DOI: 10.1002/ejic.201200248

Microwave-Assisted Synthesis of (N-Heterocyclic carbene)MCl Complexes of Group 11 Metals

Brant Landers[a] **and Oscar Navarro***[a]

Keywords: Microwave heating / N-Heterocyclic carbenes / Copper / Silver / Gold

The use of microwave heating for the synthesis of (N-heterocyclic carbene)-bearing complexes of Cu, Ag and Au allows for a drastic reduction of the reaction times required by conventional heating, while affording comparable or better yields of the desired complexes.

Introduction

The vast number of research articles and reviews on N-heterocyclic carbenes (NHCs) in the literature is a clear sign of the impact and ubiquity of these σ-donor ligands in nowadays organometallic chemistry.[1–3] Since their first use as ligands in a metal-catalysed process by Herrmann and co-workers in 1995,[4] the number of metals utilized and the applications developed has constantly increased.

In the last years, the interest in NHC-bearing complexes of Group 11 metal complexes has grown considerably. Most applications of silver(I) complexes focused in their ability to transmetalate the NHC to a less "friendly" metal that would not accept the NHC directly (or would do it in very low yields),[5] although some other uses of (NHC)Ag^I complexes have also been reported.[1,6] On the other hand and since their appearance, (NHC)Cu^I and lately (NHC)Au^I complexes have increasingly found interesting applications in catalytic processes.[1,3,7] While straightforward, the synthesis of these families of complexes requires in most cases long reaction times at high reaction temperatures and therefore a considerable energy cost. Among the 12 principles of green chemistry,[8] "energy efficiency by design" is considered a top priority.[9] In addition, quick access to libraries of catalysts is crucial when optimizing reactions, both in academia and industry, and fast, robust synthetic protocols to obtain them are always desirable. In that regard, our group has reported that the use of microwave heating for the direct synthesis (from the imidazolium or imidazolidinium salt and a metal salt) of (NHC)Pd^{II}[10] complexes allows for a drastic reduction of the reaction times and therefore a considerable reduction of energy employed.[11] Herein, we wish to report the application of this technology to the synthesis of (NHC)MCl (M = Cu, Ag, Au) complexes.

Results and Discussion

Cazin and co-workers recently reported on the use of toluene or water as solvents the for the direct synthesis of (NHC)CuCl and (NHC)AgCl complexes.[12] In their communication the authors synthesized, among others, (IPr)-, (SIPr)-, (IMes)- and (SIMes)MCl (Figure 1) in very good yields at refluxing temperatures after a reaction time of 24 h. In our laboratories, attempts to speed up the synthesis in water by applying microwave heating did only reduce the reaction times to about 4–5 h, in the best cases.

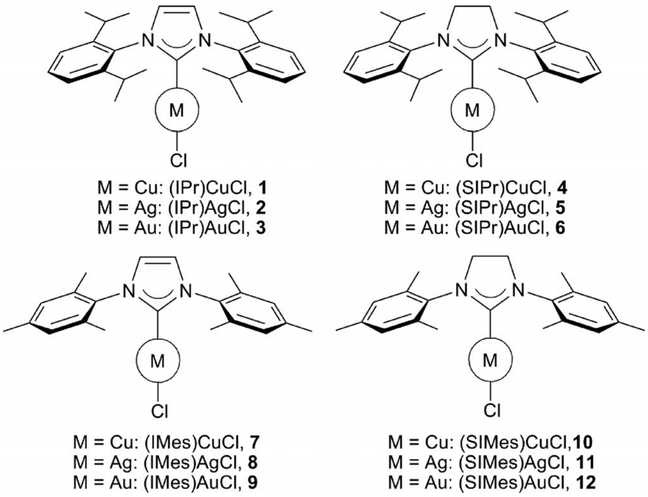


Figure 1. (NHC)MCl complexes (M = Cu, Ag, Au).

Switching the solvent to THF, on the other hand, allowed for the synthesis of the complexes in comparable yields after 0.5 h (48 times faster than the preparations in water or toluene) at 110 °C (Table 1).[13] For Cu, this protocol afforded higher yields for (IPr)- and (SIPr)-bearing complexes (Table 1, Entries 1, 2), and lower ones for (IMes)- and (SIMes)-bearing complexes (Table 1, Entries 3, 4). The trend was different for Ag: saturated ligands afforded higher yields (Table 1, Entries 6, 8), while lower

---

[a] Department of Chemistry, University of Hawaii at Manoa,
2545 McCarthy Mall, Honolulu, HI 96825, USA
Fax: +1-808-956-5908
E-mail: oscarnf@hawaii.edu

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejic.201200248.

yields were obtained with the unsaturated counterparts (Table 1, Entries 5, 7). For convenience, these reactions were set up in a glovebox and using dry THF as solvent, but we also carried out same-scale reactions without an inert gas and using technical-grade THF as solvent to prepare complexes **1** and **2**, affording 88% and 82%, respectively, of the desired products. In addition, a larger-scale reaction for the synthesis of **1** was carried out without an inert gas, affording 93% yield after 1 h.[14]

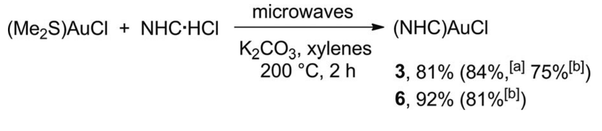
Table 1. Microwave-assisted synthesis of (NHC)CuCl and (NHC)AgCl complexes.

$$M_2O + NHC\cdot HCl \xrightarrow[\text{THF, 110 °C, 0.5 h}]{\text{microwaves}} (NHC)MCl$$

Entry	Complex	Yield[a,b]	Entry	Complex	Yield[a,b]
1	**1**	98% (94%)	5	**2**	85% (87%)
2	**4**	95% (72%)	6	**5**	92% (74%)
3	**7**	84% (98%)	7	**8**	83% (92%)[c]
4	**10**	73% (99%)	8	**11**	90% (80%)

[a] M_2O (0.65 mmol), NHC·HCl (1 mmol), THF (2 mL). [b] Yields in parentheses for conventional heating and water as solvent, 24 h.[12] [c] Reaction carried out in toluene.[12]

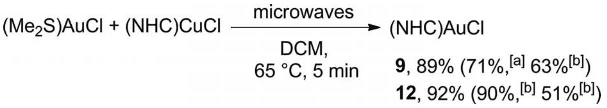
After these experiments, we directed our attention to the synthesis of (NHC)AuCl complexes. To the best of our knowledge, the direct synthesis of these complexes from Au^I salts has not been reported.[15] Reported protocols involve the combination of free carbene and an Au source, or the transmetallation from an $(NHC)Ag^I$ complex.[16] $(NHC)Cu^I$ complexes can also be used as transmetallating agents for the synthesis of some (NHC)Au complexes under very mild conditions and in very good yields.[17] Our interest focused in circumventing the need to synthesize and purify an intermediate organometallic reagent. After an optimization process, we found that the direct synthesis of (IPr)- and (SIPr)AuCl (**3** and **6**) could be achieved by using microwave heating in technical-grade xylenes in the presence of K_2CO_3 (Scheme 1). High yields were obtained, particularly keeping in mind that the synthesis of the (NHC)Cu or -Ag intermediates, which are not quantitative, was not necessary. Unfortunately, this methodology was only successful with those complexes, and mixtures of products were obtained when we attempted the synthesis of (IMes)- and (SIMes)AuCl (**9** and **12**). For these complexes, we applied a transmetallation route starting from the corresponding Cu counterparts, being able to synthesize (IMes)AuCl and (SIMes)AuCl in very good yields under microwave heating after 5 min (Scheme 2).



$$(Me_2S)AuCl + NHC\cdot HCl \xrightarrow[\text{K}_2\text{CO}_3\text{, xylenes, 200 °C, 2 h}]{\text{microwaves}} (NHC)AuCl$$

3, 81% (84%,[a] 75%[b])
6, 92% (81%[b])

Scheme 1. Microwave-assisted synthesis of (IPr)- and (SIPr)AuCl complexes. Reaction conditions: $(Me_2S)AuCl$ (0.5 mmol), NHC·HCl (0.5 mmol), xylenes (1 mL). [a] Transmetallation from (NHC)CuCl, 40 °C, DCM, 2 h.[17] [b] Reaction with free carbene, r.t., THF, 12 h.[16]



$$(Me_2S)AuCl + (NHC)CuCl \xrightarrow[\text{DCM, 65 °C, 5 min}]{\text{microwaves}} (NHC)AuCl$$

9, 89% (71%,[a] 63%[b])
12, 92% (90%,[b] 51%[b])

Scheme 2. Microwave-assisted synthesis of (IMes)- and (SIMes)AuCl complexes. Reaction conditions: $(Me_2S)AuCl$ (0.25 mmol), (NHC)CuCl (0.25 mmol), DCM (1 mL). [a] Transmetallation from (NHC)CuCl, 40 °C, DCM, 1 h.[17] [b] Transmetallation from (NHC)AgCl, r.t., DCM, 7 h.[16]

Conclusions

We have developed a microwave-assisted protocol for the synthesis of a series of (NHC)CuCl, (NHC)AgCl and (NHC)AuCl complexes. Most of these complexes could be prepared directly from the corresponding imidazolium or imidazolidinium salts and a metal salt in very short reaction times (12–48 times faster than protocols involving conventional heat)[13] and obtaining comparable or higher yields than those reported in the literature.

Experimental Section

General Procedure for the Synthesis of (NHC)CuCl and (NHC)AgCl Complexes: A 10 mL microwave vial equipped with magnetic stir bar was loaded with NHC·HCl (1.0 mmol), metal oxide (0.65 mmol) and of solvent (2 mL). The reaction mixture was heated and stirred in the microwave reactor at 110 °C for 30 min. After the reaction was complete, the mixture was cooled to room temperature. The crude mixture was then filtered through Celite (DCM). The filtrate was concentrated and the complex precipitated with hexanes. Filtering left the desired product as a white solid. The solid was vacuum-dried affording the desired (NHC)MCl complexes as a white powder.

Supporting Information (see footnote on the first page of this article): Experimental protocols and complex characterization.

Acknowledgments

The authors acknowledge the National Science Foundation (CHE 0924324) for support.

---

[1] a) C. S. J. Cazin (Ed.), *Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis*, Springer, London, **2010**; b) F. Glorius (Ed.), *N-Heterocyclic Carbenes in Transition Metal Catalysis*, Springer, Berlin, **2007**.

[2] Some recent reviews: a) M. J. Ingleson, R. A. Layfield, *Chem. Commun.* **2012**, *48*, 3579–3589; b) M. S. Viciu, O. Navarro, *Annu. Rep. Prog. Chem., Sect. B: Org. Chem.* **2011**, *107*, 226–243; c) T. Dröge, F. Glorius, *Angew. Chem. Int. Ed.* **2010**, *49*, 6940–6952.

[3] S. P. Nolan, *Acc. Chem. Res.* **2011**, *44*, 91–100; A. Correa, S. P. Nolan, L. Cavallo, *Top. Curr. Chem.* **2011**, *302*, 131–155.

[4] W. A. Herrmann, M. Elison, J. Fischer, C. Köcher, G. R. J. Artus, *Angew. Chem.* **1995**, *107*, 2602; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2371–2374.

[5] a) T. Ramnial, C. D. Abernethy, M. D. Spicer, I. D. McKenzie, I. D. Gay, J. A. C. Clyburne, *Inorg. Chem.* **2003**, *42*, 1391–1393; b) P. de Frémont, N. M. Scott, E. D. Stevens, T. Ramnial, O. C. Lightbody, C. L. B. Macdonald, J. A. C. Clyburne, C. D. Abernethy, S. P. Nolan, *Organometallics* **2005**, *24*, 6301–6309.

[6] a) M.-T. Chen, B. Landers, O. Navarro, *Org. Biomol. Chem.* **2012**, *10*, 2206–2208; b) Y. Li, X. Chen, Y. Song, L. Fang, G. Zou, *Dalton Trans.* **2011**, *40*, 2046–2052.

[7] Silvia Díez-González (Ed.), *N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools*, RSC Catalysis Series, RSC Publishing, Cambridge, **2011**.

[8] R. A. Sheldon, I. Arends, U. Hanefield, *Green Chemistry and Catalysis*, Wiley-VCH, Weinheim, **2008**.

[9] D. Dallinger, C. O. Kappe, *Chem. Rev.* **2007**, *107*, 2563–2591.

[10] O. H. Winkelmann, O. Navarro, *Adv. Synth. Catal.* **2010**, *352*, 212–214.

[11] On a laboratory scale and for most chemical transformations, energy savings up to 85-fold can be expected by using microwaves as an energy source: M. J. Gronnow, R. J. White, J. H. Clark, D. J. Macquarrie, *Org. Process Res. Dev.* **2005**, *9*, 516–518.

[12] C. A. Citadelle, E. L. Nouy, F. Bisaro, A. M. Z. Slawing, C. S. J. Cazin, *Dalton Trans.* **2010**, *39*, 4489–4491.

[13] The choice of solvent also had an effect on the reaction: with conventional heating, complex **1** could be prepared in 99% yield in refluxing THF after 6 h (51% yield after 3 h).

[14] See Supporting Information for details.

[15] Just recently, a direct synthesis from $NaAuCl_4 \cdot H_2O$ in 3-Cl-pyridine, at 80 °C for 24 h was reported: S. Zhu, R. Liang, L. Chen, C. Wang, Y. Ren, H. Jiang, *Tetrahedron Lett.* **2012**, *53*, 815–818.

[16] P. de Frémont, N. M. Scott, E. D. Stevens, S. P. Nolan, *Organometallics* **2005**, *24*, 2411–2418.

[17] M. R. L. Furst, C. S. J. Cazin, *Chem. Commun.* **2010**, *46*, 6924–6925.

Received: March 10, 2012