Sequential Catalysis

DOI: 10.1002/anie.200701727

Ruthenium(IV) Alkylidenes as Precatalysts for Direct Arylations of Alkenes with Aryl Chlorides and an Application to Sequential Catalysis**

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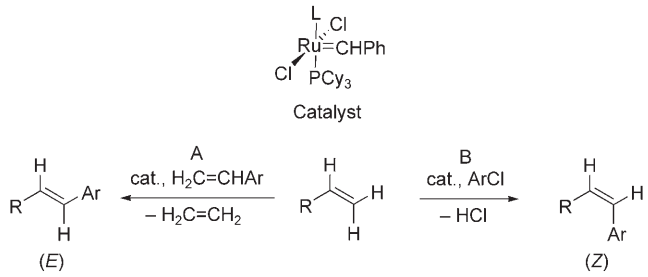
Dedicated to Professor Herbert Mayr on the occasion of his 60th birthday

The development of chemo- and regioselective intermolecular functionalization reactions of C–H bonds represents an important and long-standing goal in synthetic chemistry.[1–4] Diasteroselective olefin cross-metathesis[5–7] catalyzed by single-component ruthenium carbene complexes was recognized as an alternative for the functionalization of vinylic C–H bonds (Scheme 1, reaction A).[8] Furthermore, ruthenium(IV) alkylidene complexes enabled other valuable catalytic processes, such as isomerizations, hydrogenations, Kharasch additions, and dihydroxylations,[9] which ultimately allowed for the development of elegant sequential catalytic transformations.[10–12]

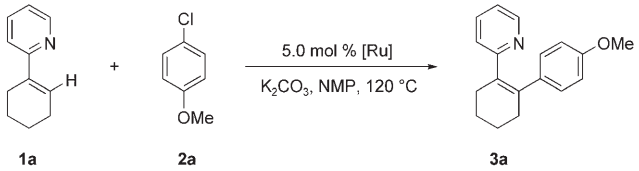


Scheme 1. Indirect (A) versus direct (B) vinylic C–H bond functionalization catalyzed by a ruthenium(IV) carbene complex.

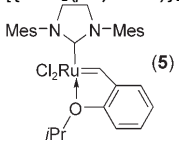
Ruthenium-catalyzed direct arylations[13] using organic electrophiles[14] have, to date, only been reported with ruthenium(II) complexes as catalysts.[15–18] While conducting mechanistic studies, we found that highly functional-group-tolerant ruthenium(IV) carbene complexes can be employed for unprecedented direct arylation reactions via C–H bond activation of alkenes[19] with readily available aryl chlorides.[20] Herein, we disclose our results on this economical and environmentally benign C–H bond functionalization process, the stereochemical outcome of which is complementary to that observed in olefin cross-metathesis reactions (Scheme 1, reaction B). The potential of our findings for tandem catalysis[21] is demonstrated with a C–H bond functionalization–hydrosilylation sequence.

At the outset of our studies we probed the catalytic performance of different ruthenium compounds in the direct arylation of alkene **1a** with electron-rich aryl chloride **2a** (Table 1 and Table S1 in the Supporting Information). Notably, we observed significant, though sluggish, product formation under phosphine-free reaction conditions (Table 1, entries 2, and 3). Significantly more efficient catalysis was accomplished with a complex derived from secondary phosphine oxide **4** (Ad = adamantyl; Table 1, entry 4). Ruthenium(IV) carbene complexes **5** and **6** showed high catalytic activities (Table 1, entries 5, and 6), while complex **7** outperformed all studied catalysts (Table 1, entry 7). In view of further catalyst development, it is notable that ruthenium(III)

Table 1: Ruthenium catalyst screening for the direct arylation of alkenes.[a]



1a **2a** **3a**

Entry	[Ru]	Yield [%][b]
1	$[Ru_3(CO)_{12}]$	–
2	$[RuCl_3 \cdot x H_2O]$	27
3	$[\{RuCl_2(p\text{-cymene})\}_2]$	34
4	$[\{RuCl_2(p\text{-cymene})\}_2]$/(1-Ad)$_2$P(O)H (**4**)	78
5	 (**5**)	54
6	$[Cl_2(PCy_3)(IMes)Ru{=}CHPh]$ (**6**)[c]	78
7	$[Cl_2(PCy_3)_2Ru{=}CHPh]$ (**7**)	85

[a] Reaction conditions: **1a** (1.0 equiv), **2a** (1.2 equiv), [Ru] (5.0 mol%), K_2CO_3 (2.0 equiv), NMP (*N*-methylpyrrolidinone, 1 mL), 120°C, 22 h. [b] Yields of isolated product. [c] IMes = *N*,*N*′-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene.

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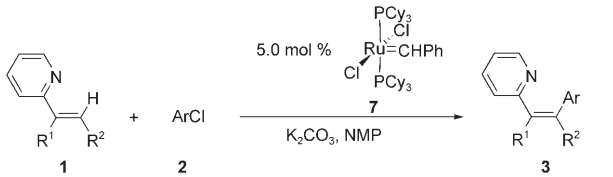
[**] Support by the DFG (Emmy Noether-Programm), the Spanish Ministerio de Educación y Ciencia (fellowship for P.A.B.), the Fonds der Chemischen Industrie, the Dr. Otto Röhm Gedächtnisstiftung, the Römer Foundation, and Sanofi-Aventis (Frankfurt) is gratefully acknowledged.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

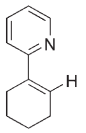
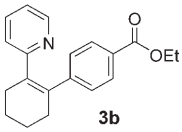
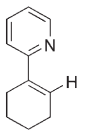
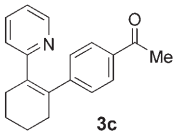
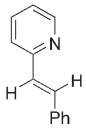
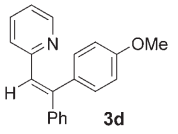
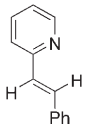
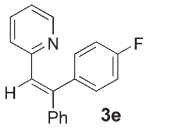
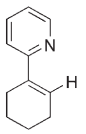
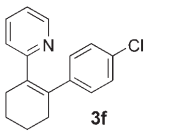
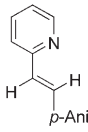
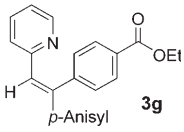
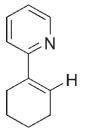
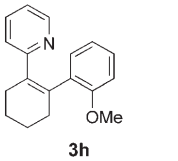
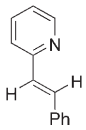
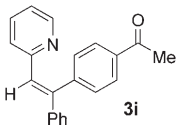
or ruthenium(IV) complexes can be used for catalytic direct arylations using organic electrophiles.

With an efficient catalyst, compound **7**, in hand, we probed its scope in direct arylation reactions of highly substituted alkenes (Table 2). Both functionalized electron-deficient and electron-rich aryl chlorides could be converted with high efficiency (Table 2, entries 1–3). Additionally, the protocol was not limited to chloride as the leaving group in the electrophile but proved applicable to bromides and iodides as well (Table 2, entries 4 and 5). Generally, coupling reactions of chlorohalobenzenes proceeded with excellent chemoselectivities (Table 2, entries 6–8). Importantly, efficient catalysis could also be achieved with an *ortho*-substituted aryl chloride (Table 2, entry 10) or at a significantly lower temperature (Table 2, entry 11).

Table 2: Scope of ruthenium(IV) carbene catalyst **7** in direct arylations of alkenes.[a]

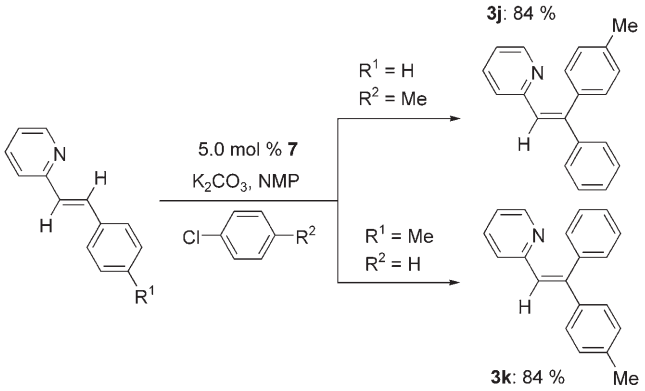


1 **2** **3**

Entry	**1**	**2**	Product	Yield [%][b]
1		4-$EtO_2CC_6H_4Cl$	 **3b**	92
2		4-$Me(O)CC_6H_4Cl$	 **3c**	88
3		4-$MeOC_6H_4Cl$	 **3d**	84
4		4-$MeOC_6H_4Br$		88
5		4-$MeOC_6H_4I$		88
6		4-FC_6H_4Cl	 **3e**	62
7		4-IC_6H_4Cl	 **3f**	48[c]
8		4-BrC_6H_4Cl		91
9		4-$EtO_2CC_6H_4Cl$	 **3g**	84
10		2-$MeOC_6H_4Cl$	 **3h**	64
11		4-$Me(O)CC_6H_4Cl$	 **3i**	88[d]

[a] Reaction conditions: **1** (1.0 equiv), **2** (1.2–2.0 equiv), **7** (5.0 mol%), K_2CO_3 (2.0 equiv), NMP (1 mL), 120°C, 22 h. [b] Yields of isolated product. [c] GC conversion. [d] 100°C.

The regio- and stereoselective synthesis of multisubstituted alkenes is among the most challenging tasks in organic synthesis.[22,23] Hence, we probed the potential of our protocol for the diastereoselective synthesis of triaryl-substituted alkenes (Scheme 2). Remarkably, the judicious choice of substrates allowed for the preparation of a given isomer with excellent selectivity.

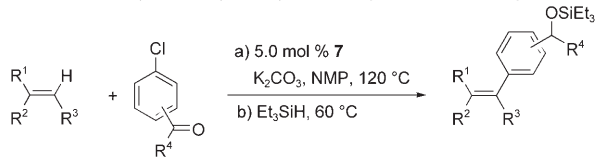


Scheme 2. Stereoselective synthesis of highly substituted alkenes.

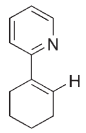
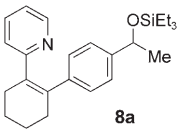
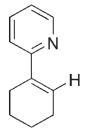
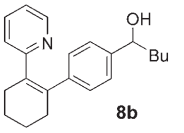
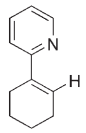
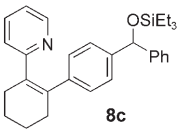
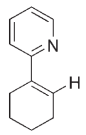
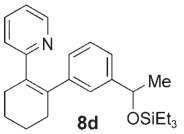
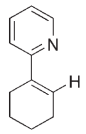
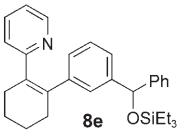
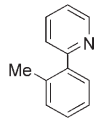
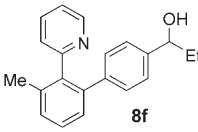
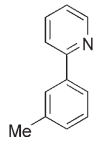
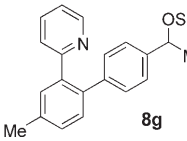
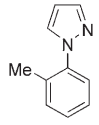
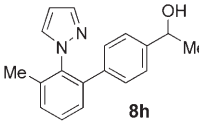
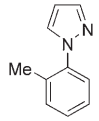
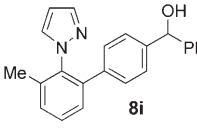
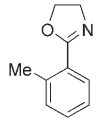
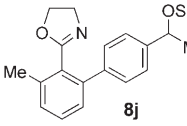
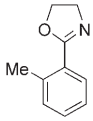
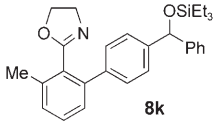
The application of a single catalyst for more than one chemical transformation in a one-pot reaction is an important goal in contemporary synthesis.[24–26] As ruthenium(IV) carbene complexes are known to catalyze a variety of important transformations,[9,11,12] we probed direct arylation-based sequential catalysis. To this end, we studied a one-pot reaction sequence consisting of a direct arylation and a hydrosilylation catalyzed by ruthenium carbene complex **7** (Table 3). A variety of differently substituted phenones proved applicable to the one-pot protocol (Table 3, entries 1–6). Importantly, the C–H bond functionalization catalyzed by the ruthenium(IV) carbene complex was not restricted to alkenes but also proved viable using arenes as pronucleophiles (Table 3, entries 7–12). The use of 2-pyridyl substituents was not a stringent requirement for the direct arylation. Thus, both pyrazolyl- (Table 3, entries 9 and 10) and oxazolinyl-substituted (Table 3, entries 11 and 12) pronucleophiles could be employed. From a practical viewpoint, it is important to note that change or removal of solvent was not required for the sequential catalysis to proceed with high yields of isolated product.

In summary, we have demonstrated that ruthenium complexes in the oxidation states +III and +IV are precatalysts for direct arylation reactions of arenes and alkenes with organic electrophiles. Remarkably, ruthenium(IV) carbene complex **7** proved most potent in the

Table 3: Direct arylation–hydrosilylation sequence with complex **7**.[a]



1 **2** **8**

Entry	1	2	Product	Yield [%][b]
1		4-Me(O)CC$_6$H$_4$Cl	 **8a**	85
2		4-Bu(O)CC$_6$H$_4$Cl	 **8b**	64[c]
3		4-Ph(O)CC$_6$H$_4$Cl	 **8c**	90
4		4-Ph(O)CC$_6$H$_4$Br		74
5		3-Me(O)CC$_6$H$_4$Cl	 **8d**	88
6		3-Ph(O)CC$_6$H$_4$Cl	 **8e**	90
7		4-Et(O)CC$_6$H$_4$Cl	 **8f**	61[c]
8		4-Me(O)CC$_6$H$_4$Cl	 **8g**	75
9		4-Me(O)CC$_6$H$_4$Cl	 **8h**	76[c]
10		4-Ph(O)CC$_6$H$_4$Cl	 **8i**	74[c]
11		4-Me(O)CC$_6$H$_4$Cl	 **8j**	85
12		4-Ph(O)CC$_6$H$_4$Cl	 **8k**	86

[a] Reaction conditions: **1** (1.0 equiv), **2** (1.2 equiv), **7** (5.0 mol%), K_2CO_3 (2.0 equiv), NMP (1 mL), 120°C, 22 h; Et_3SiH (5.0 equiv), 60°C, 22 h. [b] Yields of isolated product. [c] Isolated after deprotection with TBAF (tetrabutylammonium fluoride).

unprecedented ruthenium-catalyzed diastereoselective direct arylation of alkenes with aryl chlorides. The potential of direct arylation reactions catalyzed by ruthenium(IV) alkylidene complexes for sequential catalysis was showcased with the development of a direct arylation–hydrosilylation sequence.

Experimental Section

Representative procedure for the direct arylation–hydrosilylation sequence (Table 3, entry 1): A suspension of **7** (20.6 mg, 0.025 mmol, 5.0 mol%), K_2CO_3 (138 mg, 1.00 mmol), 2-cyclohex-1-enylpyridine (82.3 mg, 0.517 mmol) and 1-(4-chlorophenyl)ethanone (93.1 mg, 0.602 mmol) in dry NMP (1.0 mL) was stirred for 22 h at 120°C under N_2. Thereafter, Et_3SiH (293 mg, 2.52 mmol) was added by syringe at ambient temperature, and the reaction mixture was stirred for 22 h at 60°C. Et_2O (40 mL) and H_2O (40 mL) were added at ambient temperature. The separated aqueous phase was extracted with Et_2O (3×40 mL). The combined organic layers were washed with H_2O (50 mL) and brine (50 mL), dried over Na_2SO_4, and concentrated in vacuo. The remaining residue was purified by column chromatography on silica gel (*n*-pentane/Et_2O 15:1→10:1) to yield **8a** as a yellow oil (174 mg, 85%).

Received: April 18, 2007
Published online: July 19, 2007

Keywords: alkenes · C–H activation · hydrosilylation · ruthenium carbenes · sequential catalysis

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