

# One-pot terminal alkene homologation using a tandem olefin cross-metathesis/allylic carbonate reduction sequence†

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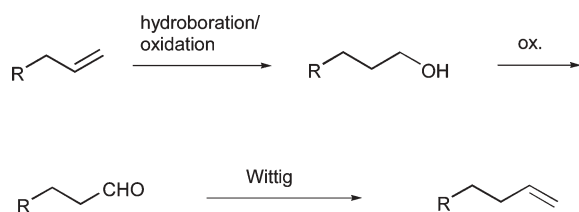
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A one-carbon homologation of terminal alkenes has been developed utilizing an olefin cross-metathesis followed by a palladium-mediated allylic carbonate reduction; various substrates were used to demonstrate the scope of the reaction, with yields ranging from 65 to 86%.

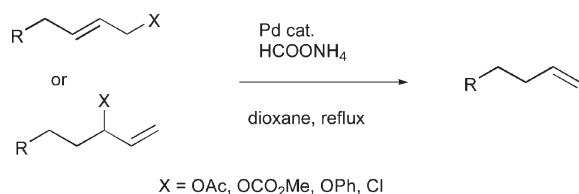
One-carbon homologation of a terminal alkene remains a difficult task in organic synthesis. To date there is no direct method to accomplish this transformation. A classical three-step sequence involves hydroboration–oxidation of a terminal alkene, oxidation to the aldehyde, and subsequent Wittig olefination (Scheme 1).



Scheme 1 Classical sequence for one carbon homologation of alkenes.

Besides being multistep, this sequence is not very functional group tolerant. In contrast, olefin cross-metathesis (CM) is very chemoselective and a convenient route to functionalized olefins.<sup>1</sup> We envisioned using a CM reaction to provide a functionalized alkene intermediate which could be easily converted *in situ* to a terminal olefin with one additional carbon in the chain.

Tsuji *et al.*<sup>2</sup> reported the conversion of allylic esters, carbonates, phenyl ethers and chlorides to terminal alkenes utilizing a palladium-catalyzed reductive cleavage (Scheme 2). Preliminary results prompted us to target allylic carbonates as intermediates for our methodology development. To the best of our knowledge

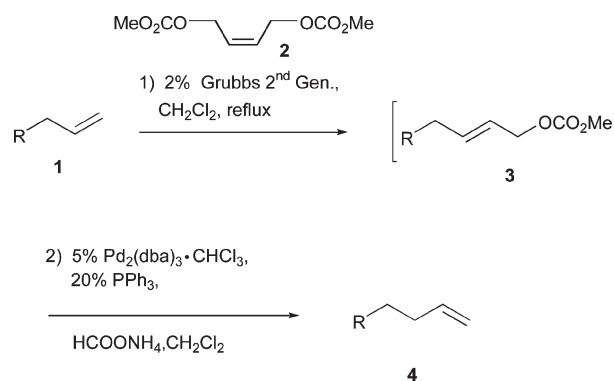


Scheme 2 Tsuji's reduction of allylic compounds.

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there is no report on a conversion of an alkene directly to an allylic carbonate. However, Grubbs *et al.* have developed chemistry where terminal olefins are converted to the corresponding allylic acetates by cross-metathesis with *cis*-2-butene-1,4-diol diacetate.<sup>3</sup> It seemed reasonable that a modification of this reaction could be utilized to make the required allylic carbonate intermediate which could then be submitted to Tsuji's conditions to form the desired terminal alkene. We decided to examine these two reactions in tandem to produce a one-pot one-carbon alkene homologation. In addition to being of general use, this methodology will extend the utility of the well established allylation reactions<sup>4</sup> by subsequent modification of the resulting terminal alkenes **1** to the one-carbon homologated butenyl derivatives **4** (Scheme 3).

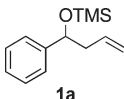
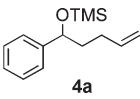
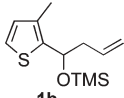
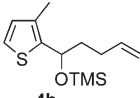
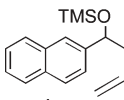
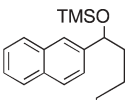
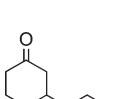
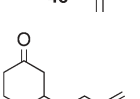
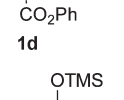
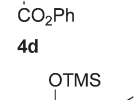
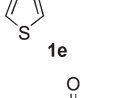
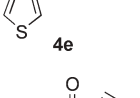
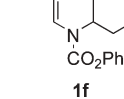
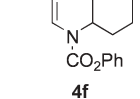


Scheme 3 One-pot terminal alkene homologation reaction.

The investigation commenced by establishing viable cross-metathesis reaction conditions of terminal alkenes with the allylic dicarbonate **2**<sup>5</sup> utilizing the Grubbs second-generation catalyst.<sup>1,3</sup> The mol percentage of catalyst was varied unveiling a 2% loading to be optimal. The concentration during the metathesis reaction was found to be essential to the success of the formation of allylic carbonate **3**. When the concentration approached 1 M, the product formation was significantly reduced. We observed that the reaction produced consistent results at a concentration of 0.1 M.

Following the optimized metathesis protocol, the intermediate carbonate was subjected to various mol percentages of Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> in the presence of PPh<sub>3</sub><sup>6</sup> and ammonium formate. Work by Braddock and Wildsmith uncovered that the success or failure of reactions involving the combination of Grubbs and Pd catalysts hinged on obtaining the correct ratio between the two.<sup>7</sup> When the ratio exceeded 2 : 1 (Grubbs cat./Pd cat.), the palladium chemistry did not work perhaps due to complexation of the PCy<sub>3</sub> to the palladium catalyst; a Grubbs cat./Pd cat. loading ratio of 1 : 2.5 proved to be optimal. After numerous solvent

**Table 1** One-pot homologation of terminal alkenes

Entry <sup>a</sup>	Substrate <b>1</b>	Product <b>4</b>	Yield <sup>b</sup> (%)
1	 <b>1a</b>	 <b>4a</b>	86
2	 <b>1b</b>	 <b>4b</b>	85
3	 <b>1c</b>	 <b>4c</b>	83
4	 <b>1d</b>	 <b>4d</b>	76
5	 <b>1e</b>	 <b>4e</b>	66
6	 <b>1f</b>	 <b>4f</b>	66
7	 <b>1g</b>	 <b>4g</b>	65

<sup>a</sup> Reactions were carried out on a 0.1–1.0 mmol scale. <sup>b</sup> Yield of pure isolated product.

studies, it was determined that methylene chloride could be used as the solvent for both reactions, eliminating the need for exchanging solvents.

The results of this study are summarized in Table 1 with product yields ranging from 65 to 86%. Entries 1–3 and 5 demonstrate

homologation of homoallylic alcohol derivatives prepared by allylation of the corresponding aldehydes. Attempts at accessing these products in the absence of a silyl protecting group were met with limited success. Entries 4, 6 and 7 show the accomplishment of the reaction in the presence of more complex substrates.

A typical procedure is as follows: the terminal alkene and bis-carbonate **2** (2 equiv.) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> and degassed. Grubbs second-generation catalyst (2%) was added and the mixture was heated at reflux for 1 d.<sup>8</sup> The solution of the *in situ* formed allylic carbonate was then cooled to rt, and PPh<sub>3</sub> (20%), Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (5%), and ammonium formate (2 equiv.) were added. The mixture was heated at reflux for 1 d and then filtered. The product was purified by silica gel chromatography.

In summary, we have developed a one-pot one-carbon alkene homologation from an existing terminal alkene, a process that should be of considerable synthetic utility.

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- The reaction is followed by TLC until the starting alkene **1** has been completely consumed.