



Synthesis of heterocycles via sequential Pd/Ru-catalysed allene insertion–nucleophile incorporation–olefin metathesis

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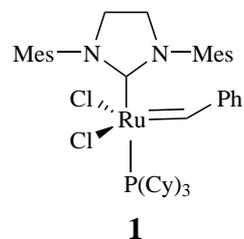
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Abstract—A novel sequential palladium/ruthenium-catalysed three-component process is described involving allenylation of aryl/heteroaryl iodides to generate (π -allyl) palladium species which are intercepted by nitrogen nucleophiles to afford 1,6- and 1,7-dienes. Subsequent ring-closing metathesis affords *N*-heterocycles in good yield. © 2001 Elsevier Science Ltd. All rights reserved.

In recent years allenes have become useful building blocks in palladium-catalysed processes.¹ We have developed a wide range of powerful and selective Pd-catalysed molecular queuing processes² whose potential would be considerably enhanced by interfacing with synthetically valuable catalytic processes mediated by other transition metals. We have recently developed such bimetallic cascades which include the electrochemically driven Pd/Cr Nozaki–Hiyama–Kishi reaction,³ Pd/In Barbier type allylation,^{4,5} Pd/Ru Heck/metathesis,^{6,7} Rh/Pd cycloaddition–cyclisation–anion capture processes⁸ and Rh/Pd cycloaddition–Friedel Craft reactions.⁹

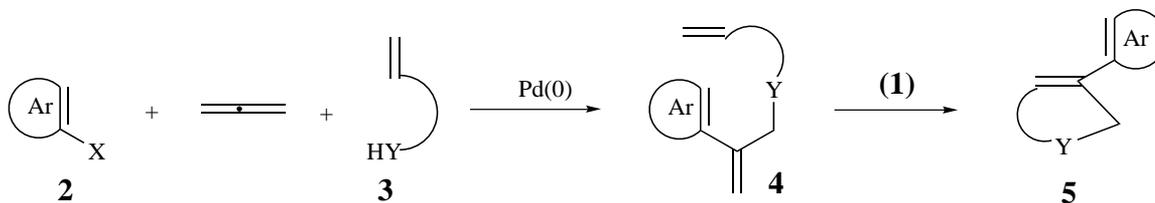
The use of ring-closing olefin metathesis in organic synthesis has seen explosive growth over the past decade. This is partly due to the discovery of second generation, air stable, Ru catalysts such as **1**^{10–12} which exhibit higher thermal stability, wider functional group

tolerance and accommodate a higher density of substituents on the double bond formed in ring-closing metathesis.



Our ongoing interest in designing palladium-catalysed allenylation processes, in combination with core reactions, has led to the three-component process (Scheme 1) involving Pd/Ru catalysis reported herein.

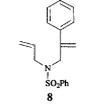
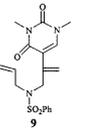
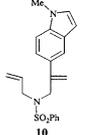
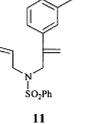
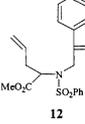
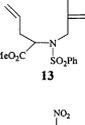
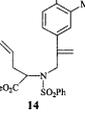
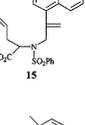
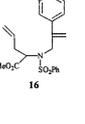
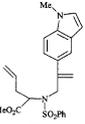
The strategy (Scheme 1) involves reaction of an aryl/vinyl halide **2** with allene and a nucleophile **3** in the



Scheme 1.

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Table 1. Three-component allenylation–amination cascades^{a,b}

Entry	Aryl Iodide	NuH ^d	Product	Yield (%) ^c
1		6		79
2		6		85
3		6		88
4		6		79
5		7		81
6		7		71
7		7		72
8		7		70
9		7		81
10		7		80

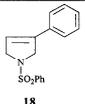
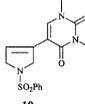
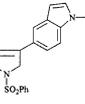
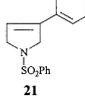
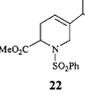
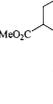
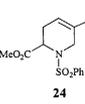
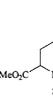
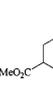
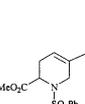
a. Reactions were carried out in toluene at 80°C for 18 h and employed 1 mmol aryl / heteroaryl / vinyl iodide, 10 mol % Pd(OAc)₂, 20 mol % PPh₃, 2 mol eq. K₂CO₃ and nucleophile 6 or 7 (1.2 mol eq.).

b. When nucleophile 7 was employed 1 mol eq. Et₄N⁺Cl⁻ was added.

c. Isolated yield.

d. Nucleophile.

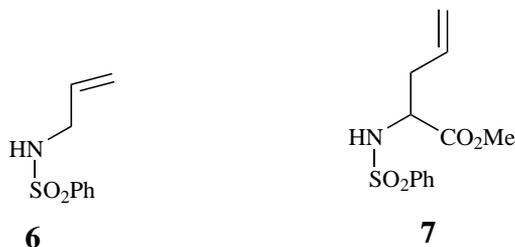
Table 2. Ring-closing metathesis process^a

Starting material	RCM Product	Yield (%) ^b
8		74
9		85
10		94
11		63
12		77
13		71
14		74
15		75
16		68
17		84

a. Reactions were carried out in toluene at 80°C for 3 h and employed 5 mol % catalyst 1.

b. Isolated yield.

presence of Pd(0) to afford 1, ω-dienes **4**, capable of undergoing a ruthenium-catalysed ring-closing metathesis to give hetero- or carbo-cycles **5**.



Thus, aryl/heteroaryl/vinyl iodides (1 mmol) reacted with allene (1 bar), Pd(OAc)₂ (10 mol%), PPh₃ (20 mol%), K₂CO₃ (2 mol equiv.) and *N*-allylbenzenesulphonamide **6** in toluene at 80°C over 18 h to afford **8–11** (Table 1, entries 1–4) in 79–88% yield.

N-Benzenesulphonyl *C*-allyl glycine methyl ester **7** was also successfully incorporated into this three-component cascade process to afford **12–17** in 70–81% yield (Table 1, entries 5–10).

The ring-closing metathesis reactions (RCM) of **8–17** were explored using catalyst **1**. Thus, **8–17** (1 mmol) treated with catalyst **1** (5 mol%) in toluene at 80°C over 3 h afforded the RCM products **18–27** in excellent yields (Table 2).

Rutijes et al.¹³ have recently reported a closely related Pd/Ru process.

In conclusion, we have demonstrated a novel sequential palladium-catalysed allene insertion/nucleophile incorporation followed by ruthenium-catalysed ring-closing metathesis for the synthesis of heterocycles. Further work is in hand incorporating substituted allenes and other nucleophiles into these processes.

Acknowledgements

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