SYNLETT Spotlight 59

NHC Ruthenium Complexes as Second Generation Grubbs Catalysts

Compiled by Javier Guerra

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Javier Guerra was born in 1978 in Ciudad Real (Spain). He studied Chemistry at the University of Castilla-La Mancha (1996–2000) where he is currently carrying out his PhD under the tutelage of Dr. Enrique Díez Barra and Dr. Juan Tejeda Sojo. His area of interest concerns the development of new pincer complexes and metallo-dendrimers as well as the study of their catalytic activity.

Facultad de Química, Universidad de Castilla-La Mancha, 13071-Ciudad Real, Spain
E-mail: fjguerra@qui-cr.uclm.es

Introduction

Developments in two seemingly unconnected fields have given rise to a new family of powerful catalysts with many applications in olefin metathesis. On the one hand, the progress made over the past decade in the synthesis of *N*-heterocyclic carbenes (NHCs) and their complexes, as well as the catalytic applications of these systems, has been impressive.^{1,2} On the other hand, the achievements in the evolution of homogeneous catalysts for olefin metathesis have turned this reaction into a common C–C coupling process³ with various possibilities including ring-opening metathesis polymerization (ROMP), ring-closing metathesis (RCM), acyclic diene metathesis polymerization (ADMET), ring-opening metathesis (ROM), and cross-metathesis (CM or XMET).

Herrmann et al.⁴ were the first to synthesize a modified Grubbs catalyst that included *N*-heterocyclic carbene ligands. The bis(NHC)-substituted derivatives **2** showed a minor improvement in terms of catalytic activity compared to conventional Grubbs catalyst **1**. Soon after, papers concurrently published by Nolans,⁵ Grubbs,⁶ and Herrmanns⁷ groups described the synthesis of mono(NHC)-substituted complexes such as those of type **3** and **4**. This new family of compounds has been called the second generation Grubbs catalysts.

The strong σ donor character of NHC ligands facilitates the dissociation of the phosphine in compounds **3** and **4** due to the *trans* effect, although the key step for olefin metathesis consists of the coordination of the olefin to the unsaturated ruthenium complex.⁸ These new compounds (**3** and **4**), which are reasonably air- and water-stable, are more active than **2** or **1** and can also tolerate the presence of different functional groups (with the ex-

ception of basic ones like nitriles and amines).^{3a} The enhanced activity of these compounds means that the reactions can be carried out under mild conditions. Three years after its synthesis,^{6b} complex **4a** [R = Mes (mesityl), R' = Cy] has become commercially available⁹ owing to its wide-ranging applications.

Compound **4a** was synthesized from **1** and the saturated 1,3-dimesityl-2,3,4,5-tetrahydro-1*H*-imidazol-2-ylidene, which was protected as the alkoxide to generate the free carbene ligands in situ.

Abstracts

Complex **4a** is able to catalyse RCM to give di-, tri- or tetra-substituted cycloolefins while complex **1** failed in the case of tri- and tetrasubstituted ones. The stability and tolerance towards different functional groups of the second generation Grubbs' catalyst has also been demonstrated.^{6b}

The syntheses of several macrocycles by ring expansion have recently been published.¹⁰ Bis-(vinylketones) and bis-acrylate systems react with a set of cycloalkenes, giving rise to a variety of structures in an atom-economical process employing only one catalyst. Factors like concentration or stoichiometry are crucial in order to control the product distribution.

En-yne CM between ethylene and alkynes substituted with a heteroatom in the propargylic or homopropargylic position failed when **1** was employed – except in the case where the heteroatom was protected. Nevertheless, even when a protection protocol is employed alcohols, ethers or silyl ethers do not react or react very poorly.¹¹ Chelation at the Ru centre is thought to be responsible for decelerating or shutting down catalysis. Complex **4a** is successful in this reaction without resorting to a protection/deprotection sequence and gives the desired products with good/excellent yields.^{12,13}

Catalyst **4a** also performs well in ROMP reactions, thus showing its ability to build polymeric structures while tolerating the presence of a huge variety of polar functional groups. Different low-strain cyclic olefins, like cyclooctene or norbornene [using 1,4-bis(acetoxy)-*cis*-2-butene as a chain transfer agent (CTA)], have also been studied.^{14,15}

References

- (1) For relevant reviews see: (a) Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39. (b) Arduengo, A. J. III *Acc. Chem. Res.* **1999**, *32*, 913. (c) Herrmann, W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290.
- (2) For recent papers see: (a) Jafarpour, L.; Heck, M. P.; Baylon, C.; Lee, H. M.; Mioskowski, C.; Nolan, S. P. *Organometallics* **2002**, *21*, 671. (b) Díez-Barra, E.; Guerra, J.; Rodríguez-Curiel, R. I.; Merino, S.; Tejeda, J. J. *Organomet. Chem.* **2002**, *660*, 50.
- (3) For relevant reviews see: (a) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (b) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012. (c) See also reference 1c. (d) A Spotlight article dealing with olefin metathesis: Chauder, B. A. *Synlett*; **1999**, 267.
- (4) Weskamp, T.; Schattenmann, W. C.; Spiegler, M.; Herrmann, W. A. *Angew. Chem. Int. Ed.* **1998**, *37*, 2490. Corrigenda. *Angew. Chem. Int. Ed.* **1999**, *38*.
- (5) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674.
- (6) (a) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247. (b) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.
- (7) (a) Weskamp, T.; Kohl, F. J.; Herrmann, W. A. *J. Organomet. Chem.* **1999**, *582*, 362. (b) Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem. Int. Ed.* **1999**, *38*, 2416. (c) Ackermann, L.; Fürstner, A.; Weskamp, T.; Kohl, F. J.; Herrmann, W. A. *Tetrahedron Lett.* **1999**, *40*, 4787.
- (8) For an exhaustive study of the mechanism see: Sandford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.*; **2001**, *123*, 6543.
- (9) Sold by Strem Chemicals Inc. (Cat. No. 44-7770); Acros Organics (Cat. No. 35616-2500); Sigma-Aldrich Co. (Cat. No. 56,974-7).
- (10) Lee, C. W.; Choi, T.-L.; Grubbs, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 3224.
- (11) (a) Kinoshita, A.; Sakakibara, N.; Mori, M. *Tetrahedron* **1999**, *55*, 8155. (b) Smulik, J. A.; Diver, S. T. *J. Org. Chem.* **2000**, *65*, 1788.
- (12) Smulik, J. A.; Diver, S. T. *Org. Lett.* **2000**, *2*, 2271.
- (13) Another study has been published that describes the reaction of mono- and disubstituted alkynes with terminal alkenes using **4a** as the catalyst: Stragies, R.; Voigtmann, U.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 5465.
- (14) Vastenamer® and Norsorex® are polymers made by ROMP from cyclooctene and norbornene respectively: Bhaduri, S.; Mukesh, D. In *Homogeneous Catalysis. Mechanisms and Industrial Applications*; John Wiley & Sons: New York, **2000**.
- (15) Bielawski, C. W.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2000**, *39*, 2903.