>a</sup> Conditions: **1a** (0.2 mmol), **1q** (0.2 mmol), **2a** (0.8 mmol), [Ru(COD)Cl<sub>2</sub>]<sub>n</sub> (0.02 mmol). Yields were determined by <sup>1</sup>H NMR analysis.

interesting chemoselectivity. A competition experiment involving both aromatic and aliphatic aldehydes led to the olefination product corresponding exclusively to the reaction of the aromatic aldehyde (Scheme 2).

**Table 2.** Substrate Scope of the Decarbonylative Addition Reaction<sup>a</sup>

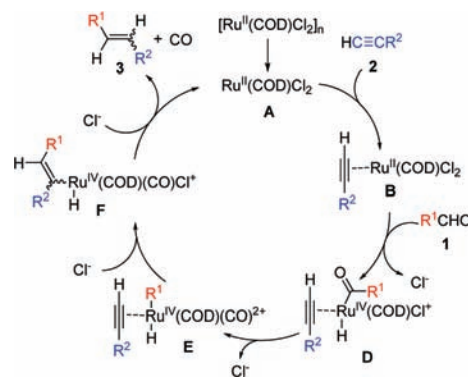
$R^1CHO + HC\equiv CR^2 \xrightarrow[5 \text{ equiv. LiCl}]{10\% [Ru(COD)Cl_2]_n, 30\% CuCl_2 \text{ hydrate}} R^1CH=CH-R^2$					
product	isolated yield <sup>c</sup> [%]	E/Z	product	isolated yield <sup>c</sup> [%]	E/Z
	75	6:1		67	2:1
	70 <sup>b</sup>	3.5:1		65	1.2:1
	72	6:1		64	1.1:1
	79	3:1		trace	N/A
	72 <sup>b</sup>	3:1			
	68	2:1			
	40	3:1			
	60	4:1			
	62	4:1			
	35	2.3:1		62	2.5:1
	25	4:1			

<sup>a</sup> Conditions: **1a** (0.2 mmol), **2a** (0.8 mmol), toluene (1 mL), 120 °C, 16 h under argon, unless otherwise noted. <sup>b</sup> At 150 °C. <sup>c</sup> Total yield of both the *E* and *Z* isomers; the *E/Z* ratio was determined by <sup>1</sup>H NMR analysis.

Electronic effects played an important role in this reaction. Aromatic aldehydes with more electron-donating groups on the phenyl ring gave much better yields than those with electron-withdrawing groups (Table 2). The yield decreased when an ester group was the substituent (**3k**). Other substrates (aldehyde and alkyne) containing ester groups, such as methyl 4-formylbenzoate, methyl propiolate, and propargyl propionate, also gave low yields, and the corresponding acids, resulting from decomposition of the esters, were found after the reaction. An unprotected hydroxyl group could also be tolerated by the reaction (**3l**). Both aromatic and aliphatic alkynes can be used as the alkyne substrate. Phenylacetylenes bearing electron-withdrawing groups gave better yields than those having electron-donating groups (**3l–3n**). It is worth noting that a conjugated aldehyde could also participate in the reaction, generating a 1,3-butadiene product (**3p**). Trans alkenes were generated as major products in all cases, and aliphatic alkynes showed better stereoselectivity than aromatic alkynes (Table 2). No product was obtained when the terminal alkynes were replaced with internal alkynes such as 2-hexyne and biphenylethyne.

A tentative mechanism to rationalize the decarbonylative addition reaction is illustrated in Scheme 3. The catalyst polymer first forms the monomer, which coordinates with the alkyne to generate intermediate **B**. A control experiment showed that no corresponding decarbonylative product was formed in the absence of alkyne. Oxidative addition with the aldehyde generates intermediate **D**, which subsequently undergoes a decarbonylative process to form intermediate **E**. Finally, reductive elimination affords the decarbonylative addition product and CO and regenerates the active ruthenium complex **A**. An IR study of the reaction residue revealed that a ruthenium carbonyl complex was formed after the reaction, which led to the termination of the catalytic cycle. The chloride ion serves as a weak coordinating ligand shuttle to facilitate these steps.

**Scheme 3.** Tentative Mechanism for the Ruthenium-Catalyzed Decarbonylative Addition Reaction



In summary, we have developed a novel method of olefination using aldehydes and alkynes via a decarbonylative addition. Various substrates were examined, and a strong electronic effect and high chemoselectivity between aromatic and aliphatic aldehydes were observed in this reaction. Further efforts to expand the scope of such an olefination based on decarbonylative addition are currently underway in our laboratory.

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**Supporting Information Available:** Experimental procedures, characterization data of new compounds, and <sup>1</sup>H and <sup>13</sup>C NMR data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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