ORGANOMETALLICS

Communications

Sequential Insertion of Carbon Monoxide and Imines into Nickel−Methyl Bonds: A New Route to Imine Hydroacylation

Jason L. Davis and Bruce A. Arndtsen*

Department of Chemistry, McGill University, 801 Sherbrooke Street West, Montreal, Quebec, Canada H3A 2K6

Summary: The sequential insertion of carbon monoxide and imines has been achieved at ambient temperatures with cationic nickel complexes, yielding the nickel-chelated amides (bipy)Ni[η^2-C(H)TolN(R)COCH$_3$]$^+$X$^-$ (bipy = 2,2′-bipyridyl; Tol = p-tolyl; R = alkyl, aryl; X = OTf, PF$_6$, SbF$_6$, B(3,5-C$_6$H$_3$(CF$_3$)$_2$)$_4$). The addition of KCN/methanol to these products of CO/imine insertion leads to cleavage of the amide ligand, providing a facile method to achieve the overall hydroacylation of imines under mild conditions.

The migratory insertion of imines into metal−acyl bonds provides a potential method to generate amides from simple and readily available R′(H)C=NR building blocks. However, while the insertion of carbon-containing unsaturated molecules (e.g., olefins or alkynes) has been explored extensively,[1−3] reports of heteroatom containing substrates (e.g., C=X; X = O, NR) undergo-

ing analogous reactions are much more rare.[4−7] Examples of the latter typically involve electropositive metal centers, which undergo insertion with a regiochemistry to generate a robust M−X bond rather than a new carbon−nitrogen bond.[4,5] The development of late-transition-metal complexes that can tolerate functionality during insertion reactions suggests they might be prime candidates for insertion of substrates such as imines.[8−11] Recently, both we[12] and others[13] have demonstrated that palladium complexes of the form L$_2$Pd-(CH$_3$)(RN=C(H)R′)$^+$X$^-$ (L$_2$ = bidentate neutral ligand;

(1) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987.

(2) For reviews of olefin polymerization, see: (a) Johnson, L. K.; Ittel, S. D.; Brookhart, M. *Chem. Rev.* **2000**, *100*, 1169. (b) Britovsek, G. J. P.; Gibson, V. C.; Wass, D. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 428. (c) Drent, E.; Budzelaar, P. H. M. *Chem. Rev.* **1996**, *96*, 663 and references therein.

(3) Brandsma, L.; Vasilevsky, S. F.; Verkruijsse, H. D. *Applications of Transition Metal Catalysts in Organic Chemistry*; Springer: Berlin, 1997.

(4) For examples of imine insertion: (a) Obora, Y.; Ohta, T.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1997**, *119*, 3745. (b) Coles, S. J.; Hursthouse, M. B.; Kelly, D. G.; Toner, A. J.; Walker, N. M. *Can. J. Chem.* **1999**, *77*, 2095.

(5) For examples of aldehyde insertions: (a) Hanna, T.; Baranger, A. M.; Bergman, R. G. *J. Org. Chem.* **1996**, *61*, 4532. (b) Han, R.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1997**, *119*, 8135.

(6) Products consistent with imine insertion have been suggested in several systems: (a) Alper, H.; Amaratunga, S. *J. Org. Chem.* **1982**, *47*, 3595. (b) Reduto, A. C.; Hegedus, L. S. *Organometallics* **1995**, *14*, 1586. (c) Muller, F.; van Koten, G.; Vrieze, K.; Heijdenrijk, D. *Organometallics* **1989**, *8*, 33.

(7) Imine insertion into metal hydrides are known and have been postulated in catalytic hydrogenations: (a) Fryzuk, M. D.; Piers, W. E. *Organometallics* **1990**, *9*, 986. (b) Debad, J. D.; Legzdins, P.; Lumb, S. A.; Batchelor, R. J.; Einstein, F. W. B. *Organometallics* **1995**, *14*, 2543. (c) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 11703 and references therein. (d) James, B. R. *Catal. Today* **1997**, *37*, 209.

(8) Abu-Surrah, A.; Rieger, B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2475.

(9) Younkin, T. R.; Connor, E. F.; Henderson, J. I.; Friedrich, S. K.; Grubbs, R. H.; Bansleben, D. A. *Science* **2000**, *287*, 460.

Table 1. Synthesis of Complexes 2a–h and 4a–g

entry	imine	R	X	yield (%) 2[a]	yield (%) 4[b]
1	**1a**	Ph	PF$_6$	64	90
2	**1b**	CH$_2$Ph	PF$_6$	84	95
3	**1c**	Me	PF$_6$	92	98
4	**1d**	Me	SbF$_6$	86	88
5	**1e**	Me	BArf[c]	85	91
6	**1f**	Me	OTf[d]	89	36
7	**1g**	^{i}Pr	PF$_6$	68	25
8	**1h**	^{t}Bu	PF$_6$	78	
9	**1i**	Me	Cl	82[e]	

[a] Isolated yields. [b] NMR yields. [c] BArf = B(3,5-C$_6$H$_3$(CF$_3$)$_2$)$_4$. [d] OTf = OSO$_2$CF$_3$. [e] Yield of (bipy)Ni(CH$_3$)Cl.

R = alkyl, aryl; R′ = aryl) can mediate the sequential insertion of carbon monoxide and imines to generate palladium-bound amides. These provide the first well-defined examples of imine insertion into a late metal–carbon bond.[6]

In an attempt to explore the scope of this reaction, as well as develop a metal complex capable of mediating imine insertion under more mild conditions, the synthesis and reactivity of the nickel complexes (bipy)Ni-(CH$_3$)(RN=C(H)Tol)$^+$X$^-$ (bipy = 2,2′-bipyridyl, Tol = p-C$_6$H$_4$CH$_3$) has been investigated. We report herein the first example of the sequential insertion of CO and imines into nickel–methyl bonds, which ultimately leads to a controlled, metal-mediated route to synthesize amides from imines.[14] Methods for the generation, characterization, and cleavage of the amide fragments from the nickel center, as well as a comparison of the relative rates of insertion to the analogous palladium complexes, are described below.

The reaction of [R(H)N=CH(Tol)]$^+$X$^-$ (**1a–h**) with (bipy)Ni(CH$_3$)$_2$ in THF at −40 °C results in the immediate liberation of methane and formation of the cationic nickel–imine complexes **2a–h** (eq 1, Table 1).[15] Com-

(1)
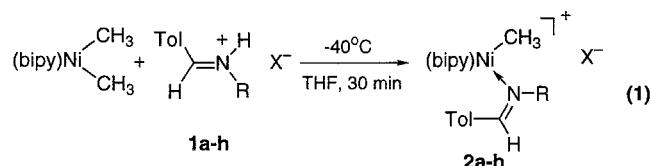
plexes **2a–h** can be isolated by precipitation with pentane, affording solids which are stable at room temperature under nitrogen. The ^{1}H and ^{13}C NMR for **2a–h** display a downfield shift in the imine resonances upon coordination,[16] consistent with η^1-binding of the imine through the nitrogen.[12]

No evidence for imine insertion into the Ni–CH$_3$ bond of complexes **2a–h** was observed at ambient temperature, and heating to 70 °C resulted only in the decomposition of the complex to liberate free imine. Thus, similar to the analogous palladium complexes,[12] **2a–h** have a significant kinetic barrier to imine insertion into the nickel–alkyl bond. However, the exposure of com-

Scheme 1
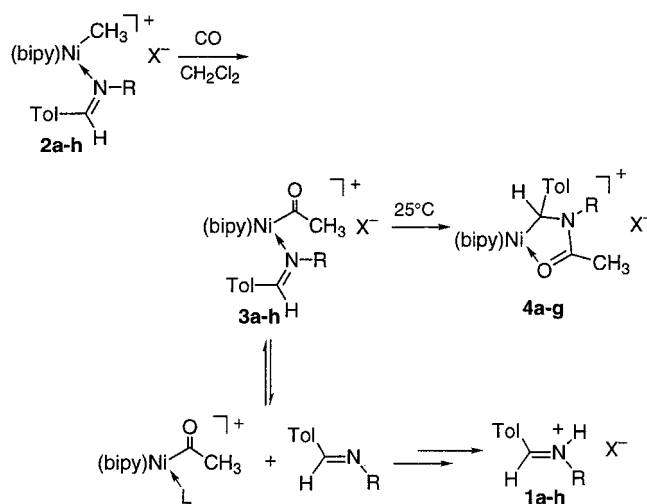
plexes **2a–h** to 1 atm of carbon monoxide results in the rapid insertion of CO to form the nickel–acyl complexes **3a–h**. Unlike **2a–h**, nickel–acyl complexes **3a–g** do react upon standing for several hours in CD$_2$Cl$_2$ solution, resulting in the formation of the product of imine insertion into the nickel–acyl bond (**4a–g**) (Scheme 1). The same reaction at 70 °C results in complete conversion to **4a–g** in under 30 min.

Complexes **4a–g** have been characterized by ^{1}H and ^{13}C NMR, IR, and, in the case of **4b**, X-ray structural analysis. In all cases, only one regioisomer of complexes **4a–g** is obtained, in which imine insertion has occurred to form an amide bond and a new nickel–carbon bond. The formation of a robust amide bond likely provides the driving force for imine insertion into the nickel–acyl bond, which does not exist in nickel–methyl complexes **2a–h**.

The yield of the imine insertion products is sensitive to the imine and counteranion employed. Use of more strongly coordinating counterions dramatically reduces the yield of **4** (Table 1, entries 6 and 9). In the case of **1i**, the chloride counteranion is found to coordinate preferentially over imine in both the nickel–methyl (**2**) and –acyl complexes (**3**), and no evidence for imine insertion is observed. Replacing the primary alkyl substituent on imine nitrogen (entries 2–6) with a secondary ^{i}Pr substituent greatly reduces both the rate of insertion and the yield (entry 7), while the N(^{t}Bu)-substituted imine (**3h**) does not undergo insertion (entry 8). Monitoring the reaction of **3g** (or **3h**) by ^{1}H NMR (CD$_2$Cl$_2$) reveals the competitive formation of the protonated iminium salt **1g** in 21% yield (**1h**: 40% yield) in the product mixture. Similarly, the use of a less basic N-phenyl-substituted imine in **3a** also leads to the low-yield formation of **1a** (6% yield) in addition to **4a**, as does the more coordinating OTf$^-$ counteranion in **3f**

(10) (a) Mecking, S.; Johnson, L. K.; Wang, L.; Brookhart, M. *J. Am. Chem. Soc.* **1998**, *120*, 888. (b) Johnson, L. K.; Mecking, S.; Brookhart, M. *J. Am. Chem. Soc.* **1996**, *118*, 267.

(11) Morimoto, T.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1999**, *121*, 1758.
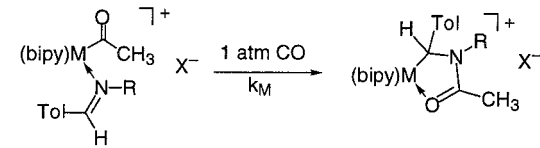
(12) Dghaym, R. D.; Yaccato, K. J.; Arndtsen, B. A. *Organometallics* **1998**, *17*, 4.

(13) Kacker, S.; Kim, J.; Sen, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 1251.

(14) For examples of metal-mediated imine hydroacylation, see: (a) Vasapollo, G.; Alper, H. *Tetrahedron Lett.* **1988**, *29*, 5113. (b) Alper, H.; Amaratunga, S. *Tetrahedron Lett.* **1981**, *22*, 3811. (c) Zhou, Z.; James, B.; Alper, H. *Organometallics* **1995**, *14*, 4209. (d) Antebi, S.; Alper, H. *Can. J. Chem.* **1986**, *64*, 2010. (e) Morimoto, T.; Achiwa, K. *Tetrahedron: Asymmetry* **1995**, *6*, 2661.

(15) Wilke, G.; Herrmann, G. *Angew. Chem., Int. Ed. Engl.* **1966**, *6*, 581.

(16) Complex **2c**: ^{1}H NMR (CD$_2$Cl$_2$) δ 8.56 (s, =C(H)Tol); ^{13}C NMR δ 169.7 (s, =C(H)Tol). Free MeN=C(H)Tol: ^{1}H NMR (CD$_2$Cl$_2$) δ 8.42 (=C(H)Tol); ^{13}C NMR δ 160.6 (=C(H)Tol).

Table 2. Rates of Imine Insertion with 3a−c and 5a−c

3a-c (M = Ni); **5a-c** (M = Pd)

	R	$k_{Ni}{}^a$ $(10^{-3}\,s^{-1})$	$\Delta G^\ddagger$(40 °C) (kcal/mol)	$k_{Pd}{}^b$ $(\times 10^{-4}\,s^{-1})$	$\Delta G^\ddagger$(90 °C) (kcal/mol)	$\Delta\Delta G^\ddagger$
a	Ph	1.5	22.7	0.84	28.2	5.5
b	PhCH$_2$	0.27	23.8	0.93	28.1	4.3
c	CH$_3$	0.89	23.1	2.3	27.4	4.3

^{a} Rate of disappearance of **3a−c** at 45 °C in CD$_2$Cl$_2$. ^{b} Rate of disappearance of **5a−c** (X = BArf) at 90 °C in d_5-PhBr.[18]

(**1f**: 42% yield). The generation of protonated iminium salts with less basic or more slowly inserting imines, or more strongly coordinating anions, implies that decoordination of the imine to form (bipy)Ni(COCH$_3$)-L$^+$ (L = CO, X) may lead to decomposition. Consistent with this observation, the addition of excess PhN=C(H)-Tol to the reaction of **2a** with CO completely suppresses the formation of the protonated imine products and generates complex **4a** in quantitative yield.[17]

The insertion of imines into the nickel−acyl bond of **3a−g** occurs with a lower barrier than that of the analogous palladium complexes, which require prolonged heating at 70 °C. To quantify the influence of the metal center on insertion rates, the first-order rate constants for the insertion of imines with a number of isoelectronic nickel− and palladium−acyl complexes have been determined. As shown in Table 2, the nickel complexes all display a ca. 4.3−5.5 kcal/mol lower barrier for imine insertion than the analogous palladium complexes.

The lower barrier to imine insertion with nickel complexes is not surprising and is similar to that observed in ethylene insertion into isoelectronic cationic nickel and palladium complexes.[19,20] It has been suggested that the more rapid insertion of olefins with first-row transition metals may arise from either a weakened metal−olefin bond or perhaps a weaker metal−alkyl bond.[21] While we do not have sufficient evidence to distinguish between these possibilities for imine insertion, our data are consistent with a more labile imine σ-coordination in the nickel complexes. This is shown qualitatively by the rapid equilibrium coordination of

imine in **2a−c** in acetonitrile solvent. In contrast to the behavior of palladium complexes **5a−c** in CD$_3$CN, where (bipy)Pd(CH$_3$)(RN=C(H)Tol)$^+$X$^-$ and (bipy)Pd(CH$_3$)-(NCCD$_3$)$^+$X$^-$ can be clearly distinguished at ambient temperature by ^{1}H NMR,[12] the analogous equilibrium with nickel complexes **2a−c** and the solvated complex is much more rapid, resulting in broadened ^{1}H NMR resonances at temperatures down to −40 °C.

The sequential insertion of carbon monoxide and imine into the nickel−methyl bond of **2** allows the formation of nickel-bound amides under very mild conditions (i.e., ambient temperature and 1 atm of CO). In addition, the amide ligand in **4a−c** can be readily cleaved from the nickel center, providing a metal-mediated route to generate amides from imines and CO. The addition of KCN to a methanol solution of **4a** results in the immediate generation of a colorless solution. Removal of the solvent, followed by an ether extraction and acid wash with 10% HCl, provides amide **6a** in >95% isolated yield. A similar process can be performed with complexes **4b,c**, in all cases leading to the production of amides in near-quantitative yields. Overall, this reaction represents a relatively straightforward two-step method to hydroacylate imines via the sequential insertion of carbon monoxide and imine into a nickel−methyl bond (eq 2). To our knowledge, the only other report of

(2)

1a-c   **6a-c**
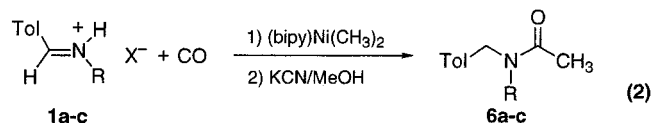
imine hydroacylation with carbon monoxide is that by Alper and co-workers,[14a−d] which utilizes cobalt carbonyl catalysts at elevated temperatures.

In conclusion, we have presented the first example of imine insertion into a nickel−acyl bond to form the five-membered metallocycles **4a−g**. This sequential insertion of carbon monoxide and imine occurs with a significantly lower barrier with nickel complexes **2a−g** than the isoelectronic palladium complexes and provides a new and controlled route to generate both nickel-bound and free amides. Considering that these amides are formed via the well-defined insertion of imines into a Ni−C bond, the induction of asymmetry into this process, and the incorporation of other insertion monomers into the amide products, should prove to be viable extensions of this work. Studies directed toward the latter will be the subject of future reports.

Supporting Information Available: Text and figures giving details of the synthesis and characterization data for **2a−h** and **4a−g**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM000685B

(17) The added PhN=C(Tol) does not significantly perturb the rate of formation of **4a**, suggesting that imine insertion is an intramolecular process from **3a**. A manuscript describing the complete mechanistic details of imine insertion with the isoelectronic palladium complexes is currently in preparation.

(18) Dghaym, R. D.; Arndtsen, B. A. Unpublished results.

(19) Rix, C. F.; Brookhart, M. *J. Am. Chem. Soc.* **1995**, *117*, 1137.

(20) Svejda, S. A.; Johnson, L. K.; Brookhart, M. *J. Am. Chem. Soc.* **1999**, *121*, 10634.

(21) (a) Han, Y.; Deng. L.; Ziegler, T. *J. Am. Chem. Soc.* **1997**, *119*, 5939. (b) Deng, L.; Margi, P.; Ziegler, T. *J. Am. Chem. Soc.* **1997**, *119*, 1094.