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Dramatic Influence on the Olefinic Geometry in the Nickel(0)-Catalyzed Coupling Reaction of 1,3-Dienes and Aldehydes Using N-Heterocyclic Carbene as a Ligand

Yoshihiro Sato, Rieko Sawaki, and Miwako Mori*

Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan

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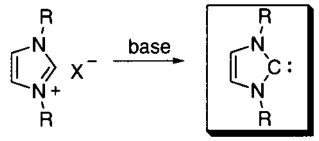
Summary: The use of N-heterocyclic carbene **2** *as a ligand in a nickel(0)-catalyzed coupling reaction of 1,3-diene and aldehyde was investigated. It was found that the Ni(0)−carbene complex showed a unique property in the reaction of 1,3-diene* **4** *and aldehyde* **5** *to give the coupling product* ***Z*-6**, *having a (Z)-olefin in high yield in a highly stereoselective manner. Since the same reaction using the Ni(0)−PPh$_3$ complex gave* ***E*-6a** *in a stereoselective manner, this result indicates that the Ni(0)−carbene complex has a property different from that of the traditional Ni(0)−phosphine complex.*

Since the first report of the isolation and X-ray crystallographical characterization of N-heterocyclic carbenes (imidazol-2-ylidenes, **2**; Scheme 1) was published in 1991 by Arduengo,[1] these compounds have attracted much attention not only as a stable isolable carbene species but also as molecules to coordinate to various transition metals.[2] These transition-metal complexes coordinated by the N-heterocyclic carbene **2** were expected to have different reactivities compared with those coordinated by traditional ligands such as phosphines. Indeed, some transition-metal-catalyzed reactions using **2** as a ligand in which the reactivity and yield were greatly enhanced have recently been reported.[3] The unique property of this new type of ligand prompted us to apply the ligand to nickel(0)-catalyzed coupling reactions of 1,3-dienes and aldehydes.[4]

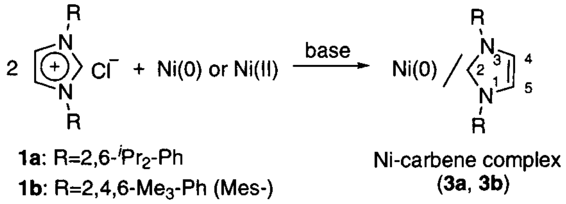
Scheme 1



1 **2**

Initially, we investigated the preparation of Ni(0)−carbene complex **3** in situ (Table 1).[5] A mixture of the zerovalent nickel complex Ni(cod)$_2$ (1 equiv) and the imidazolium salt **1a** (2 equiv) in THF was treated with ^{t}BuOK (2 equiv)[6] at 0 °C, and the mixture was stirred at the same temperature for 20 min. The mixture was then monitored by ^{13}C NMR at room temperature, and the signal of the carbene carbon (C2) was observed at 219.4 ppm (run 1). On the other hand, when a mixture of NiCl$_2$ (1 equiv) and **1a** (2 equiv) in THF was treated with 4 equiv of BuLi under similar conditions, a distinctive peak of the carbene carbon was again observed at 220.5 ppm in the ^{13}C NMR spectrum (run 2). The result indicates that the reduction of NiCl$_2$ and the formation of the N-heterocyclic carbene from **1a** are simultaneously caused by BuLi in a one-pot reaction. It is interesting that none of the peaks attributable to the C2 carbon of the N-heterocyclic carbene were observed in a ^{13}C NMR spectrum of the mixture obtained from NiCl$_2$, **1a**, and PhMgBr (run 3). Similarly, the Ni(0)−carbene complex **3b** was prepared in situ from NiCl$_2$ and 2 equiv of imidazolium salt **1b** in C$_6$D$_6$ by treatment with BuLi (hexane solution) (run 4). The ^{13}C chemical shift of the carbene carbon in **3b** appears at 219.8 ppm, which is substantially downfield from the reported chemical shift (193.2 ppm) of **3b′** formed from Ni(cod)$_2$ and free carbene **2b** (R = mesityl), which has been reported by Arduengo et al.[7,8] Although the complete characterization of Ni(0)−carbene complexes **3** has not been achieved yet, the present procedure would provide a simple way to prepare various Ni(0)−carbene complexes from chemically stable reagents such as NiCl$_2$ and imidazolium salts.

Table 1. Preparation of Ni(0)−Carbene Complex 3 in Situ from Imidazolium Salt 1 and Ni Complex



run[a]	Ni complex	imidazolium salt	base	C$_2$ (δ(^{13}C), ppm)
1	Ni(cod)$_2$	**1a**	^{t}BuOK^b	219.4
2	NiCl$_2$	**1a**	BuLi^c	220.5
3	NiCl$_2$	**1a**	PhMgBr^c	*d*
4	NiCl$_2$	**1b**	BuLi^c	219.8

[a] All reactions (except for run 4) were carried out in THF at 0 °C in a NMR tube. The reaction for run 4 was carried out in C$_6$D$_6$ in a similar manner. After they were stirred for 20 min, the reaction mixtures were directly monitored by ^{13}C NMR at 23 °C. [b] Two molar equivalents of the base was used. [c] Four molar equivalents of the base was used. [d] The corresponding peak was not observed.

Having established in situ preparation of Ni(0)−carbene complexes, we turned our attention to the coupling reaction of 1,3-diene **4** and aldehyde **5** (Scheme 2).[4] At first, the reaction of **4** (1 equiv) and **5a** (1 equiv) was investigated using the Ni(0)−carbene complex **3a**

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* To whom correspondence should be addressed. E-mail: mori@pharm.hokudai.ac.jp.

[1] Arduengo, A. J., III; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361.

[2] For reviews, see: Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39. Herrmann, W. A.; Köcher, C. *Angew. Chem., Int. Ed.* **1997**, *36*, 2162.

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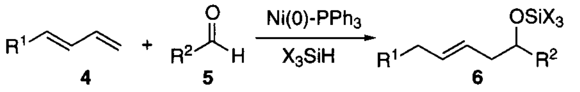
Scheme 2



Scheme 3

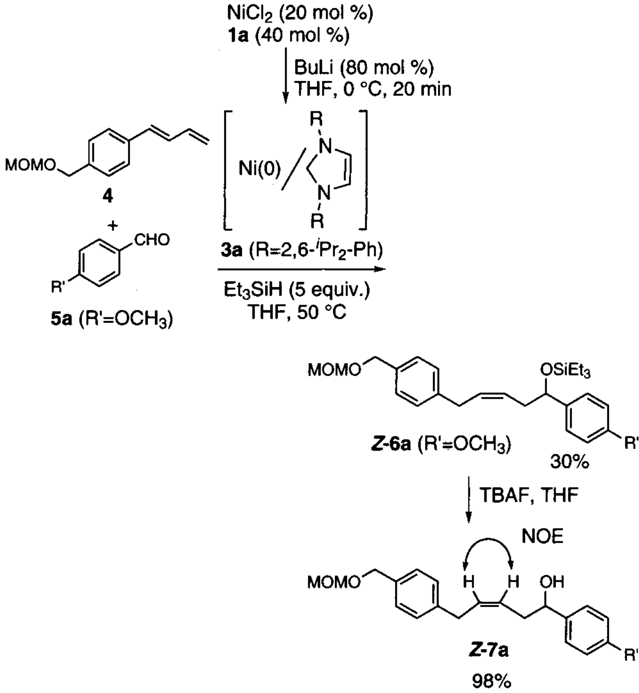
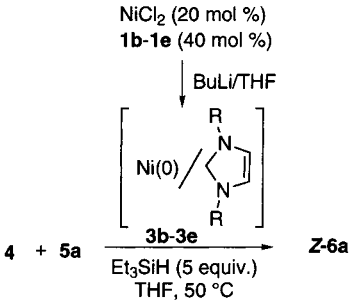
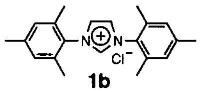
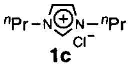
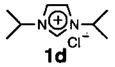
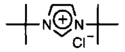
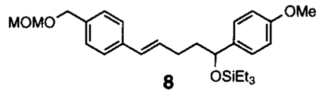


Table 2. Intermolecular Coupling Reaction of 1,3−Diene 4 and Aldehyde 5a Using Ni Complexes 3b−e



run	imidazolium salt	time (h)	yield (%)	recovery of **4** (%)
1	 **1b**	21	38	51
2	 **1c**	18	10	77
3	 **1d**	24	49	39
4[a]	 **1e**	15	2	0

[a] **8** was obtained in 36% yield.



in the presence of Et_3SiH (5 equiv) in THF at 50 °C (Scheme 3). Interestingly, the coupling product ***Z*-6a** was obtained in 30% yield along with the recovery of **4** (52%) (Scheme 3). The olefinic geometry of ***Z*-6a** was unambiguously determined to a be *Z* configuration by both the coupling constant of olefinic protons (10.9 Hz) in ^1H NMR and an NOE experiment in ***Z*-7a**. Since the same reaction using the Ni(0)−PPh_3 complex gave ***E*-6a** in a stereoselective manner (Scheme 2), which had previously been reported by us,[9] this result indicates that the Ni(0)−carbene complex has the properties different from those of the traditional Ni(0)−phosphine complex. The reaction of **4** and **5a** was carried out using various complexes **3b**−**e** prepared from $NiCl_2$ (20 mol %), imidazolium salts **1b**−**e** (40 mol %), and BuLi (80 mol %) (Table 2). The yield of ***Z*-6a** varied from 2% to 49%, depending on the substituent of the N-heterocyclic carbene in the complex, and the use of Ni(0)−carbene complex **3d** gave the best result (run 3).

It is noteworthy that the reaction of **4** and **5a** using 20 mol % of the Ni(0)−carbene complex generated from $NiCl_2$ (20 mol %) and imidazolium salt **1d** (20 mol %) with BuLi (60 mol %) stereoselectively produced ***Z*-6a** in 87% yield as the sole product. This result indicates that the Ni(0)−carbene complex (Ni(0)/carbene = 1/1) generated from $NiCl_2$ and an equimolar amount of the

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(3) For Heck reactions, see: (a) Herrmann, W. A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G. R. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2371. (b) Enders, D.; Gielen, H.; Raabe, G.; Runsink, J.; Teles, H. *Chem. Ber.* **1996**, *129*, 1483. (c) McGuinness, D. S.; Green, M. J.; Cavell, K. J.; Skelton, B. W.; White, A. H. *J. Organomet. Chem.* **1998**, *565*, 165. (d) Clyne, D. S.; Jin, J.; Genest, E.; Gallucci, J. C.; RajanBabu, T. V. *Org. Lett.* **2000**, *2*, 1125. For Suzuki−Miyaura coupling reactions, see: (e) Herrmann, W. A.; Reisinger, C. P.; Spiegler, M. *J. Organomet. Chem.* **1998**, *557*, 93. (f) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804. (g) Zhang, C.; Trudell, M. L. *Tetrahedron Lett.* **2000**, *41*, 595. (h) Fürstner, A.; Leitner, A. *Synlett* **2001**, 290. For Kumada−Tamao cross-coupling reactions, see: (i) Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* **1999**, *121*, 9889. (j) Böhm, V. P. W.; Weskamp, T.; Gstöttmayr, C. W. K.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2000**, 39, 1602. For Stille coupling reactions, see: (k) Weskamp, T.; Böhm, V. P. W.; Herrmann, W. A. *J. Organomet. Chem.* **1999**, *585*, 348. (l) Grasa, G. A.; Nolan, S. P. *Org. Lett.* **2001**, *3*, 119. For amination of aryl halides, see: (m) Huang, J.; Grasa, G.; Nolan, S. P. *Org. Lett.* **1999**, *1*, 1307. (n) Stauffer, S. R.; Lee, S.; Stambuli, J. P.; Hauck, S. I.; Hartwig, J. F. *Org. Lett.* **2000**, *2*, 1423. For coupling reactions of aryl halides with organosilicon reagent, see: (o) Lee, H. M.; Nolan, S. P. *Org. Lett.* **2000**, *2*, 2053. For olefin metathesis, see: (p) Weskamp, T.; Schattenmann, W. C.; Spiegler, M.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 2490. (q) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674. (r) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247. For hydroformylation of styrene derivatives, see: (s) Chen, A. C.; Ren, L.; Decken, A.; Crudden, C. M. *Organometallics* **2000**, *19*, 3459.

(4) (a) Takimoto, M.; Hiraga, Y.; Sato, Y.; Mori, M. *Tetrahedron Lett.* **1998**, *39*, 4543. (b) Sato, Y.; Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2000**, 122, 1624.

(5) Recently, a Ni(II), Pd(II), or Pd(0) complex with imidazolium salts in the presence of an excess of base have been reported in some reactions.[3f−j,l−o] In those reactions, the formation of a Ni(0)− or Pd(0)−carbene complex was assumed.

(6) It was reported that free N-heterocyclic carbenes **2** were prepared by treatment of the corresponding imidazolium salts **1** with a strong base (e.g., ^{t}BuOK and $NaNH_2$).[1,2]

(7) Arduengo, A. J., III; Gamper, S. F.; Calabrese, J. C.; Davidson, F. *J. Am. Chem. Soc.* **1994**, *116*, 4391.

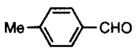
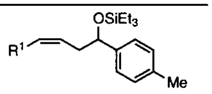
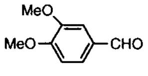
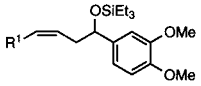
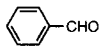
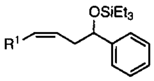
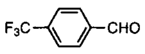
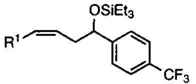
(8) All peaks except for the carbene carbon (C2) of the ^{13}C NMR spectrum of **3b** were almost identical with those of the corresponding Ni(0)−carbene complex **3b′**[7] (see the Supporting Information). It was thought that this discrepancy would result from the presence of LiCl and hexane, which were derived from the reaction of $NiCl_2$ and BuLi (hexane solution). However, removal of those or isolation of **3b** from the catalyst mixture was unfruitful.

(9) The reaction of **4**, **5a**, and Et_3SiH using $Ni(cod)_2$ (20 mol %) and PPh_3 (40 mol %) under the same conditions gave ***E*-6a** in 76% yield.[4a]

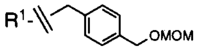
Table 3. Reaction of 4 with Various Aldehydes 5

$\mathrm{NiCl_2}$ (5 or 10 mol %)
1d (5 or 10 mol %)
$\downarrow$ BuLi/THF

$$\mathbf{4} + \mathbf{5} \xrightarrow[\text{Et}_3\text{SiH, THF, 50 °C}]{\text{Ni-carbene complex}} \mathbf{\textit{Z}\text{-}6}$$

run	aldehyde	time, yield
1[a]	 **5b**	 ***Z*-6b** (28 h, 95%)
2	 **5c**	 ***Z*-6c** (24 h, 79%)
3	 **5d**	 ***Z*-6d** (40 h, 74%)
4	 **5e**	 ***Z*-6e** (40 h, 54%)[b]

[a] 5 mol % of Ni(0)-carbene complex was used. [b] Diene **4** was recovered in 25%.



imidazolium salt **1d** has a greater activity toward the coupling reaction compared with the Ni(0)−carbene complex (Ni(0)/carbene = 1/2), which afforded ***Z*-6a** in 49% yield under similar conditions (Table 2, run 3). The high activity of this Ni(0)−carbene complex (Ni(0)/carbene = 1/1) enabled reduction of the amount of the catalyst to 5%, and the product ***Z*-6a** was obtained in 79% yield in a completely stereoselective manner.

Reactions of **4** and various aldehydes **5b**−**e** with this Ni(0)−carbene complex (5 or 10 mol %) were investigated (Table 3). The aldehyde **5b** or **5c**, having an electron-donating substituent on the aromatic ring, seemed to be more reactive than benzaldehyde (**5d**) to give the corresponding product in 95% (***Z*-6b**) and 79% (***Z*-6c**) yield. Although the reaction rate was relatively slow, an electron-withdrawing group (**5e**, run 4) was tolerated in this reaction, producing ***Z*-6e** in 54% yield (in 72% conversion yield). It was remarkable that the geometry of olefin in the coupling products was exclusively controlled to be a *Z* configuration in all cases.

In summary, it was found that the Ni(0)−carbene complex showed a unique property in the reaction of 1,3-diene **4** and aldehyde **5** to give the coupling product ***Z*-6**, having the (*Z*)-olefin in good yield in a highly stereoselective manner. This indicates that the Ni(0)−carbene complex has reactivities quite different from those of the Ni(0)−phosphine complex, although the mechanism of the formation of ***Z*-6** is still not clear. In addition, Ni(0)−carbene complexes **3** prepared by treatment of $\mathrm{NiCl_2}$ and the corresponding imidazolium salts **1** with BuLi were used in this study. Although the precise characterization of the Ni(0)−carbene catalyst **3** used in our procedure has not been rigorously established, its generation is experimentally simple and reproducibly provides synthetic results that are complementary to those of phosphine-based catalysts. Further studies, including studies on the mechanism, are in progress.

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Supporting Information Available: Figures giving ^{13}C NMR spectra of Ni(0)−carbene complexes **3a**,**b** prepared in situ from $\mathrm{NiCl_2}$, imidazolium salts **1a**,**b**, and BuLi and text giving a typical procedure for the coupling reaction of **4** and **5b** (Table 3, run 1) and spectral data of ***Z*-6a**, ***Z*-6b**, ***Z*-6c**, ***Z*-6d**, ***Z*-6e**, and ***Z*-7a**. This material is available free of charge via the Internet at http://pubs.ac.org.

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