Imidazol(in)ium-2-Carboxylates as Efficient Precursors to N-Heterocyclic Carbene Complexes of Copper and Silver

Tomasz K. Olszewski and Dagmara E. Jaskólska

Apeiron Synthesis, Klecińska 125, 54-413, Wroclaw, Poland

Received 23 May 2012; revised 19 August 2012

ABSTRACT: Copper and silver N-heterocyclic carbene (NHC) complexes were prepared through a simple, base-free protocol involving the decomposition of corresponding imidazol(in)ium-2-carboxylates under thermolytic conditions and a subsequent reaction of the in situ generated carbenes with copper(I) or silver(I) chloride, respectively. The desired NHC metal complexes were isolated with good yields after simple crystallization. © 2012 Wiley Periodicals, Inc. Heteroatom Chem 23:605–609, 2012; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21056

INTRODUCTION

N-Heterocyclic carbene (NHC) complexes are established as an important class of ligands for homogeneous catalysis, and their catalytic applications are frequently reported [1]. The electronic and steric modularity associated with the resulting complexes has made the NHCs excellent candidates when designing new metal complexes for catalysis. In that respect, the syntheses of catalysts based on affordable metals are eagerly sought thus, making the NHC copper species of type [CuCl(NHC)] of significant importance. These complexes were already found to be very effective in several catalytic transformations such as hydrosilylation of ketones [2], reduction of carbonyl compounds [3], hydroamination of alkenes [4], Huisgen [3+2] cycloaddition [5], aziridination [6], cyclopropanation [7], methylenation [8], and copper-catalyzed enantioselective transformations with high levels of selectivity [9]. In addition to their many successful applications in catalysis, NHC-copper complexes were also reported to exhibit biological activity as antitumor agents [10].

The NHC copper species of type [CuCl(NHC)] are not the only NHC complexes of interest in group 11 of elements. Their silver analogues of type [AgCl(NHC)] have also attracted significant interest and nowadays are commonly used as NHC transfer agents in transition metal chemistry [11] and additionally have displayed interesting antimicrobial activity [12]. In light of the aforementioned interesting catalytic and biological applications of [CuCl(NHC)] and [AgCl(NHC)] complexes, facile synthetic routes leading to high yields of those compounds are highly desirable. In general, copper-NHC complexes are prepared using either basemediated deprotonations [13], or via transmetalation from the corresponding silver-NHC complexes [14], or more recently by a reaction of copper(I) oxide with imidazolium salts [15]. In turn, the synthesis of silver-NHC complexes usually involves the reaction of imidazolium salts with silver(I) oxide [15b,16].

To the best of our knowledge, the application of imidazol(in)ium-2-carboxylates as intermediates for the synthesis of [CuCl(NHC)] and [AgCl(NHC)] complexes is unknown [17]. For the application of NHC-CO₂ adducts as substrates in the synthesis of NHC complexes with Rh, Ir, Ru, Pd, and Ti, see a comprehensive review in [18]. Herein, we report on

Correspondence to: T. K. Olszewski; e-mail: tomasz.olszewski@ apeiron-synthesis.com.

^{© 2012} Wiley Periodicals, Inc.



SCHEME 1 Proposed synthesis of [CuCl(NHC)] and [AgCl(NHC)] with the use of NHC-CO₂ zwitterions.

efficient synthesis of [CuCl(NHC)] and [AgCl(NHC)] complexes with the use of those useful intermediates. The presented simple and base-free protocol involves decomposition of the imidazol(in)ium-2-carboxylates under thermolytic conditions and a reaction of the in situ generated carbenes with copper(I) or silver(I) chloride, respectively.

RESULTS AND DISCUSSION

NHC based on the imidazole ring upon a reaction with carbon dioxide forms inner salts, which can be stored and handled with no particular precautions [19]. Such NHC-CO₂ zwitterions readily lose their CO_2 moiety upon heating or dissolution; hence, they act as convenient surrogates to air- and moisturesensitive free carbenes for organometallic synthesis and organocatalytic applications [18]. We took advantage of the liability of the NHC-CO₂ zwitterions to generate active species in the preparation of [CuCl(NHC)] and [AgCl(NHC)] complexes (Scheme 1). Four representative and most com-



SCHEME 2 Imidazol(in)ium-2-carboxylates used in this study.

monly used NHCs, i.e., SIPr, IPr, SIMes, and IMes, were used as substrates in the present study, and their corresponding CO_2 adducts were synthesized (Scheme 2).

Having in hand a palette of NHC-CO₂ betaines, we examined their application as substrates for the synthesis of [CuCl(NHC)] complexes. Initially, the preparation of the IPrCuCl complex using IPrCO₂ betaine, as a model substrate, was investigated (Table 1).

Knowing that the reactivity of the free carbene with copper(I) chloride can be strongly modulated by the reaction medium, we carried out the preliminary experiments in different solvents. Reaction run with 1.2 equiv of CuCl in CHCl₃ at 23°C resulted in formation of desired IPrCuCl product, albeit





^aExperiments were carried out using 1.1 mmol (500 mg) of IPrCO₂ and 1.2 equiv (1.32 mmol, 130 mg) of CuCl in 15 mL of appropriate solvent for 12 h. Reactions were monitored by TLC. Products could be easily distinguished as the [(IPr)₂Cu⁺]Cl⁻ is much more polar than the IPrCuCl. ^bEntry 2 mixture of IPrCuCl and [(IPr)₂Cu]⁺Cl⁻ in a ratio of 50:50; entry 3 mixture of IPrCuCl and [(IPr)₂Cu]⁺Cl⁻ in a ratio of 30:70. ^cYield given for isolated product after recrystallization from the CH₂Cl₂/Et₂O mixture.

		$R^{-N} \stackrel{\text{MCI}}{\underset{0}{\oplus} 0} N_{-R} \xrightarrow{\text{MCI}}_{\text{toluene}}$ $110 ^{\circ}C$ $12 h$	R [∽] N → N M CI	
Entry	Substrate	Metal Source (MCI)	Product	Yield (%) ^b
1	IPrCO ₂	CuCl	IPrCuCl	90
2	IMesCO ₂	CuCl	IMesCuCl	88
3	SIPrCO ₂	CuCl	SIPrCuCl	85
4	SIMesCO ₂	CuCl	SIMesCuCl	80
5	IPrCO ₂	AgCl	IPrAgCI	95
6	IMesCO ₂	AgCl	IMesAgCl	92
7	SIPrCO ₂	AgCl	SIPrAgCl	82
8	SIMesCO ₂	AğCl	SIMesĂgCl	88

TABLE 2 Synthesis of [CuCl(NHC)] and [AgCl(NHC)] Complexes from Zwitterionic Carboxylates--Substrate Scope^a

^aExperiments were carried out using 1.1 mmol of appropriate imidazol(in)ium-2-carboxylate and 1.2 equiv of CuCl or AgCl in 15 mL of toluene at 110°C for 12 h.

^bYield given for isolated product after recrystallization from the CH₂Cl₂/Et₂O mixture.

accompanied by its bis-complex $[(IPr)_2Cu^+]Cl^-$ and a starting material IPrCO₂ (Table 1, entry 1). In turn, heating of the IPrCO₂ with 1.2 equiv of CuCl in CHCl₃ at 60°C resulted in total consumption of IPrCO₂ and yielded a mixture of both $[(IPr)_2Cu^+]Cl^$ and IPrCuCl complexes. Experiment run in CH₃CN again led to formation of a mixture of $[(IPr)_2Cu^+]Cl^$ and IPrCuCl; albeit, this time the latter was in the minority (Table 1, entry 3). These results are in agreement with the literature reports and show that increasing the polarity of the solvent (dielectric constant for $CHCl_3 = 4.2$ and for $CH_3CN = 37.5$ [20] leads to an increase in the amount of the bis-NHC carbene [21]. Finally, and to our satisfaction, a reaction performed in toluene (dielectric constant = 2.3) [20] at 110°C furnished almost exclusively the desired IPrCuCl complex with 90% yield (traces of the [(IPr)₂Cu⁺]Cl⁻ were removed by recrystallization of the crude from a mixture of CH_2Cl_2/Et_2O) (Table 1, entry 4).

Having the optimized reaction conditions in hand, a selected spectrum of NHC-CO₂ zwitterions was examined to test the scope of the presented protocol (Table 2).

Different saturated and unsaturated imidazol (in)ium-2-carboxylates were tolerated under the presented, optimized reaction conditions. Pure copper complexes of type [CuCl(NHC)] were obtained in good yields and high purity after simple recrystallization from the CH_2Cl_2/Et_2O mixture (Table 2 entries 1–4). It has to be mentioned that the advantage of the applied decarboxylation method is the absence of a strong base, usually needed for the generation

of carbene. It is known that the presence of potassium *tert*-butoxide in the synthesis of copper NHC complexes is a source of undesired side products of type Cu(NHC)(Ot-Bu) [5].

Subsequently, encouraged by the optimistic result obtained for the synthesis of [CuCl(NHC)] complexes, we decided to further examine the synthetic utility of imidazol(in)ium-2-carboxylates as substrates in the preparation of silver complexes of type [AgCl(NHC)]. For that purpose, we applied the above-mentioned optimized copper protocol using AgCl, instead of CuCl, as the silver source (Table 2). The presented protocol worked well for different saturated and unsaturated imidazol (in)ium-2-carboxylates, and to our satisfaction pure silver complexes of type [AgCl(NHC)] were easily obtained and in good yields as well as with high purity after simple recrystallization from the CH_2Cl_2/Et_2O mixture (Table 2 entries 5–8).

conclusion, we have In shown that imidazol(in)ium-2-carboxylates, readily available, isolable, air- and moisture-stable reagents, offer an efficient route to NHC complexes of copper and silver. By avoiding the strong base needed in the free carbene route, our method minimizes possible side reactions. The presented chemistry provides an interesting and alternative synthetic pathway to NHC copper and silver complexes of type [CuCl(NHC)] and [AgCl(NHC)], respectively, that have already found countless applications in organocatalysis and organometallic chemistry and additionally posses very interesting biological activity.

EXPERIMENTAL

All imidazol(in)ium-2-carboxylates used in this study were prepared according to the procedure described earlier in the literature from appropriate commercially available imidazol(in)ium chlorides, potassium *tert*-butoxide (1 M solution in toluene), and CO₂ using toluene as a reaction solvent [19a]. Their structures were unambiguously confirmed by standard spectroscopic techniques, and the obtained data were in agreement with the literature reports: IPrCO₂ [19b], IMesCO₂ [19b], SIPrCO₂ [22], and SIMesCO₂ [22].

General Protocol for the Preparation of [*CuCl(NHC)*] and [AgCl(NHC)] Complexes from Imidazol(in)ium-2-carboxylates

A 50-mL two-necked round-bottom flask equipped with a magnetic stirring bar, a condenser, and a three-way stopcock was charged with appropriate imidazol(in)ium-2-carboxylate (1.1 mmol) and CuCl or AgCl (1.32 mmol). The flask was purged with argon prior to addition of degassed, dry toluene (15 mL), and the resulting reaction mixture was stirred at 110°C for 12 h. Shorter reaction times resulted in the formation of the desired NHC metal complexes, albeit in lower yields. Experiments with AgCl were carried out in the absence of light. After that time, the reaction mixture was cooled down to room temperature and filtered through a filter paper. The filtrate was diluted with CH_2Cl_2 (25 mL) and washed with H_2O (2 × 15 mL). The organic phase was dried over anhydrous MgSO₄ and evaporated to dryness under vacuum. The resulting crude was dissolved in a little amount of CH_2Cl_2 , and Et_2O was added to precipitate the product. The precipitated [CuCl(NHC)] and [AgCl(NHC)] complexes as white solids were collected by filtration and dried on vacuum. The NMR spectra obtained for the isolated complexes were consistent with the literature reports: IPrCuCl [3b], IMesCuCl [15b], SIPrCuCl [23], SIMesCuCl [2b], and IPrAgCl, IMesAgCl, SIPrAgCl, and SIMesAgCl [15b],[21].

ACKNOWLEDGMENT

Apeiron Synthesis acknowledges the Operation Programme Innovative Economy (PO IG) for financial support within the PO IG 1.4-4.1. Programme.

REFERENCES

[1] (a) Benhamou, L.; Chardon, E.; Lavigne, G.; Bellemin-Laponnaz, S.; Cesar, V. Chem Rev 2011, 111, 2705; (b) Cabeza, J. A.; Garcia-Alvarez, P. Chem Soc Rev 2011, 40, 5389; (c) John, A.; Ghosh, P. Dalton Trans 2010, 39, 7183; (d) Nair, V.; Vellalath, S.; Babu, B. P. Chem Soc Rev 2008, 37, 2691; (e) Peris, E.; Crabtree, R. H. Coord Chem Rev 2004, 248, 2239; (f) Herrmann, W. A. Angew Chem, Int Ed 2002, 41, 1290; (g) Viciu, M. S.; Germaneau, R. F.; Nolan, S. P. Org Lett 2002, 4, 4053; (h) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. Chem Rev 2000, 100, 39; (i) Herrmann, W. A.; Kocher, C. Angew Chem, Int Ed 1997, 36, 2163.

- [2] (a) Diez-Gonzalez, S.; Stevens, E. D.; Scott, N. M.; Petersen, J. L.; Nolan, S. P. Chem Eur J 2008, 14, 158; (b) Díez-González, S.; Scott, N. M.; Nolan, S. P. Organometallics 2006, 25, 2355; (c) Diez-Gonzalez, S.; Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. J Org Chem 2005, 70, 4784.
- [3] (a) Diez-Gonzalez, S.; Nolan, S. P. Acc Chem Res 2008, 41, 349; (b) Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. Organometallics 2004, 23, 1157.
- [4] (a) Munro-Leighton, C.; Delp, S. A.; Blue, E. D; Gunnoe, T. B. Organometallics 2007, 26, 1483;
 (b) Delp, S. A.; Munro-Leighton, C.; Goj, L. A.; Ramirez, M. A.; Gunnoe, T. B.; Petersen, J. L.; Boyle, P. D. Inorg Chem 2007, 46, 2365; (c) Munro-Leighton, C.; Blue, E. D.; Gunnoe, T. B. J Am Chem Soc 2006, 128, 1446.
- [5] Diez-Gonzalez, S.; Correa, A.; Cavallo, L.; Nolan, S. P. Chem Eur J 2006, 12, 7558.
- [6] (a) Liu, R.; Herron, S. R.; Fleming, S. A. J Org Chem 2007, 72, 5587; (b) Trost, B. M.; Dong, G. J Am Chem Soc 2006, 128, 6054.
- [7] Fructos, M. R.; Belderrain, T. R.; Nicasio, M. C.; Nolan, S. P.; Kaur, H.; Diaz-Requejo, M. M.; Perez, P. J. J Am Chem Soc 2004, 126, 10846.
- [8] Lebel, H.; Davi, M.; Diez-Gonzalez, S.; Nolan, S. P. J Org Chem 2007, 72, 144.
- [9] (a) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. Angew. Chem. Int. Ed. 2007, 46, 1097; (b) Lee, K. S.; Brown, M. K.; Hird, A. W.; Hoveyda, A. H. J Am Chem Soc 2006, 128, 7182; (c) Martin, D.; Kehrli, S.; d'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A. J Am Chem Soc 2006, 128, 8416; (d) Winn, C. L.; Guillen, F.; Pytkowicz, J.; Roland, S.; Mangeney, P.; Alexakis, A. J Organomet Chem 2005, 690, 5672; (e) Van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. J Am Chem Soc 2005, 127, 6877; (f) Tominaga, S.; Oi, Y.; Kato, T.; An, D. K.; Okamoto, S. Tetrahedron Lett 2004, 45, 5585.
- [10] (a) Teyssot, M. L.; Jarousse, A. S.; Chevry, A.; De Haze, A.; Beaudoin, C.; Manin, M.; Nolan, S. P.; Diez-Gonzalez, S.; Morel, L.; Gautier, A. Chem Eur J 2009, 15, 314; (b) Teyssot, M. L.; Jarousse, A. S.; Manin, M.; Chevry, A.; Roche, S.; Norre, F.; Beaudoin, C.; Morel, L.; Boyer, D.; Mahiou, R.; Gautier, A. Dalton Trans 2009, 6894.
- [11] For a recent example of silver–NHC complex as transfer agent on Rh, Pd, and Au, see: Boronat, M.; Corma, A.; Gonzalez-Arellano, C.; Iglesias, M.; Sanchez, F. Organometallics 2010, 29, 134.
- [12] Hindi, K. M.; Panzner, M. J.; Tessier, C. A.; Cannon, C. L.; Youngs, W. J. Chem Rev 2009, 109, 3859.
- [13] For application of Cu(I), see: (a) Michon, C.; Ellern,
 A.; Angelici, R. J. Inorg. Chim. Acta 2006, 359, 4549;
 (b) Schneider, N.; Cesar, V.; Bellemin-Laponnaz, S.;

Gade, L. H. J Organomet Chem 2005, 690, 5556; (c) Mankad, N. P.; Gray, T. G.; Laitar, D. S.; Sadighi, J. P. Organometallics 2004, 23, 1191. For application of Cu(II), see; (d) Yun, J.; Kim, D.; Yun, H. Chem Commun 2005, 5181; (e) Hu, X.; Castro-Rodriguez, I.; Meyer, K. J Am Chem Soc 2003, 125, 12237.

- [14] (a) Winkelmann, O.; Nather, C.; Luning, U. J Organomet Chem 2008, 693, 923; (b) Wan, X.-J.; Xu, F.-B.; Li, Q.-S.; Song, H.-B.; Zhang, Z.-Z. Inorg Chem Commun 2005, 8, 1053; (c) Larsen, A. O.; Leu, W.; Nieto Oberhuber, C.; Campbell, J. E.; Hoveyda, A. H. J Am Chem Soc 2004, 126, 11130.
- [15] (a) Chun, J.; Lee, H. S.; Jung, I. G.; Lee, S. W.; Kim, J. H.; Son, S. U. Organometallics 2010, 29, 1518; (b) Citadelle, C. A.; Le Nouy, E.; Bisaro, F.; Slawin, A. M. Z.; Cazin, C. S. J. Dalton Trans 2010, 39, 4489; (c) Simonovic, S.; Whitwood, A. C.; Clegg, W.; Harrington, R. W.; Hursthouse, M. B.; Male, L.; Douthwaite, R. E. Eur J Inorg Chem 2009, 1786; (d) Tulloch, A. A. D.; Danopoulos, A. A.; Kleinhenz, S.; Light, M. E.; Hursthouse, M. B.; Eastham, G. Organometallics 2001, 20, 2027.
- [16] (a) Lin, J. C. Y.; Huang, R. T. W.; Lee, C. S.; Bhattacharyya, A.; Hwang, W. S.; Lin, I. J. B. Chem Rev 2009, 109, 3561; (b) Lee, C. S.; Pal, S.; Yang, W. S.; Hwangi, W. S.; Lin, J. B. J Mol Catal, A: Chem 2008, 280, 115; (c) Garrison, J. C.; Youngs, W. J. Chem Rev 2005, 105, 3978; (d) Viciano, M.;

Mas-Marza, E.; Poyatos, M.; Sanau, M.; Crabtree, R. H.; Peris, E. Angew Chem, Int Ed 2005, 44, 444; (e) Kascatan-Nebioglu, A.; Panzner, M. J.; Garrison, J. C.; Tessier, C. A.; Youngs, W. J. Organometallics 2004, 23, 1928; (f) Lin, I. J. B.; Vasam, C. S. Comments Inorg Chem 2004, 25, 75; (g) Quezada, C. A.; Garrison, J. C.; Panzner, M. J.; Tessier, C. A.; Youngs, W. J. Organometallics 2004, 23, 4846.

- [17] Hahn, F. E.; Jahnke, M. C. Angew Chem, Int Ed 2008, 47, 3122.
- [18] For a comprehensive review, see: Delaude, L. Eur J Inorg Chem 2009, 1681.
- [19] (a) Van Ausdall, B. R.; Glass, J. L.; Wiggins, K. M.; Aarif, A. M.; Louie, J. J Org Chem 2009, 74, 7935; (b) Duong, H. A.; Tekavec, T. N.; Arif, A. M.; Louie, J. Chem Commun 2004, 112; (c) Kuhn, N.; Steimann, M.; Weyers, G. Z Naturforsch, B 1999, 54, 427.
- [20] Linde, D. R. Handbook of Chemistry and Physics, 85th ed.; CRC Press: Boca Raton, FL, 2004-2005; Section 8, p. 141.
- [21] Fremont P.; Scott M. N.; Stevens E. D.; Ramnial T.; Lightbody O. C.; Macdonald C. L. B.; Clyburne J. A. C.; Abernethy C. D.; Nolan S. P. Organometallics 2005, 24, 6301.
- [22] Tudose, A.; Delaude, L.; Andre, B.; Demonceau, A. Tetrahedron Lett. 2006, 48, 8529.
- [23] Goj, L. A.; Blue, E. D.; Delp, S. A.; Gunnoe, T. B.; Cundari, T. R.; Pierpont, A. W.; Petersen, J.; Boyle, P. D. Inorg Chem 2006, 45, 9032.