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Imidazol(in)ium-2-Carboxylates as N-Heterocyclic Carbene Ligand Precursors for Ruthenium Metathesis Initiators

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Summary: Imidazol(in)ium-2-carboxylates were used as N-heterocyclic carbene (NHC) ligand precursors to convert the $[RuCl_2(p\text{-cymene})]_2$ dimer into three ruthenium-arene complexes of the $[RuCl_2(p\text{-cymene})(NHC)]$ type. The decarboxylation of $NHC \cdot CO_2$ betaines also provided a convenient synthetic path to prepare five well-known ruthenium-NHC catalysts for olefin metathesis and related reactions, including the second generation Grubbs and Hoveyda–Grubbs catalysts, *via* ligand exchange with phosphine-containing, first generation ruthenium-benzylidene or indenylidene complexes. Both procedures are particularly attractive from a practical point of view, because $NHC \cdot CO_2$ adducts are stable zwitterionic compounds that can be stored and handled with no particular precautions.

Keywords: arene ligands; betaines; organometallic catalysts; ring-opening metathesis polymerization (ROMP); zwitterions

Introduction

Stable N-heterocyclic carbenes (NHCs) have become ubiquitous ligands in organometallic chemistry and in homogeneous catalysis.[1-3] Currently, the NHCs most commonly encountered are imidazolin-2-ylidene and imidazolidin-2-ylidene derivatives (structure **1** with or without a formal double bond between C4 and C5, respectively). Due to their high sensitivity toward oxygen and moisture, these species are often generated *in situ* from more stable precursors. The simplest option is to add both an imidazol(in)ium salt and a strong base to a suitable metal compound (Scheme 1). Alternatively, we[4,5] and others[6,7] have shown that imidazol(in)ium-2-carboxylates readily lost their CO_2 moiety upon heating or dissolution and could serve as efficient carbene precursors in organocatalytic processes[7-10] or for the synthesis of various transition metal-NHC complexes[11] (Scheme 1).

In this article, we describe the efficient synthesis of three ruthenium-arene and five ruthenium-alkylidene complexes bearing NHC ligands upon thermolysis of $NHC \cdot CO_2$ adducts. Most of these species are well-known second generation catalyst precursors for various types of olefin metathesis and related reactions.

Synthesis of Ruthenium-Arene Complexes

In a first series of experiments, the $[RuCl_2(p\text{-cymene})]_2$ dimer (**2**) was refluxed for 2 h in THF with 2 equiv. of $ICy \cdot CO_2$, $IMes \cdot CO_2$, or $IDip \cdot CO_2$. A slow stream of argon was applied on top of the condenser to help displace carbon dioxide. After work-up and purification by column chromatography, the corresponding $[RuCl_2(p\text{-cymene})(NHC)]$ complexes (**3**–**5**) were isolated in ca. 70–90% yields (Scheme 2).[12] These neutral,

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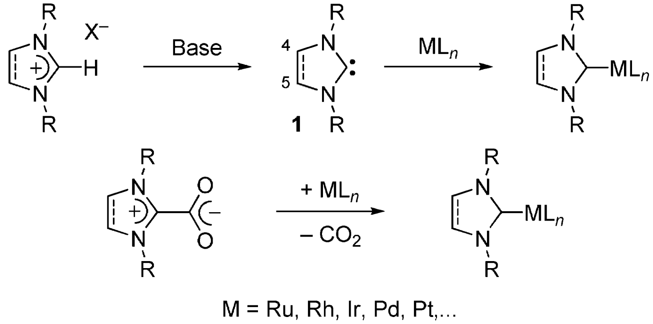
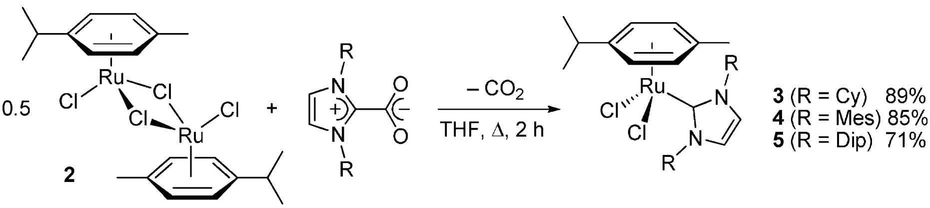


Scheme 1.
Formation of transition metal-NHC complexes by deprotonation or decarboxylation of suitable imidazol(in)ium precursors.



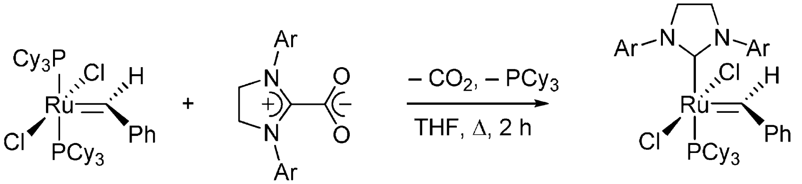
Scheme 2.
Synthesis of ruthenium-arene complexes **3–5** from $[RuCl_2(p\text{-cymene})]_2$ (**2**) and NHC · CO_2 betaines.

18-electron species are well-known catalyst precursors for several ruthenium-mediated organic transformations,[13,14] including ring-opening metathesis polymerization (ROMP)[15] and atom transfer radical polymerization (ATRP).[16] Their synthesis from $[RuCl_2(p\text{–cymene})]_2$ and free NHCs has already been reported in the literature.[17-20] From a practical point of view, the recourse to NHC · CO_2 adducts as carbene transfer agents provides a convenient alternative to the use of air- and moisture-sensitive carbene reagents, while ensuring high yields of organometallic products. It should be noted also that the carboxylate zwitterions proved far superior to the corresponding imidazol(in)ium acid salts to generate active species *in situ* in the ROMP of cyclooctene at room temperature.[4] Indeed, a 1:2 molar combination of dimer **2** and NHC · CO_2 adducts displayed the same level of activity as the preformed $[RuCl_2(p\text{–cymene})(IMes)]$ complex (**4**), whereas mixtures of $[RuCl_2(p\text{–cymene})]_2$, NHC · HX (H = Cl, BF_4), and potassium *tert*-butoxide were almost totally inactive under the same reaction conditions.

Synthesis of Ruthenium-Benzylidene Complexes

The experimental procedure devised for the preparation of ruthenium-arene complexes **3–5** was successfully extended to other classes of well-defined alkene metathesis initiators.[21] Thus, the second generation Grubbs catalyst (**7**)[22] was obtained in high yield and purity from the reaction of its diphosphine parent (**6**)[23] with SIMes · CO_2 (Scheme 3). A similar ligand exchange carried out with SIDip · CO_2 afforded the known complex **8**[24] in 70% isolated yield.

It should be pointed out that complex **8** is significantly less stable in solution than its sibling **7** and totally decomposed on silica gel plates used for TLC analysis. Therefore, it was purified by a quick wash with



6

7 (Ar = Mes) 90%
8 (Ar = Dip) 70%

Scheme 3.
Synthesis of ruthenium-benzylidene complexes **7** and **8** from the first generation Grubbs catalyst (**6**) and NHC · CO_2 betaines.

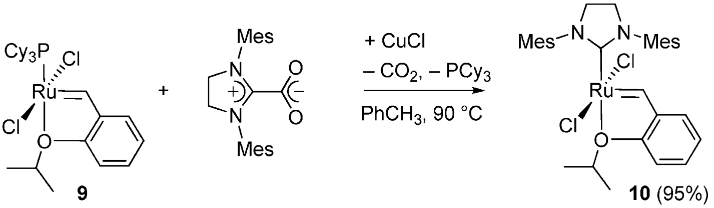
methanol instead of column chromatography. The lower stability in solution of ruthenium-benzylidene or indenylidene complexes bearing the SIDip ligand compared to analogous species containing IMes or IDip, such as complexes **7** or **13**, was already pointed out by Clavier and Nolan, who suggested that the more sterically demanding SIDip ligand should ease phosphine dissociation.[25] Furthermore, Fürstner *et al.* observed the formation of a hydridic by-product during the preparation of complex **8** from its parent **6** and the *tert*-butanol adduct SIDip(H)(O-*t*-Bu).[24]

We also investigated the formation of the second generation Hoveyda–Grubbs catalyst (**10**)[26] starting from the isopropoxybenzylidene complex (**9**)[27] and a small excess of SIMes · CO_2 (Scheme 4).[21] ^{31}P NMR analysis revealed that conversion was not complete after 3 h in toluene at 90 °C. Thus, the reaction mixture was further heated for 3 h at 90 °C in the presence of 1.2 equiv. of copper(I) chloride to help displace tricyclohexylphosphine. Under these conditions, the final chelated product (**10**) was isolated as a green microcrystalline solid in almost quantitative yield.

Synthesis of Ruthenium-Indenylidene Complexes

To complement our investigations on ruthenium-benzylidene complexes, we decided to prepare second generation ruthenium-indenylidene catalysts using imidazol(in)ium-2-carboxylate zwitterions as NHC ligand precursors (Scheme 5).[21] The reaction of diphosphine complex **11**[28] with SIMes · CO_2 was investigated in refluxing THF. After 1.5 h, ^{31}P NMR analysis showed that the starting material had been fully consumed. Work-up and purification by flash column chromatography afforded the Neolyst™ M2 catalyst (**12**)[29] in 86% isolated yield.

The synthesis of $[RuCl_2(PCy_3)(IMes)(3\text{-phenyl-1-indenylidene})]$ (**13**) was achieved using the same experimental protocol with IMes generated *in situ* from IMes · CO_2 instead of adding the free NHC ligand to the starting complex, as originally



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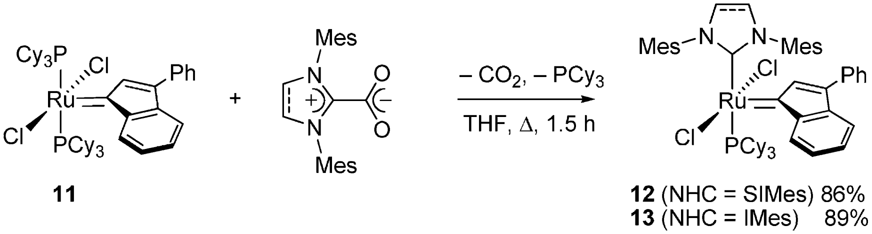
10 (95%)

Scheme 4.
Synthesis of the second generation Hoveyda–Grubbs catalyst (**10**) from its first generation parent (**9**) and IMes · CO_2.



Scheme 5.
Synthesis of second generation ruthenium-indenylidene complexes **12** and **13** from catalyst **11** and NHC · CO_2 betaines.

described in the literature.[30] Under these revised conditions, a full conversion of the starting material took place within 1.5 h and catMETium® IMesPCy catalyst (**13**) was isolated in 89% yield after purification by flash chromatography to remove the excess of carboxylate reagent, tricyclohexylphosphine, and its oxide (Scheme 5).[21]

Conclusion

The decarboxylation of imidazol(in)ium-2-carboxylates provides a convenient synthetic path to efficiently convert various ruthenium complexes into valuable second generation olefin metathesis initiators. Because NHC · CO_2 betaines are readily available, air- and moisture-stable reagents, this procedure is particularly attractive from a practical point of view. Other studies have shown that it is applicable to a wide range of transition metal complexes, and we are confident that zwitterionic adducts of NHCs are promised a bright future in various fields of organic synthesis and catalysis.[31]

[1] "*N-Heterocyclic Carbenes in Synthesis*", S. P. Nolan, Ed., Wiley-VCH, Weinheim **2006**.

[2] "*N-Heterocyclic Carbenes in Transition Metal Catalysis*", *Topics in Organometallic Chemistry*, Vol. *21*, F. Glorius, Ed., Springer, Berlin **2007**.

[3] A. J. Arduengo, G. Bertrand, *Chem. Rev.* **2009**, *109*, 3209 and following articles in this issue.

[4] A. Tudose, A. Demonceau, L. Delaude, *J. Organomet. Chem.* **2006**, *691*, 5356.

[5] A. Tudose, L. Delaude, B. André, A. Demonceau, *Tetrahedron Lett.* **2006**, *47*, 8529.

[6] H. A. Duong, T. N. Tekavec, A. M. Arif, J. Louie, *Chem. Commun.* **2004**, 112.

[7] H. Zhou, W.-Z. Zhang, C.-H. Liu, J.-P. Qu, X.-B. Lu, *J. Org. Chem.* **2008**, *73*, 8039.

[8] B. Bantu, G. M. Pawar, U. Decker, K. Wurst, A. M. Schmidt, M. R. Buchmeiser, *Chem. Eur. J.* **2009**, *15*, 3103.

[9] B. Bantu, G. M. Pawar, K. Wurst, U. Decker, A. M. Schmidt, M. R. Buchmeiser, *Eur. J. Inorg. Chem.* **2009**, 1970.

[10] Y. Kayaki, M. Yamamoto, T. Ikariya, *Angew. Chem. Int. Ed.* **2009**, *48*, 4194.

[11] A. M. Voutchkova, M. Feliz, E. Clot, O. Eisenstein, R. H. Crabtree, *J. Am. Chem. Soc.* **2007**, *129*, 12834.

[12] L. Delaude, X. Sauvage, A. Demonceau, J. Wouters, *Organometallics* **2009**, *28*, 4056.

[13] L. Delaude, A. Demonceau, A. F. Noels, *Curr. Org. Chem.* **2006**, *10*, 203.

[14] V. Dragutan, I. Dragutan, L. Delaude, A. Demonceau, *Coord. Chem. Rev.* **2007**, *251*, 765.

[15] L. Delaude, A. Demonceau, A. F. Noels, *Chem. Commun.* **2001**, 986.

[16] L. Delaude, S. Delfosse, A. Richel, A. Demonceau, A. F. Noels, *Chem. Commun.* **2003**, 1526.

[17] W. A. Herrmann, C. Köcher, L. J. Goossen, G. R. J. Artus, *Chem. Eur. J.* **1996**, *2*, 1627.

[18] L. Jafarpour, J. Huang, E. D. Stevens, S. P. Nolan, *Organometallics* **1999**, *18*, 3760.

[19] C. Lo, R. Cariou, C. Fischmeister, P. H. Dixneuf, *Adv. Synth. Catal.* **2007**, *349*, 546.

[20] N. Ledoux, B. Allaert, F. Verpoort, *Eur. J. Org. Chem.* **2007**, 5578.

[21] X. Sauvage, A. Demonceau, L. Delaude, *Adv. Synth. Catal.* **2009**, *351*, 2031.

[22] M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953.

[23] P. Schwab, M. B. France, J. W. Ziller, R. H. Grubbs, *Angew. Chem. Int. Ed.* **1995**, *34*, 2039.

[24] A. Fürstner, L. Ackermann, B. Gabor, R. Goddard, C. W. Lehmann, R. Mynott, F. Stelzer, O. R. Thiel, *Chem. Eur. J.* **2001**, *7*, 3236.

[25] H. Clavier, C. A. Urbina-Blanco, S. P. Nolan, *Organometallics* **2009**, *28*, 2848.

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

[27] J. S. Kingsbury, J. P. A. Harrity, P. .J Bonitatebus, Jr., A. H. Hoveyda, *J. Am. Chem. Soc.* **1999**, *121*, 791.

[28] R. Dorta, R. A. Kelly, III, S. P. Nolan, *Adv. Synth. Catal.* **2004**, *346*, 917.

[29] S. Monsaert, R. Drozdzak, V. Dragutan, I. Dragutan, F. Verpoort, *Eur. J. Inorg. Chem.* **2008**, 432.

[30] L. Jafarpour, H.-J. Schanz, E. D. Stevens, S. P. Nolan, *Organometallics* **1999**, *18*, 5416.

[31] L. Delaude, *Eur. J. Inorg. Chem.* **2009**, 1681.