Effective and Inexpensive Acrylonitrile Cross-Metathesis: Utilisation of Grubbs II Precatalyst in the Presence of Copper(I) Chloride

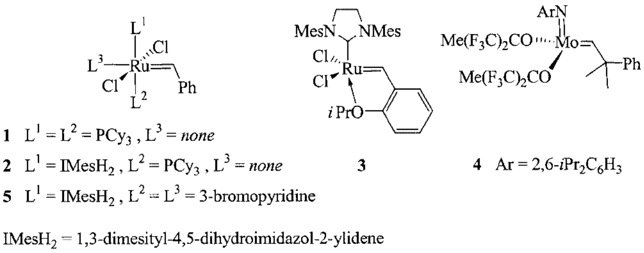
Michael Rivard[a] **and Siegfried Blechert***[a]

Keywords: Ruthenium / Copper / Metathesis / Synthetic methods

The efficient selective cross-metathesis (CM) of acrylonitrile using unmodified precatalyst **2** is reported. The use of copper(I) chloride as an additive and phosphane scavenger is described and significant turnover enhancement upon addition of a metallic salt in selective CM is observed for the first time. The influence of catalyst decomposition and other experimental parameters (concentration, amount of acrylonitrile used) on conversion is also demonstrated.

Introduction

Over the past five years, selective cross-metathesis (CM) has appeared as a powerful and efficient method for the formation of C-C double bonds.[1] Whereas the bis(tricyclohexylphosphane) complex **1** (Scheme 1) has proved to be promising in selective CM,[2] it nevertheless remains incompatible with nonterminal or conjugated olefins. The emergence of the N-heterocyclic carbene (NHC) coordinated precatalysts,[3] such as the second generation Grubbs catalyst **2**, has largely solved this problem,[4] except for some conjugated olefins, most notably acrylonitrile.[4f,5] However, this substrate has been successfully employed in CM with the phosphane-free precatalyst **3**[5b,6] (prepared from **2**[7]) or the molybdenum-based Schrock precatalyst **4**,[8] which nevertheless exhibits a higher sensitivity to oxygen than its Ru analogues.



Scheme 1. Olefin metathesis catalysts

Recent alternatives involved the use of purified acrylonitrile[9] or the use of precatalyst **5**[10] (also obtained from **2**), bearing two bromopyridine ligands in place of a tricyclohexyphosphane ligand. More important than the ability of the precatalyst to generate catalytically active species (which should be identical in the case of **2** and **3**), it seems that the presence of free phosphane in the reaction mixture during acrylonitrile CM has an inhibiting effect on conversion. However, the known phosphane-free precatalysts are more expensive than their precursor **2**. Therefore, it was of interest to study the effect of a phosphane scavenger on CM catalysed by **2**.

It should be pointed out that enhancement of reactivity by abstraction of free phosphane has already been mentioned in Ru-carbene catalysed metathesis.[4g,11] However, there are no reports of a turnover enhancement in selective CM by the means of metallic salts. It should also be noted that the higher reactivity observed when using a phosphane scavenger is also associated with a shorter lifetime of the active species,[11d,12] sometimes leading to incomplete reactions and decreased turnover numbers (TON). In the case of **1**, this shorter lifetime has been explained by the formation of highly reactive heterobimetallic copper-ruthenium complexes.[13]

Results and Discussion

To determine the additive and conditions giving optimal turnover enhancement, several metallic salts were tested. Among the compounds tested [CuCl, CuBr, CuI, CuOAc, $(CuOTf)_2 \cdot PhMe$, $CuCl_2$, $CuOTf_2$, $Ni(COD)_2$], CuCl proved to be the most effective and the use of four equivalents relative to ruthenium gave the most satisfactory result (Table 1, entries 1−4). Interestingly, the reaction mixture was always heterogeneous, due to the low solubility of copper chloride. Varying the batch of CuCl to see the influence of different particle size showed no effect on the conversion. It should also be pointed out that whereas this metallic salt is known to act as a “phosphane sponge”, the structure of the resulting $CuCl \cdot PR_3$ complex remains ill-defined.[11d,12,13] The

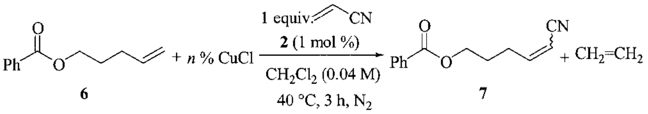
---

[a] Technische Universität Berlin,
Strasse des 17. Juni 135, 10623 Berlin, Germany.
Fax: (internat.) +49-(0)3031423619
E-mail: blechert@chem.tu-berlin.de

DOI: 10.1002/ejoc.200300215

lower conversion observed with larger amounts of copper chloride (Table 1, entries 3 and 4) remainsunclear and further investigations are under way to explain it.

Table 1. Effect of CuCl in cross metathesis



Entry	n	Conversion (%)[a]
1	0	40
2	4	65, (49)[b]
3	8	63
4	16	46
5	4[c]	30
6	4[d]	35

[a] Determined by ^{1}H NMR spectroscopy. [b] Concentration: 0.16 M. [c] 4.0 equiv. acrylonitrile. [d] Reaction done in the presence of decomposed catalyst.

Table 1 also shows that an excess of acrylonitrile (Table 1, entry 5) or higher concentrations (Table 1, entry 2) significantly decreases the conversion of this reaction. The known instability of enoic carbenes[14] led us to rationalise this behaviour as being due to the decomposition of highly reactive, phosphane-free, 14-electron species bearing a cyano-substituted alkylidene.

In our attempt to achieve higher conversions, we observed a nonlinear relationship between conversion and catalyst loading and a dramatic decrease of the effective turnover with high concentration of catalyst (Figure 1): in the presence of copper, 1 mol % of **2** efficiently proceeds to 65% conversion. The use of three times the amount of catalyst does not yield a conversion in excess of 91% (this trend is even more visible in the absence of CuCl).

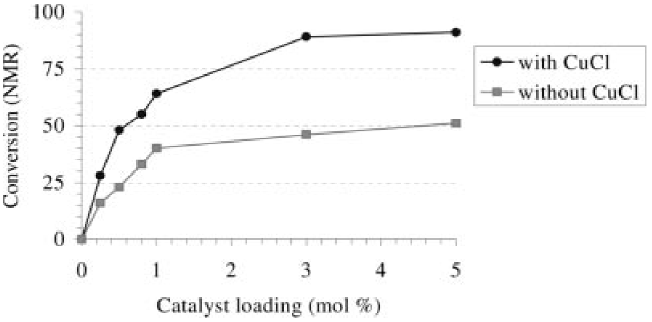


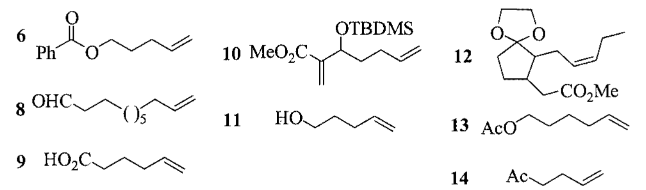
Figure 1. Conversion in acrylonitrile CM catalysed by **2**; conditions: ratio **2**/CuCl:1:4, 1 equiv. acrylonitrile, CH$_2$Cl$_2$ (0.04 M), 40 °C, 3 h, N$_2$; conversions determined by ^{1}H NMR spectroscopy

As already noticed in several previous experiments performed in our laboratories, this behaviour could be explained either by an inhibition due to an interaction between the cross-metathesis product and the catalyst, or an accelerated decomposition with higher loading of catalyst; a combination of both effects is also possible. Since the addition of cross-metathesis product **7** has proved to have no effect on the acrylonitrile CM of **6**, catalyst inhibition was rejected. On the other hand, to appreciate the effect of decomposition of the catalyst on the course of the reaction, the following experiment was carried out. Firstly, diallyl ether ring-closing metathesis catalysed by **2** was performed under an inert atmosphere. Once the reaction reached completion, solvent and cyclised product were removed under a stream of nitrogen. Then, in the same vessel and in the presence of decomposed catalyst, acrylonitrile CM of **6** was done: a significant loss of activity of the catalyst was observed (Table 1, entry 6). It appears that the ruthenium species resulting from the decomposition of the catalyst can themselves decompose the ruthenium carbene complexes. The non-linear behaviour of the curves shown in Figure 1 may therefore be explained by an auto-catalysed decomposition of the catalyst.

Despite this, 91% conversion of the benzoate **6** was obtained when using 5 mol % of **2** and 20 mol % of CuCl, showing the potential of this readily available method with a view to application in synthesis. The efficiency of this method is also apparent when comparing this result with the significantly lower conversion (51%) obtained with the same amount of catalyst without additive. Additionally, the dramatic effective turnover improvement obtained by addition of CuCl is clearly demonstrated when considering the effective TON for 50% conversion. The modest result in the absence of CuCl (TON = 10) is enhanced 10-fold in the presence of phosphane scavenger (TON = 97).

The same conversions obtained after 3 h (Table 1, entry 2) and 16 h (Table 2, entry 1) confirmed the shorter lifetime of the catalyst when a phosphane scavenger is added (vide supra). Table 2 also highlights that the positive effect of copper observed with **6** as it was extended to include other

Table 2. Acrylonitrile CM with various electron rich olefins



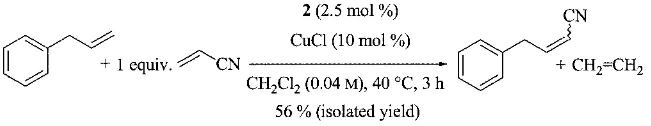
Entry[a]	Substrate	Yield (%) with CuCl[b]	Yield (%) without CuCl[c]
1	**6**	65	45
2	**8**	74	48
3	**9**	34	10
4	**10**	52[c]	42[c]
5	**11**	53	29
6	**12**	57	42
7	**13**	64	52
8	**14**	27	16

[a] conditions: **2** (1.0% mol.), 1.0 equiv. acrylonitrile, CH$_2$Cl$_2$ (0.04 M), 40 °C, overnight, N$_2$. [b] Unless specified, yields were determined by ^{1}H NMR spectroscopy with the use of tetramethylbenzene as external standard. [c] *trans*-stilbene used as external standard.

substrates (Table 2, entry 2−8). It is important to emphasise that these results were obtained with only 1 mol % of **2**: the use of larger amounts of catalyst results in higher yields (91% conversion of **6** with 5 mol % of **2** in the presence of copper).

Interestingly, the *E*/*Z* ratio of cross-metathesis product (not mentioned in the table) remains unchanged upon addition of CuCl. This indicates that the environment of the metallic centre when the cross-metathesis occurs is the same, whatever the role of the copper salt during the reaction.

The isolated yield of cross-metathesis product obtained from allybenzene (see below), clearly identifies this protocol as an alternative method to the others previously used in acrylonitrile CM to date.



Despite these interesting results, the low to modest conversions observed in acrylonitrile CM without copper remain unexplained. We can suggest a possible reaction between the activated olefin and the nucleophilic phosphane (possibly promoted by ruthenium itself, thus playing the role of a Lewis acid), with the resulting phosphonium ylide causing the decomposition of the ruthenium carbene species. However, it has been shown that even in the absence of the additive, unmodified precatalyst **2** is able to cross metathesise acrylonitrile, whereas this substrate was initially considered as unreactive with phosphane-ligated NHC Ru-carbene complexes.

Conclusion

In the course of our studies, we have shown that unmodified phosphane-ligated precatalyst **2** could efficiently promote acrylonitrile CM. We have also shown the effect of copper(I) chloride as a phosphane scavenger and described for the first time a significant turnover enhancement in selective cross-metathesis upon additon of a metallic salt. This protocol appears, due to its simplicity, to be an attractive and less expensive alternative to the other methods requiring modified precatalysts **3** or **5**. Further investigations are in progress in our laboratories to determine the nature of the catalytic species involved during the reaction.

Experimental Section

Copper(I)chloride (10 mg, 0.1 mmol) was added to a dried, two-necked flask equipped with a reflux condenser and containing an equimolar solution of allylbenzene (120 mg, 1.01 mmol) and acrylonitrile (54 mg, 1.01 mmol) in CH_2Cl_2 (22 mL). Precatalyst **2** (21.5 mg, 0.025 mmol) was then added and, after passing a stream of N_2 through the flask for a short time, the resulting mixture was stirred at 40 °C for 3 h. The reaction was quenched by addition of ethyl vinyl ether and the solvent removed under reduced pressure. The crude mixture was purified by column chromatography on silica (*n*-pentane/Et_2O = 9:1) yielding the expected product (82 mg, 56%) as an oil.

Acknowledgments

This work was supported by the Fonds der Chemischen Industrie.

---

[1] [1a] S. J. Connon, S. Blechert, *Angew. Chem.* **2003**, *115*, 1944−1968; *Angew. Chem. Int. Ed.* **2003**, *42*, 1900−1923. [1b] S. E. Gibson, S. P. Keen, *Top. Organomet. Chem.* **1998**, 155−181.

[2] For examples of ene-ene CM catalysed by **1** see: [2a] C. Pietraszuk, H. Fisher, M. Kujawa, B. Marciniec, *Tetrahedron Lett.* **2001**, *42*, 1175−1178. [2b] M. Ahmed, T. Arnauld, A. G. M. Barret, D. C. Braddock, K. Flack, P. A. Procopiou, *Org. Lett.* **2000**, *2*, 551−553. [2c] H. E. Blackwell, D. J. O'Leary, A. K. Chatterjee, R. A. Washenfelder, D. A. Bussmann, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 58−71. [2d] H. Seshadri, C. J. Lovely, *Org. Lett.* **2000**, *2*, 327−330. [2e] Y. J. Hu, R. Roy, *Tetrahedron Lett.* **1999**, *40*, 3305−3308. [2f] S. C. G. Biagini, S. E. Gibson, S. P. Keen, *J. Chem. Soc., Perkin Trans. 1* **1998**, 2485−2499. For examples of ene-yne CM catalysed by **1** see: [2g] A. Kinoshita, N. Sakakibara, M. Mori, *Tetrahedron* **1999**, *55*, 8155−8167. [2h] R. Stragies, M. Schuster, S. Blechert, *Chem. Commun.* **1999**, 237−238. [2i] S. C. Schürer, S. Blechert, *Synlett* **1999**, 1879−1882.

[3] [3a] A. Fürstner, O. R. Thiel, C. W. Lehmann, *Organometallics* **2002**, *21*, 331−335. [3b] L. Jafarpour, A. C. Hillier, S. P. Nolan, *Organometallics* **2002**, *21*, 442−444. [3c] M. Scholl, T. M. Trnka, J. P. Morgan, R. H. Grubbs, *Tetrahedron Lett.* **1999**, *40*, 2247−2250.

[4] [4a] J. P. Morgan, C. Morrill, R. H. Grubbs, *Org. Lett.* **2002**, *4*, 67−70. [4b] A. K. Chatterjee, D. P. Sanders, R. H. Grubbs, *Org. Lett.* **2002**, *4*, 1939−1942. [4c] T. L. Choi, A. K. Chatterjee, R. H. Grubbs, *Angew. Chem.* **2001**, *113*, 1317−1319; *Angew. Chem. Int. Ed.* **2001**, *40*, 1277−1279. [4d] M. Lera, C. J. Hayes, *Org. Lett.* **2001**, *3*, 2765−2768. [4e] R. Stragies, U. Voigtmann, S. Blechert, *Tetrahedron Lett.* **2000**, *41*, 5465−5468. [4f] A. K. Chatterjee, J. P. Morgan, M. Scholl, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 3783−3784. [4g] J. P. Morgan, R. H. Grubbs, *Org. Lett.* **2000**, *2*, 3153−3155. [4h] A. K. Chatterjee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 1751−1753.

[5] [5a] D. L. Wright, L. C. Usher, M. Esterella-Jimenez, *Org. Lett.* **2001**, *3*, 4275−4277. [5b] S. Gessler, S. Randl, S. Blechert, *Tetrahedron Lett.* **2000**, *41*, 9973−9976. Except for: [5c] O. M. Blanco, L. Castedo, *Synlett* **1999**, 557−558.

[6] [6a] S. Randl, N. Buschmann, S. J. Connon, S. Blechert, *Synlett* **2001**, 1547−1550. [6b] S. Randl, S. Gessler, H. Wakamatsu, S. Blechert, *Synlett* **2001**, 430−432.

[7] S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179.

[8] [8a] O. Brümmer, A. Rückert, S. Blechert, *Chem. Eur. J.* **1997**, *3*, 441−446. [8b] W. E. Crowe, D. R. Goldberg, *J. Am. Chem. Soc.* **1995**, *117*, 5162−5163.

[9] T. M. Cameron, A. S. Gamble, K. A. Abboud, J. M. Boncella, *Chem. Commun.* **2002**, 1148−1149.

[10] J. A. Love, J. P. Morgan, T. M. Trnka, R. H. Grubbs, *Angew. Chem.* **2002**, *114*, 4207−4209; *Angew. Chem. Int. Ed.* **2002**, *41*, 4035−4037.

[11] [11a] J. Huang, H. J. Schanz, E. D. Stevens, S. P. Nolan, *Organometallics* **1999**, *18*, 5375−5380. [11b] D. M. Lynn, B. Mohr,

R. H. Grubbs, *J. Am. Chem. Soc.* **1998**, *120*, 1627−1628. [11c] M. S. Sanford, L. M. Henling, R. H. Grubbs, *Organometallics* **1998**, *17*, 5384−5389. [11d] E. L. Dias, S. T. Nguyen, R. H Grubbs, *J. Am. Chem. Soc.* **1997**, *119*, 3887−3897.

[12] M. Ulman, R. H. Grubbs, *J. Org. Chem.* **1999**, *64*, 7202−7207.

[13] E. L. Dias, R. H. Grubbs, *Organometallics* **1998**, *17*, 2758−2767.

[14] M. Ulman, T. R. Belderrain, R. H. Grubbs, *Tetrahedron Lett.* **2000**, *41*, 4689−4693.

[15] For studies concerning the thermal stability of NHC-coordinated ruthenium complexes see ref 11a.

Received April 4, 2003