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Regioselective allylic alkylation and etherification catalyzed by in situ generated *N*-heterocyclic carbene ruthenium complexes

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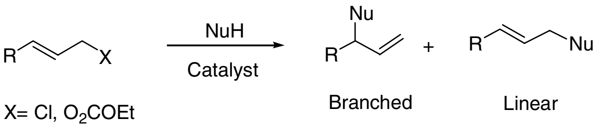
Abstract—Benzimidazolium halides are used for the first time as ligand precursors in ruthenium-catalyzed substitution of allylic carbonates and chlorides by carbon nucleophiles and phenols, respectively. After generation of diaminocarbene species upon deprotonation by *t*BuOK, their association with $[Cp^*Ru(MeCN)_3]PF_6$ induces a very high regioselectivity in favor of the branched isomers when cinnamyl derivatives are used as starting substrates. They also provide good regioselectivities for the allylation of phenols by unsymmetrical aliphatic allylic substrates such as 3-chloro-4-phenylbut-1-ene, and thus provide a straightforward access to new allylic phenyl ethers.

Metal-catalyzed allylic substitution is recognized as a useful process in organic synthesis for C–C and C-heteroatom bond forming reaction.[1] In this context, the control of the regioselectivity is of crucial importance when unsymmetrical allylic derivatives are used as substrates.



For this type of nucleophilic substitution, pentamethylcyclopentadienyl ruthenium catalysts have already disclosed promising properties with respect to regioselectivity in favor of the branched isomer.[2] Thus, $[Cp^*(MeCN)_3Ru][PF_6]$ bearing labile ligands was recently shown to be appropriate for the synthesis of aryl allyl ethers starting from allylic halides and phenols.[3] Remarkably, Cp*(bipy)Ru precursors have revealed a catalytic activity allowing the direct involvement of neutral undeprotonated soft carbon pronucleophiles.[4,5] On the other hand, *N*-heterocyclic carbenes (NHC) have attracted considerable attention, not only as isolable species,[6,7] but also as ligands for transition-metal catalysts.[8] They have offered very active systems for catalytic hydrogenation,[9] C–C coupling,[10] olefin metathesis,[11] amination of aryl halides,[12] cyclopropanation,[13] and cycloisomerization reactions,[14] but only Mori and co-workers have involved NHC ligands in palladium complexes to achieve allylic substitution.[15]

We report herein that a combination of a Cp*Ru moiety and NHC ligand allows the achievement and improvement of both catalytic activity and regioselectivity as compared to (i), Cp*(bipy)Ru precursors toward soft carbon nucleophiles and (ii), $[Cp^*(MeCN)_3Ru][PF_6]$ toward aryl oxide anions.

For this study, the catalysts were prepared starting from $[Cp^*(MeCN)_3Ru][PF_6]$ **1** that contains very labile acetonitrile ligands, and 1,3-dialkylbenzimidazolium salts

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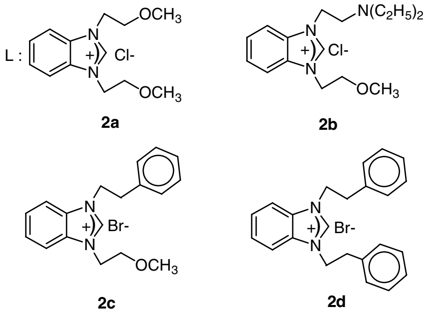


Scheme 1.

2a–**d** (Scheme 1). These salts quantitatively result from quaternization of 1-alkylbenzimidazolines in DMF.[16,17]

Under basic conditions **2a**–**d** generated the corresponding NHC species that were reacted in situ with **1**. As bipyridine ligands, *N*-heterocyclic carbenes are strong σ-donors and poor π-acceptors. Whereas bipyridine ligands act as robust chelates, coordination of only one NHC might be expected on the basis of previous works.[18] An additional stabilization of the metal center may be gained through the presence of weakly coordinating oxygen or nitrogen atoms located in the side arms of the NHC arising from **2a**–**c** (Scheme 1). For each experiment, the catalytic material was prepared as follows: the appropriate amount of **2a**–**d** (2 mol per Ru atom) was treated with a stoichiometric amount of *t*-BuOK in THF (5 mL) at 50 °C for 2 h. [Cp*Ru(CH_3CN)$_3$][PF_6] was then added and the mixture was heated at 50 °C for 2 h. THF was subsequently removed under vacuum to leave a solid that was immediately involved as catalytic material. Even if we were not able to fully characterize the organometallic complex, it is assumed that [Ru-carbene] species are formed.[18,19] Then, the reaction of carbonate **3** with dimethylmalonate **4** was investigated by successively adding carbonate **3** (0.5 mmol) and malonate **4** (0.6 mmol) to the catalytic material (0.015 mmol based on ruthenium) dissolved in acetonitrile (4 mL). The resulting solution was stirred overnight at room temperature, concentrated under vacuum and then filtered on silica gel. ^{1}H NMR spectroscopic analysis of the crude product indicated completion of the reaction affording the desired product **7** (Eq. 1), and a high (**7B**/**7L**) branched to linear ratio (Table 1). A blank experiment, carried out according to the same procedure but without any ruthenium source, led to no conversion of the starting substrates.

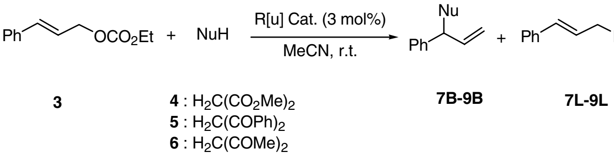
Indeed, the regioselectivities were fairly good (ranging between 71:29 with ligand **2d** and 88:12 with ligand **2b**, Table 1, entries 1–4). Since **1** is unable to catalyze allylic alkylation without prior formation of the stabilized carbonucleophiles via deprotonation of malonate,[3] these results provide a clear evidence of the crucial role of the carbene ligand in the new catalytic system, wherein a preliminary preparation of sodiodimethylmalonate is avoided. The extension of this reaction to the stabilized carbon pronucleophiles **5** (Eq. 1) also led to good results as the branched isomer **8B** was the major compound (Table 1, entries 5–8). However, with penta-2,4-dione **6** and using the **2a**-based catalyst, the linear product **9L** and the branched isomer **9B** were isolated in an almost 1:1 ratio (Table 1, entry 9). Finally, these results emphasize the potential of Cp*Ru–NHC catalysts for the regioselective nucleophilic substitution of allylic carbonates. It is also worth noting that the regioselectivity is opposite to that obtained in the palladium–NHC-catalyzed reaction that produces the linear isomer as the major product.[15]

Table 1. Ruthenium-catalyzed allylic alkylation of cinnamyl carbonate **3**[a]

Entry	NHC precursor	Nucleophile	Product	Ratio[b] **B/L**
1	**2a**	**4**	**7**	85/15
2	**2b**	**4**	**7**	88/12
3	**2c**	**4**	**7**	82/18
4	**2d**	**4**	**7**	71/29
5	**2a**	**5**	**8**	74/26
6	**2b**	**5**	**8**	75/25
7	**2c**	**5**	**8**	60/40
8	**2d**	**5**	**8**	62/38
9	**2a**	**6**	**9**	46/54

[a] Conditions: 0.6 mmol of pronucleophile **4**–**6**, 0.5 mmol of cinnamyl carbonate **3**, 0.015 mmol (based on ruthenium) of (**2a**–**d**)-based catalyst in 4 mL of CH_3CN at room temperature for 16 h.

[b] As determined by ^{1}H NMR spectroscopy, complete conversion of **3**.



(1)

In order to evaluate the scope of this catalytic system, the range of nucleophiles was extended to phenol derivatives. Using experimental conditions very similar to those reported when **1** was used as a catalyst,[3] reaction of phenol with cinnamyl chloride in the presence of the **2a**-catalyst and potassium carbonate in acetonitrile (Eq. 2) led to the formation of the allyl phenyl ether **11** in a 94:6 branched to linear ratio (Table 2, entry 1). In this case, the blank experiment showed the formation of the sole linear derivative but in a very low yield. The regioselectivities observed in acetonitrile, THF and methanol (Table 2, entries 1–3) were quite similar (94:6, 93:7, 89:11, respectively). This observation indicated a slight effect of the solvent and is in sharp contrast with the results obtained with **1** as catalyst: in the same solvents, the regioselectivities are 98:2, 86:14 and 60:40, respectively.[20] Quite good regioselectivities were retained when (**2b**–**d**)-catalysts were involved (Table 2, entries 4–6). These catalytic systems based on (**2a**–**d**) tolerate the presence of an electron-donating group (such as a methoxy group) or an electron-withdrawing group (such as an halide) as *para*-substituent on the phenyl ring. Thus, good regioselectivities were obtained

Table 2. Ruthenium-catalyzed allylic etherification of cinnamyl chloride by aryl oxide anions[a]

Entry	NHC precursor	Ar	Product	Ratio[b] **B/L**
1	**2a**	C_6H_5	**11**	94/6
2[c]	**2a**	C_6H_5	**11**	93/7
3[d]	**2a**	C_6H_5	**11**	89/11
4	**2b**	C_6H_5	**11**	92/8
5	**2c**	C_6H_5	**11**	90/10
6	**2d**	C_6H_5	**11**	88/12
7	**2a**	4-Cl–C_6H_4	**12**	89/11
8	**2b**	4-Cl–C_6H_4	**12**	89/11
9	**2c**	4-Cl–C_6H_4	**12**	88/12
10	**2d**	4-Cl–C_6H_4	**12**	87/13
11	**2a**	4-MeO–C_6H_4	**13**	94/6
12	**2b**	4-MeO–C_6H_4	**13**	93/7
13	**2c**	4-MeO–C_6H_4	**13**	93/7
14	**2d**	4-MeO–C_6H_4	**13**	92/8
15	**2a**	2-Cl–C_6H_4	**14**	32/68
16	**2b**	2-Cl–C_6H_4	**14**	64/36
17	**2c**	2-Cl–C_6H_4	**14**	49/51
18	**2d**	2-Cl–C_6H_4	**14**	60/40

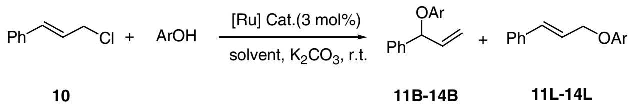
[a] Conditions: 1.2 mmol of ArOH, 1.2 mmol of K_2CO_3, 1 mmol of cinnamyl chloride **10**, 0.03 mmol (based on ruthenium) of (**2a**–**d**)-based catalyst in 6 mL of MeCN, room temperature, 16 h.

[b] As determined by ^{1}H NMR spectroscopy, complete conversion of **10**.

[c] THF as solvent.

[d] MeOH as solvent.

for *p*-substituted phenols and changing the electronic properties of the substituent had little influence on regioselectivity (Table 2, entries 7–14). However, chloro-substitution at the *ortho*-position had a detrimental effect on the regioselectivity (Table 2, entries 15–18). In these reactions, the catalysis may be slowed and the non-catalyzed reaction may become competitive. Indeed, under the same reaction conditions but without any ruthenium complex, 2-chlorophenol reacted with cinnamyl chloride **10** to produce the sole linear derivative **14L** in 75% yield after 16 h. The same lack of regioselectivity was observed with 2-chlorophenol when [Cp*Ru(CH_3CN)$_3$][PF_6] was used as catalyst precursor.[3]



(2)

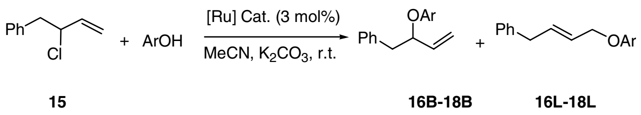
Table 3. Ruthenium-catalyzed allylic etherification of **15** by aryl oxide anions[a]

Entry	NHC precursor	Ar	Product	Ratio[b] **B/L**
1	**2a**	C_6H_5	**16**	83/17
2	**2b**	C_6H_5	**16**	64/36
3	**2c**	C_6H_5	**16**	78/22
4	**2d**	C_6H_5	**16**	67/33
5	**2a**	4-Cl–C_6H_4	**17**	67/33
6	**2b**	4-Cl–C_6H_4	**17**	83/17
7	**2c**	4-Cl–C_6H_4	**17**	86/14
8	**2d**	4-Cl–C_6H_4	**17**	87/13
9	**2a**	4-MeO–C_6H_4	**18**	69/31
10	**2b**	4-MeO–C_6H_4	**18**	80/20
11	**2c**	4-MeO–C_6H_4	**18**	74/26
12	**2d**	4-MeO–C_6H_4	**18**	77/23

[a] Conditions: 1.2 mmol of ArOH, 1.2 mmol of K_2CO_3, 1 mmol of allylic chloride **15**, 0.03 mmol (based on ruthenium) of (**2a**–**d**)-based catalyst in 6 mL of MeCN at room temperature for 16 h.

[b] As determined by ^{1}H NMR spectroscopy, complete conversion of **15**.

Allyl aryl ethers arising from cinnamyl derivatives are valuable intermediates in organic chemistry,[21] but it is also of interest to develop an efficient access to branched allylic aryl ethers starting from aliphatic allylic halides (vs cinnamyl chloride type substrates). For this study, 3-chloro-4-phenylbut-1-ene **15**, which offered both conveniences of low volatility facilitating experimental work and easy synthesis,[22] was chosen as allylic substrate. The reaction of phenoxide anion with **15** in the presence of 3 mol % of **1** in acetonitrile at room temperature quantitatively afforded the phenyl ethers **16B** and **16L** (Eq. 3) but a 1.5/1 **B/L** ratio indicated a rather moderate regioselectivity.[20] Significantly increased regioselectivities (Table 3, entries 1–4, **B/L** ratio average: 73/27) were reached when (**2a**–**d**)-based catalysts were used instead of **1**. Thus, a 83/17 ratio was obtained when the NHC precursor **2a** was used. Good regioselectivities were also obtained when *p*-chlorophenol (Table 3, entries 5–8, **17B/17L** ratio up to 87/13) and *p*-methoxyphenol (Table 3, entries 9–12, **18B/18L** ratio up to 80/20) were involved as nucleophiles. Compounds **16B**–**18B** are new compounds, which are conveniently and selectively prepared by this ruthenium-catalyzed reaction.



(3)

In conclusion, we have disclosed that the coordination of *N*-heterocyclic carbenes to a Cp*Ru center generates useful catalyst precursors for allylic substitution reactions starting from unsymmetrical allylic carbonates or halides. Among the different precursors **2a**–**d**, it is difficult to select one for its better efficiency as the observed regioselectivities are quite similar and slightly depend on the nature of the nucleophile. This new catalytic system achieved high regioselectivities with different nucleophiles (soft carbon nucleophiles, aryl oxide anions) and significantly improved regioselectivities when aliphatic allylic halides were used.

Acknowledgments

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References and notes

1. Tsuji, J. In *Transition Metal Reagents and Catalysts. Innovations in Organic Synthesis*; Wiley: Chichester, 2000; p 109.
2. (a) Kondo, T.; Ono, H.; Satake, N.; Mitsudo, T.; Watanabe, Y. *Organometallics* **1995**, *14*, 1945; (b) Kondo, T.; Mitsudo, T. In *Ruthenium in Organic Synthesis*; Murahashi, S.-I., Ed.; VCH: Weinheim, 2004; pp 129–151.
3. Mbaye, M. D.; Demerseman, B.; Renaud, J.-L.; Toupet, L.; Bruneau, C. *Adv. Synth. Catal.* **2004**, *346*, 835.
4. Mbaye, M. D.; Demerseman, B.; Renaud, J.-L.; Toupet, L.; Bruneau, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5066.
5. Hubert, C.; Renaud, J.-L.; Demerseman, B.; Fischmeister, C.; Bruneau, C. *J. Mol. Catal.* **2005**, *237*, 161–164.
6. Arduengo, A. J., III. *Acc. Chem. Res.* **1999**, *32*, 913.
7. Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39.
8. (a) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290; (b) Herrmann, W. A. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Eds.; VCH: Weinheim, 1996; p 712.
9. (a) Perry, M. C.; Cui, X.; Powell, M. T.; Hou, D.-R.; Reibenspies, J. H.; Burgess, K. *J. Am. Chem. Soc.* **2003**, *125*, 113; (b) Cui, X.; Burgess, K. *J. Am. Chem. Soc.* **2003**, *125*, 14212; (c) Fan, Y.; Cui, X.; Burgess, K.; Hall, M. B. *J. Am. Chem. Soc.* **2004**, *126*, 16688.
10. (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457; (b) Özdemir, I.; Demir, S.; Yaşar, S.; Çetinkaya, B. *Appl. Organomet. Chem.* **2005**, *19*, 550; (c) Clavier, H.; Coutable, L.; Guillemin, J.-C.; Mauduit, M. *Tetrahedron: Asymmetry* **2005**, *16*, 921.
11. (a) Sémeril, D.; Bruneau, C.; Dixneuf, P. H. *Adv. Synth. Catal.* **2002**, *344*, 585; (b) Trnka, T. M.; Grubbs, R. *Acc. Chem. Res.* **2001**, *34*, 18; (c) Clavier, H.; Audic, N.; Mauduit, M.; Guillemin, J.-C. *Chem. Commun.* **2004**, 2282.
12. (a) Stauffer, S. R.; Lee, S.; Stambouli, J. P.; Hanck, S. I.; Hartwig, J. F. *Org. Lett.* **2000**, *2*, 1423; (b) Grasa, G. A.; Viciu, M. S.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729.
13. Çetinkaya, B.; Özdemir, I.; Dixneuf, P. H. *J. Organomet. Chem.* **1997**, *534*, 153.
14. (a) Çetinkaya, B.; Demir, S.; Özdemir, I.; Toupet, L.; Sémeril, D.; Bruneau, C.; Dixneuf, P. H. *New J. Chem.* **2001**, *25*, 519; (b) Çetinkaya, B.; Demir, S.; Özdemir, I.; Toupet, L.; Sémeril, D.; Bruneau, C.; Dixneuf, P. H. *Chem. Eur. J.* **2003**, *9*, 2323.
15. (a) Sato, Y.; Yoshino, T.; Mori, M. *Org. Lett.* **2003**, *5*, 31; (b) Sato, Y.; Yoshino, T.; Mori, M. *J. Organomet. Chem.* **2005**, *690*, 5753.
16. For the synthesis of salts **2a**,**b**,**d** see: Özdemir, I.; Gök, Y.; Gürbüz, N.; Çetinkaya, E.; Çetinkaya, B. *Heterocycl. Chem.* **2005**, *42*, 303.
17. For the synthesis of salt **2c** see: Özdemir, I.; Gök, Y.; Gürbüz, N.; Yaçar, S.; Çetinkaya, E.; Çetinkaya, B. *Pol. J. Chem.* **2004**, *78*, 2141.
18. Baratta, W.; Herdtweck, E.; Herrmann, W. A.; Rigo, P.; Schwarz, J. *Organometallics* **2002**, *21*, 2101.
19. Dragutan, V.; Dragutan, I.; Demonceau, A. *Platinum Metals Rev.* **2005**, *49*, 123.
20. Mbaye, M. D. PhD thesis, University of Rennes 1, 2004.
21. (a) Labrosse, J.-R.; Poncet, C.; Lhoste, P.; Sinou, D. *Tetrahedron: Asymmetry* **1999**, *10*, 1069; (b) Trost, B. M.; Thiel, O. R.; Tsui, A.-C. *J. Am. Chem. Soc.* **2002**, *124*, 11616; (c) Trost, B. M.; Tang, W. *J. Am. Chem. Soc.* **2002**, *124*, 14542.
22. Julia, M.; Verpeaux, J. N.; Zahneissen, T. *Bull. Soc. Chim. Fr.* **1994**, *131*, 539.