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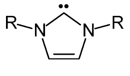
EDITORIAL

Diverse Chemical Applications of N-Heterocyclic Carbenes

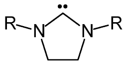
N-Heterocyclic carbenes, or NHCs as they are commonly abbreviated, have attracted significant interest over the past decade due to their widespread utility in chemical transformations. As ligands on transition metals, NHCs have been found to have properties similar to those of the widely employed phosphine ligand, due to their ability to act as both a Lewis base and a Lewis acid at the same time. In addition, the ability to prepare a number of derivatives allows control of both sterics and electronics, also reminiscent of the capabilities of phosphines.

JACS Select is a collection of previously published work, intended to capture recent interest in a topic of increased importance to the chemical community. In 2008−09, over 100 publications have appeared in *JACS* featuring chemistry involving NHCs, either attached to a transition metal complex or as integral components in the chemistry being reported. This sixth issue of *JACS* Select contains 20 reports chosen to demonstrate the variety of chemistry that can be accomplished with these versatile molecules.

First, it is worth examining the structures of typical NHCs that are currently being examined. Structure **A** shows the presence of a carbene moiety stabilized by two adjacent π-donating atoms. The unsaturation in the backbone makes this an aromatic system, so that the carbine p-orbital is available to act as a π-acid. In comparison, use of the corresponding NHC with a saturated backbone (**B**) leaves the carbene with two π-donor atoms attached, decreasing its Lewis acidity. In fact, the back-filling of the carbene p-orbital has led to these species being drawn as shown in **C**, which represents the NHC as a strong σ-donor ligand with little π-acceptor character.



A



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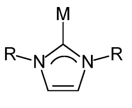

C

In addition to acting as ligands on transition metals, the ability of NHCs to act as both electron donors and acceptors permits them to serve as organocatalysts in a variety of coupling reactions. Four publications have been chosen that highlight this activity. **Bode** reported a simple and broadly applicable NHC-catalyzed annulation based on an α-hydroxyenone surrogate for α,β-unsaturated aldehydes.[1] Here, the NHC forms a reactive enol that can be used to make cyclopentenes and γ-lactams that include an assortment of heterocyclic substituents. Another use of an NHC in organocatalysis was reported by **Rovis**, in which triazolium species act as catalysts for the intermolecular reaction of glyoxamides with alkylidenemalonates to give asymmetric aldehyde addition products.[2] **Waymouth** has found new NHC initiators that enable polmerization of lactides to cyclic polylactides as a result of faster initiation and slower cyclization as compared to 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene(Imes).[3] Poly(ethylene glycol) (PEG or PEO) is a widely used biocompatible polymer, easily prepared via ring-opening polymerization. While this route does not easily adapt to the preparation of functionalized derivatives, **Gnanou and Taton** have reported that the NHC 1,3-bis(diisopropyl)imidazol-2-ylidene (IPr) serves as an efficient catalyst for ethylene oxide polymerization to give α,ω-difunctionalized PEOs with polydispersities near 1.0.[4]

N-Heterocyclic carbenes have also figured prominently in metathesis catalysis, and three contributions have been selected that display some highlights of NHC-based improvements. In the Grubbs II olefin metathesis catalyst, an NHC group replaces a phosphine ligand in the Grubbs I catalyst. **Grubbs** has prepared an NHC derivative in which the organocarbene ligand responsible for metathesis on the ruthenium metal center is tethered to the NHC ligand.[5] In

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(1) Chiang, P.-C.; Rommel, M.; Bode, J. W. *J. Am. Chem. Soc.* **2009**, *131*, 8714–8718.
(2) Liu, Q.; Perreault, S.; Rovis, T. *J. Am. Chem. Soc.* **2008**, *130*, 14066–14067.
(3) Jeong, W.; Shin, E. J.; Culkin, D. A.; Hedrick, J. L.; Waymouth, R. M. *J. Am. Chem. Soc.* **2009**, *131*, 4884–4891.
(4) Raynaud, J.; Absalon, C.; Gnanou, Y.; Taton, D. *J. Am. Chem. Soc.* **2009**, *131*, 3201–3209.
(5) Boydston, A. J.; Xia, Y.; Kornfield, J. A.; Gorodetskaya, I. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2008**, *130*, 12775–12782.

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doing so, ring-expansion metathesis polymerization with cyclooctene leads to the formation of a macrocycle that is eventually ejected from the metal, producing polymer rings of about 150 kDa. **Fréchet** has used a specially designed Ru-tethered NHC catalyst for the synthesis of a cyclic dendronized polymer from a dendronized macromonomer.[6] The combination of tether size and NHC saturation was used to achieve the desired relative rates of propagation vs catalyst release. In Grubbs's NHC-containing metathesis catalyst (Grubbs II), occasionally the carbene is seen to undergo insertion side reactions. **Keister and Diver** have found that addition of CO or isocyanide triggers carbene insertion into an aromatic ring on the NHC nitrogen to give a cycloheptatriene, a reaction related to the Buchner insertion for cyclopropanation of aromatic rings.[7] Study of this decomposition route is important to prepare metathesis catalysts that can operate with lower catalyst loadings.

Two interesting applications of NHCs in main group chemistry have appeared recently. N-Heterocyclic carbenes have been shown to stabilize Si═Si double bonds. **Driess** has used this capability to prepare a stable silylene (R_2Si**:**), which can be oxidized to give the first example of a Si═O double bond.[8] **Roesky** has prepared and studied the addition reactions of NHCs, N-heterocyclic silylenes, and N-heterocyclic germylenes.[9] Distinct reactivity is seen with ammonia and aminoboranes, leading to a simple N−H insertion adduct with the former but net hydrogenation with the latter.

Use of NHC-containing complexes also promotes insertion reactions of alkynes and cyclizations. **Bertrand** reported an easily synthesized, sterically hindered NHC that allows low-coordinate gold(I) to be prepared.[10] This species was shown to be an efficient catalyst for the addition of secondary dialkylamines to internal alkynes, a process that has little precedent. As analogues of phosphines, NHC-derived catalysts are expected to have similar chemistry. **Tsuji** has found an iridium catalyst for the addition of acid chlorides across terminal alkynes in which the phosphine-based catalyst results in decarbonylative addition, whereas the bulky NHC-based catalyst gives exclusively the acyl chloride addition product.[11] **Nolan** has reported a gold(I) NHC cation that catalyzes the efficient hydration of alkynes to give ketones.[12] The success of the reaction is limited to the IPr ligand and the weakly coordinating solvent dioxane with a non-coordinating anion. A variety of carbonyl complexes were prepared with catalyst loadings as low as 50 ppm. Au(I) coordinated with an NHC ligand has been shown by **Horino and Toste** to catalyze sequential cycloisomerization/sp^3 C−H bond functionalization of 1,5-enynes and 1,4-enallenes to provide tetracyclododecane and tetracyclotridecane derivatives.[13] In this complex sequence of tandem reactions, the NHC and phosphine complexes give comparable results. A useful catalyst for the [3 + 2] addition of alkynes and α-aryldiazoesters to yield indenes has been reported by **Chang**.[14] The ionic $Cu(IPr)^+B(ArF)_4^-$ catalyst is proposed to react via a carbenoid species with the alkyne to undergo electrophilic cyclization with the arene.

Three Communications demonstrate the utility of NHC ligands in group-transfer reactions. The planar coordination geometry of NHCs has been put to use by **Lammertsma** in the synthesis of a novel ruthenium phosphinidene complex, in which the perpendicular relationship between these two groups changes the σ-donor/π-acceptor properties of the NHC.[15] The enhanced σ-donor properties are thought to enhance the polarity of the Ru═PR bond, thereby enhancing the reactivity of the group toward phosphinidine transfer. The utility of organofluorine compounds in medicinal, materials, and agricultural fields requires the development of new methods for the introduction of fluorine-containing functional groups into organic molecules. **Vicic** has reported a new copper-NHC trifluoromethyl derivative that can convert aryl iodides into trifluoromethyl derivatives in good yields.[16] **Hoveyda** has reported a protocol for catalytic boron−copper addition to acyclic and cyclic aryl olefins.[17] These saturated-NHC copper(I)

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(6) Boydston, A. J.; Holcombe, T. W.; Unruh, D. A.; Fréchet, J. M. J.; Grubbs, R. H. *J. Am. Chem. Soc.* **2009**, *131*, 5388–5389.

(7) Galan, B. R.; Pitak, M.; Gembicky, M.; Keister, J. B.; Diver, S. T. *J. Am. Chem. Soc.* **2009**, *131*, 6822–6832.

(8) Xiong, Y.; Yao, S.; Driess, M. *J. Am. Chem. Soc.* **2009**, *131*, 7562–7563.

(9) Jana, A.; Schulzke, C.; Roesky, H. W. *J. Am. Chem. Soc.* **2009**, *131*, 4600–4601.

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(12) Marion, N.; Ramón, R. S.; Nolan, S. P. *J. Am. Chem. Soc.* **2009**, *131*, 448–449.

(13) Horino, Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2809–2811.

(14) Park, E. J.; Kim, S. H.; Chang, S. *J. Am. Chem. Soc.* **2008**, *130*, 17268–17269.

(15) Aktas, H.; Slootweg, J. C.; Schakel, M.; Ehlers, A. W.; Lutz, M.; Spek, A. L.; Lammertsma, K. *J. Am. Chem. Soc.* **2009**, *131*, 6666–6667.

(16) Dubinina, G. G.; Furutachi, H.; Vicic, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 8600–8601.

(17) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.

catalysts give high yields of a single boronate diastereomer. Furthermore, use of a chelating NHC allowed for a highly enantioselective borylation of β-methylstyrene and related cyclic olefins.

N-Heterocyclic carbenes have also made their way into materials chemistry. **Yam** has synthesized a series of diarylethene-containing NHC complexes of Au(I), Ag(I), and Pd(II).[18] These materials have been demonstrated to undergo photochromic reactions that may provide opportunities for materials and catalysts with photoswitchable functions.

N-Heterocyclic carbene ligands are useful in many complexes due to the steric protection they offer while maintaining a low coordination number. However, in some cases intramolecular reactions can occur, as seen in the case of the Keister/Diver study. **Macgregor and Whittlesey** have seen the deprotonation of an agostic methyl C−H bond of an $\mathrm{I^iPr_2}$ NHC ligand; however, calculations indicate that the proton removed is not the agostic hydrogen but one that is geminal on the same methyl group.[19] This conclusion suggests that similar pathways should be considered in electrophilic methane activation reactions. Finally, a ruthenium complex containing an NHC ligand has been found by **Madsen** to promote the remarkable reaction of primary amines and primary alcohols to give amides with loss of 2 equiv of H_2.[20] A proposed pathway involves initial conversion of the alcohol to an aldehyde, followed by attack of the amine and dehydrogenation to give the amide.

As mentioned above, these reports represent only a small fraction of the work that is going on employing N-heterocyclic carbenes in chemical synthesis. We hope that portraying some of these examples will stimulate thinking of additional ways that readers can find uses for these unusual molecules.

William D. Jones, Associate Editor

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