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Comparison of Imine to Olefin Insertion Reactions: Generation of Five- and Six-Membered Lactams via a Nickel-Mediated CO, Olefin, CO, Imine Insertion Cascade

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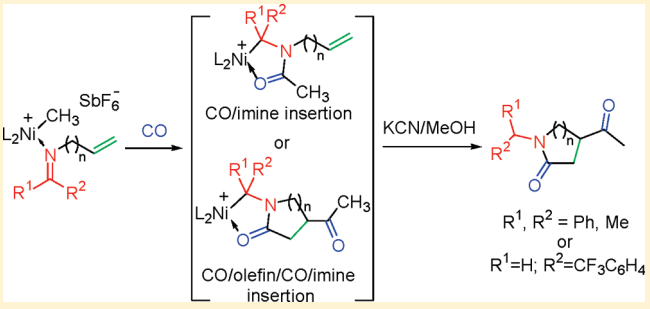
Supporting Information

ABSTRACT: Cationic nickel complexes of the form $L_2Ni(CH_3)(RN{=}C(H)R)^+$ (L_2 = bidentate nitrogen donor) have been probed for their ability to mediate olefin and imine migratory insertion reactions. While these complexes do not undergo alkene insertion into the nickel−methyl bond, the use of olefin-tethered imines $CH_2{=}CH(CH_2)_nN{=}C(R)$aryl ($n$ = 1−3; R = H, methyl, phenyl) and the addition of CO initiates competitive olefin and imine insertion into the in situ generated nickel−acyl complex. The insertion selectivity shows clear steric and electronic influences and suggests that strong imine coordination can allow it to compete with the more rapid insertion of alkenes. This reactivity has been employed to develop a CO/alkene/CO/imine insertion cascade to synthesize five- and six-membered-ring lactams.

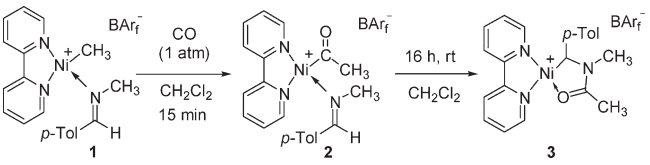


Transition-metal-mediated carbon−carbon and carbon−nitrogen bond forming reactions have become important fundamental reactions in synthetic chemistry. While many variants of these reactions exist, those that incorporate unsaturated molecules via their migratory insertion into metal−ligand bonds have seen extensive use, especially with alkenes as substrates (e.g., alkene hydrogenation,[1] hydroformylation,[2] Heck couplings,[3] olefin polymerization,[4] and related reactions). However, analogous transformations employing heteroatom-containing unsaturated substrates such as imines and aldehydes are less common, despite their structural similarity. Perhaps the most established of these are catalytic hydrogenation or related reductions.[5] More recently, the metal-catalyzed addition of organometallic reagents to imines and aldehydes has also been achieved.[6]

The extensive use of alkene insertion reactions in synthetic processes suggests that the analogous reaction with imines could provide an effective method for generating carbon−nitrogen bonds. However, until only recently, examples of even the stoichiometric insertion of imines into late-metal−carbon bonds in a fashion analogous to that for alkenes were rare.[7−11] This has been postulated to be at least partially based upon thermodynamics, where the insertion of an imine into a metal−carbon bond to cleave a carbon−nitrogen π bond and form a new carbon−nitrogen σ bond is not expected to be nearly as exothermic as is observed with alkene insertion.[7,12]

Both ourselves[7,8] and others[9−11] have demonstrated that CO and imines can undergo sequential migratory insertion into late-transition-metal−carbon bonds to yield products analogous to those of CO/alkene insertion. For example, imines readily undergo insertion into the in situ generated nickel−acyl bond of **2** to form metal-chelated amides (Scheme 1).[8] The generation of a strong amide bond is believed to provide the driving force for these reactions. Considering that these same nickel complexes have been demonstrated to readily undergo alkene insertion reactions,[13] this system provides an intriguing opportunity to probe the relative insertion propensity of these two distinct units. To our knowledge, this fundamental comparison of imine and olefin insertion has not been previously explored and could be important in the development of synthetic processes that utilize both alkenes and imines as insertion substrates. We report below the results of these efforts, which examine the steric, electronic, and regiochemical effects governing competitive insertion between α-olefins and imines. This reactivity has been used to

Scheme 1. Sequential Insertion of CO and Imine into Nickel−Alkyl Bonds



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design a nickel-mediated, four-component insertion cascade to construct five- and six-membered lactams.

RESULTS AND DISCUSSION

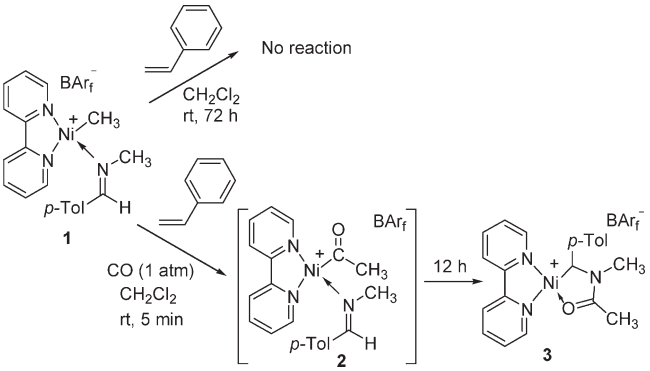
We have previously demonstrated that imines bound to cationic nickel complexes of the form **1** (Scheme 1; BAr_f = $B(3,5\text{-}C_6H_3(CF_3)_2)_4$, *p*-Tol = *p*-$C_6H_4CH_3$) do not undergo insertion into the nickel−methyl bond, even at elevated temperature.[8] However, exposure of these complexes to 1 atm of carbon monoxide leads to the formation of the analogous Ni−acyl complex **2**, which can undergo imine migratory insertion into the Ni−$COCH_3$ bond to generate the stable metallacycle **3**. The kinetic barrier to this imine insertion ($\Delta G^{\ddagger}$ = 23 kcal/mol at 40 °C) is significantly higher than that previously reported for alkene insertions into analogous nickel−carbon bonds (e.g., $\Delta G^{\ddagger}$ = 14 kcal/mol at −40 °C for styrene).[13,14] This rate difference, as well as the prerequisite CO insertion, led us to question the ability of imines to undergo competitive insertion in the presence of olefins. However, migratory insertion is considered to be an intramolecular reaction from the coordinated unsaturated substrate, and the basicity of the imine nitrogen should compete favorably with olefins for binding to the nickel center.

As an initial probe of this competition, 2 equiv of styrene was added to the nickel−imine complex **1** (Scheme 1). While the analogous non-imine-coordinated Ni−alkyl complexes are known to mediate the insertion of α-olefins very rapidly at ambient temperature,[15] complex **1** does not react with styrene after several days, and no evidence is observed for decomposition of complex **1** or olefin consumption. This lack of reactivity, and no visible signal broadening in the ^{1}H NMR spectrum, suggested that imine remains bound to the metal center during the reaction, effectively blocking olefin coordination for insertion. This is notable, since previous studies have determined that the imines in these nickel complexes are relatively labile and could be rapidly replaced by other nitrogen donors (e.g., other imines or CH_3CN).[8]

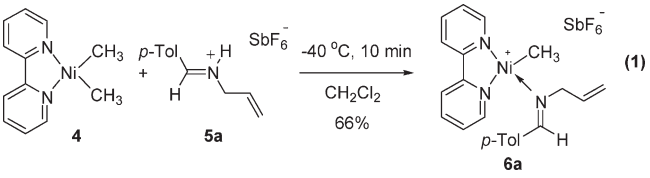
In an effort to initiate imine dissociation and subsequent insertion, carbon monoxide was added to the reaction mixture. This leads to the rapid insertion of carbon monoxide to form **2**, which subsequently converts to the imine insertion product **3** (Scheme 2), and no evidence for styrene insertion is observed.

The observation that a relatively bulky, trans-disubstituted imine can undergo preferential insertion relative to an α-olefin into the nickel−carbon bond is not consistent with their relative insertion rates. However, it does correlate with the stronger binding of the Lewis basic imine to the cationic nickel center. We rationalized that

Scheme 2. Selective Insertion of CO and Imine into Nickel−Methyl Bonds in the Presence of Styrene

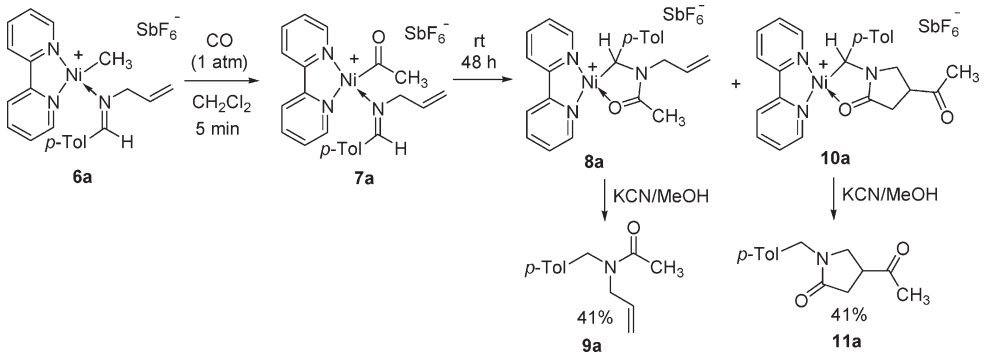


introducing a tethered α-olefin into the system, which may potentiallly undergo associative ligand substitution more readily than a free alkene, might allow for competitive insertion with imines. The alkene-tethered imine complex can be prepared by the addition of the iminium salt **5a** to (bipy)Ni$(CH_3)_2$ (**4**; bipy = 2,2′-bipyridyl) in CH_2Cl_2, which affords the deep red cationic complex **6a**, along with the rapid liberation of methane (eq 1). No evidence for olefin coordination or insertion was observed in **6a**, and the ^{1}H and ^{13}C NMR spectra display a single nickel−methyl signal (^{1}H NMR (CD_2Cl_2) δ 0.09 (s, 3H, Ni−CH_3)]), as well as downfield shifts in the imine resonances (^{1}H NMR δ 8.40 (s, =C(*H*)-*p*-Tol), ^{13}C NMR δ 169.1 (s, =C(H)-*p*-Tol); free imine, ^{1}H NMR δ 8.27 (s, =C(*H*)-*p*-Tol), ^{13}C NMR δ 161.4 (s, =*C*(H)*p*-Tol)), consistent with η^1 binding of the imine through the nitrogen lone pair.[7−9] These complexes are stable at room temperature in solution and can be isolated as solids. They are thermally unstable, however, and upon heating undergo complex decomposition, during which the ^{1}H NMR signals associated with the olefin are consumed.



Adding 1 atm of carbon monoxide to **6a** in CD_2Cl_2 and monitoring the reaction by ^{1}H NMR shows the rapid, in situ

Scheme 3. Products of Competitive Insertion with Olefin-Tethered Imines



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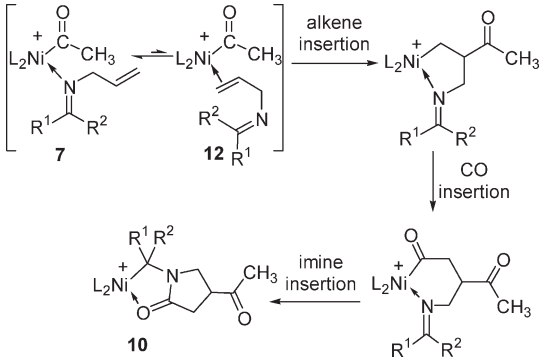
Scheme 4. CO/Olefin/CO/Imine Insertion Cascade

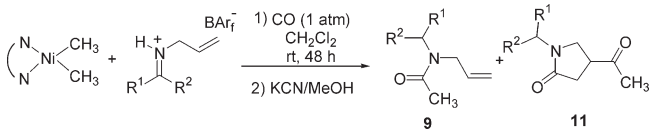


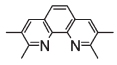
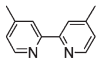
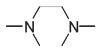
formation of the Ni−acyl complex **7a** (Scheme 3) within 5 min (Ni(COCH_3), δ 2.60 ppm).[16] This CO insertion initiates the competitive insertion of the olefin or imine unit into the newly generated nickel−acyl bond. After 48 h, the product of imine insertion (**8a**), as well as the bicyclic complex **10a** (as a mixture of diastereomers) are observed in a ca. 1:1 ratio.[17] Nickel complex **10a** represents the unusual product of the insertion cascade illustrated in Scheme 4, where olefin insertion into the Ni−acyl bond leads to the formation of a new Ni−alkyl bond, which can undergo insertion of a second equivalent of CO, followed by cyclization via imine insertion. Consistent with our previous observations, the metal-chelated amides are inert to further insertion reactions. The addition of a KCN/MeOH solution to these complexes readily cleaves the organic fragments from the metal center, affording the hydroacylated imine **9a** and the lactam **11a**.

Carbon monoxide appears to play a critical role in this reaction, as both an insertion monomer and an initiator for imine and alkene insertion. As was previously demonstrated, imine insertion requires the formation of a nickel−acyl ligand to be more thermodynamically viable.[8] The reason for alkene insertion proceeding only after CO insertion is less clear, though it may be due to the olefin being able to compete more favorably with the imine for coordination to the Ni−acyl complex, perhaps by CO behaving as a ligand to initiate an associative exchange process between imine and the alkene. Alternatively, the steric requirement of the nickel−acyl ligand may favor imine displacement. While no evidence for alkene coordination is observed, given the much faster rates of alkene insertion, even a small equilibrium formation of **12** (Scheme 4) should allow for competitive olefin insertion.

On the basis of this analysis, it was rationalized that modifying the ability of the imine to bind to the metal center should provide some degree of control over the relative insertion propensity of olefins and imines. For example, the use of electron-withdrawing substituents on the imine reduces its ability to bind to the metal center and favors cyclization by initial olefin insertion to form product **11** (Table 1, entry b). Conversely, more electron rich imines favor the formation of the imine insertion product **9** (Table 1, entry c). The ratio of products is also affected by the ligands on the metal center, where increasing electron density on the ligand (Table 1, entries d and e) favor lactam formation. The latter may result from the more electron rich and more strongly back-bonding nickel center favoring coordination to the alkene. Use of the harder tetramethylethylenediamine ligand yields only the product of imine insertion (Table 1, entry f).

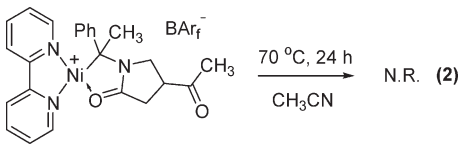
Table 1. Steric and Electronic Effects on Competitive Insertion[a]



Entry	R^1	R^2	Ligand	**9**	**11**
a	H	p-$CH_3C_6H_4$	2,2'-bipyridyl	41%	41%
b	H	p-$CF_3C_6H_4$	2,2'-bipyridyl	--	78%
c	H	p-$CH_3OC_6H_4$	2,2'-bipyridyl	61%	21%
d[b]	H	p-$CH_3C_6H_4$		10%	70%
e[b]	H	p-$CH_3C_6H_4$		10%	70%
f	H	p-$CH_3C_6H_4$		93%	--
g	CH_3	Ph	bipy	--	75%
h	Ph	Ph	bipy	--	77%

[a] (bipy)Ni(Me)$_2$ (200 mg, 0.85 mmol) and iminium salt (0.85 mmol) in 20 mL of CH_2Cl_2, 1 atm of CO, for 48 h at room temperature. [b] (L)$NiMe_2$ complexes generated in situ from (tmeda)$NiMe_2$.

Product selectivity also exhibits strong steric trends. Not surprisingly, use of the more sterically encumbered trisubstituted imines derived from acetophenone and benzophenone greatly reduced its ability to compete for insertion with the alkene (Table 1, entries g and h). Nevertheless, these imines undergo intramolecular insertion at room temperature to form the lactam in good yield. While β-hydride elimination is often the final step in many insertion-based cascade reactions, these metallacycles appear to be particularly resistant to further reaction, even upon prolonged heating (eq 2).[18] This is presumably due to the restricted rotation induced by tight chelation to the amide oxygen, which may prevent the β-hydrogens from adopting the syn orientation required for elimination to occur.



(2)

Control over the relative rates of insertion provided an unusual route to synthesize substituted lactams (**11**) via four separate insertion steps (CO, olefin, CO, and imine). In an effort to further probe the generality of this insertion cascade, longer tethers between the imine and olefin were employed. When the tether length was increased by one carbon, the six-membered lactam (**13**) was formed in only 20% yield, with the major product being instead the five-membered exo-cyclization product (**14**, 60%) (Scheme 5).

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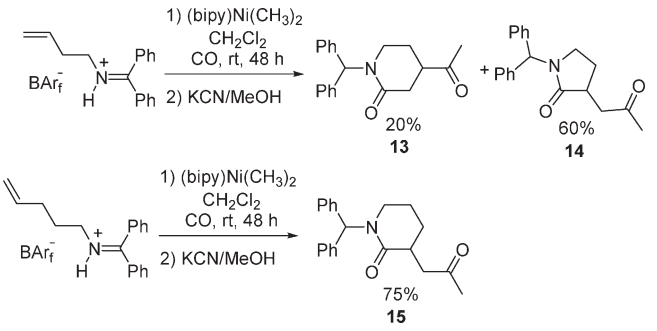
Scheme 5. Synthesis of Five- and Six-Membered Lactams



Extension of the tether to three methylene units provided the six-membered lactam (**15**) with almost complete selectivity (72% yield) and none (<5%) of the seven-membered lactam.

The change in regioselectivity in the olefin insertion step appears to be directly related to the length of the tether, though the exact nature of the directing influences on this reaction remains unclear. The *N*-allyl-substituted imines show complete selectivity for the sterically less congested 1,2-insertion product. This selectivity may be a result of the sterically bulky imine unit directing the orientation of olefin coordination prior to insertion (Scheme 6), or perhaps by the imine remaining coordinated to the nickel throughout the reaction, which would favor the formation of the five-membered chelate product **16** (n = 1). As the length of the tether is increased, the steric interactions at the nickel center should become less pronounced, and chelation of the imine should stabilize the generation of the smaller ring intermediate **17** (n = 2, 3). This 2,1-insertion regioselectivity is also that most commonly found in systems bearing smaller bite angle ligands (e.g., 2,2′-bipyridyl).[19] While the selectivity of olefin insertion is reversed with longer tether lengths, the regiochemistry of imine insertion remains unchanged, and in all cases, insertion occurs such that an amide bond is formed.

CONCLUSIONS

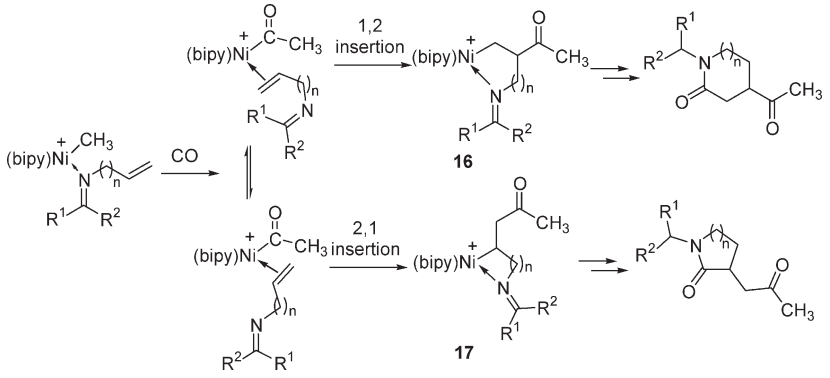
In conclusion, the above results suggest that imines and olefins are unusually competitive in their insertion propensity into nickel−carbon bonds. This is despite the larger steric requirement of substituted imines and their generally higher barriers to imine insertion. The relative insertion propensity shows clear steric and electronic effects and indicates that the superior coordinating ability of imines is a major factor in these reactions. These effects can be used to direct the reaction toward either imine hydroacylation or cyclization to form lactams. The latter has been used to design a new, nickel-mediated one-pot insertion cascade of CO, olefin, a second unit of CO, and imine, to synthesize five- and six-membered lactams in good yield under mild conditions. Further investigation into the relative insertion propensity of imines with other types of unsaturated monomers, as well as studies directed toward the coupling of these cyclizations into catalytic reactions (e.g., cross-coupling), should further expand the scope and utility of this chemistry.

EXPERIMENTAL SECTION

General Procedures. Unless otherwise noted, all manipulations were carried out under an inert atmosphere in a drybox or using standard Schlenk or vacuum line techniques. ^{1}H and ^{13}C NMR spectra were obtained on 300 or 400 MHz instruments. Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. Liquids were freeze−pump−thawed three times to degas before use. Diethyl ether was distilled from sodium benzophenone. Pentane, methylene chloride, and chlorobenzene were distilled from CaH_2. Deuterated solvents were dried as their protonated analogues but were vacuum-transferred from the drying agent. Ultrahigh-purity carbon monoxide was used in the reactions. Imines were prepared by standard procedures from the corresponding aldehyde and amine in THF at room temperature with magnesium sulfate as the drying agent. Benzophenone-derived imines were prepared by the reaction of benzophenone with the appropriate amine-HCl salt at room temperature overnight in methylene chloride. The solution was then filtered and the solvent removed under vacuum to give the desired imine as a colorless oil. (bipy)$NiMe_2$[20] and (4,4′-dimethylbipyridyl)$NiMe_2$[21] were prepared as described in the literature from (tmeda)$NiMe_2$[22] and the appropriate ligand. (2,3,8,9-tetramethyl-1,10-phenanthroline)$NiMe_2$ was prepared in a similar fashion as an insoluble green solid and used in situ without further purification for the experiment in Table 1. Iminium salts were prepared via addition of 1.1 equiv of anhydrous HCl in diethyl ether to the appropriate imine, followed by removal of the ether in vacuo and the addition of desired counterion salt (i.e., $AgSbF_6$, NaBArf[23]) in CH_2Cl_2 for 4 h. The precipitate was removed by filtration and the filtrate pumped to dryness and used in situ without further purification.

Synthesis of [(bipy)Ni(CH$_3$)(CH$_2$=CHCH$_2$N=(H)Tol]$^+$SbF$_6^-$ (6a). (bipy)$Ni(CH_3)_2$ (75 mg, 0.307 mmol) was suspended in THF (10 mL) and cooled to −40 °C to give an intensely dark green solution. In a separate vessel [CH_2=$CHCH_2$(H)N=$CH(p$-$C_6H_4CH_3$)]$^+SbF_6^-$ (124 mg, 0.307 mmol) was dissolved in THF (10 mL) and cooled

Scheme 6. Postulated Insertion Pathways for Five- and Six-Membered Lactam Formation



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to −40 °C. The iminium salt was then added to the rapidly stirred solution of (bipy)Ni(CH_3)$_2$ over 3 min via pipet. Near the end of the addition the dark green solution changed to a deep red color. The solution was cooled to −40 °C for 30 min and then filtered through Celite and recrystallized from diethyl ether (50 mL) at −40 °C. After 12 h the clear solvent mixture was decanted, and the solid residue was washed with pentane (3 × 5 mL) and then dried under vacuum to yield an orange powder (112 mg, 64% yield). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 9.39 (d, J = 11.6 Hz, 2H), 8.40 (s, 1H, C(H)-p-Tol), 8.36 (d, J = 5.6 Hz, 1H), 8.15−8.01 (m, 4H), 7.63−7.54 (m, 2H), 7.41−7.30 (m, 3H), 6.50−6.36 (m, 1H, CH_2CH=CH_2), 5.58 (d, J = 18.0 Hz, 1H, CH_2CH=CH_2), 5.36−5.30 (d, J = 10.9 Hz, 1H, CH_2CH=CH_2), 4.65 (d, J = 5.4 Hz, 2H, CH_2CH=CH_2), 2.38 (s, 3H, $C_6H_4CH_3$), 0.09 (s, 3H, Ni−CH_3). ^{13}C NMR (126 MHz, CD_2Cl_2): δ 169.1, 157.2, 156.4, 153.1, 149.8, 147.1, 146.1, 141.1, 136.6, 134.0, 129.3, 128.2, 127.7, 127.2, 123.4, 122.5, 115.5, 63.5, 21.4, −1.5. Anal. Calcd for $C_{22}H_{24}F_6N_3NiSb$: C, 42.29; H, 3.87; N, 6.72. Found: C, 41.97; H, 3.77; N, 6.55.

In Situ Generation of [(bipy)Ni(COCH$_3$)(CH$_2$=CHCH$_2$N=(H)-Tol)]$^+$SbF$_6^-$ (7a). Complex **6a** (10 mg, 0.016 mmol) was dissolved in 0.5 mL of CD_2Cl_2. The solution was transferred to a J. Young NMR tube and frozen in a liquid-nitrogen bath, the tube was evacuated, and 1 atm of carbon monoxide was added. Immediate ^{1}H NMR analysis showed that **7a** was formed within 5 min at ambient temperature, along with small amounts of the subsequent imine and/or olefin insertion products. In situ ^{1}H NMR analysis is consistent with this structure.[8] ^{1}H NMR (300 MHz, CD_2Cl_2): δ 9.51 (d, J = 7.7 Hz, 2H), 8.52 (s, 1H, C(H)-p-Tol), 8.18−8.01 (m, 4H), 7.88 (br, 1H), 7.65−7.30 (m, 5H), 6.33 (br, 1H, CH_2CH=CH_2), 5.64 (d, J = 19.9 Hz, 1H, CH_2CH=CH_2), 5.36 (d, J = 10.9 Hz, 1H, CH_2CH=CH_2), 4.65 (m, 2H, CH_2CH=CH_2), 2.54 (s, 3H ($NiCOCH_3$), 2.32 (s, 3H, $C_6H_4CH_3$).

General Procedure for the Cyclocarbonylation of Imines. (bipy)NiMe_2 (200 mg, 0.846 mmol) was dissolved in 10 mL of dry methylene chloride to give an intensely blue-green solution. One equivalent of iminum salt was dissolved in 10 mL of methylene chloride and added dropwise to a stirred solution of (bipy)NiMe_2. The solution rapidly turned deep red near the end of the addition, and the evolution of methane was noted. The solution was then transferred to a 300 mL reaction bomb and frozen in a liquid nitrogen bath, the bomb was evacuated, and 1 atm of carbon monoxide was added. The mixture was warmed to room temperature and stirred for 48 h. The organic products were then cleaved from the nickel center by addition of a saturated solution of KCN/MeOH. This was accompanied by a rapid color change from deep red to pale yellow. The solvent was removed in vacuo, the residue was dissolved in methylene chloride, this solution was filtered through Celite, and the solvent was removed again. The resulting oil was then dissolved in ethyl acetate, washed twice with 10% HCl solution, and purified by silica gel column chromatography. The identity of **11g** was confirmed by comparison of ^{1}H and ^{13}C NMR data to those of the known compound.[24]

*N-Allyl-N-(4-methylbenzyl)acetamide (**9a**).* Yield: 41% isolated, oil. The product was observed as a mixture of amide rotamers at ambient temperature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20−7.00 (m, 4H), 5.81−5.65 (m, 1H), 5.24−5.04 (m, 2H), 4.75 (s, 2H, major rotamer), 4.43 (s, 2H, minor rotamer), 3.98 (d, 2H, J = 7.6 Hz, minor), 3.79 (d, 2H, J = 7.6 Hz, major), 2.38 (s, 3H, minor), 2.31 (s, 3H, major), 2.38 (s, 3H, minor), 2.36 (s, 3H, major). ^{13}C NMR (126 MHz, $CDCl_3$): δ 171.1, 169.8, 137.5, 137.3, 134.7, 133.2, 132.6, 129.8, 129.5, 128.5, 126.5, 117.7, 117.0, 50.8, 49.9, 48.0, 47.9, 21.8, 21.6, 21.4, 21.3. IR (KBr): ν_{CO} 1650 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C 76.41; H, 8.72; N, 7.23.

*N-Allyl-N-(4-methoxybenzyl)acetamide **(9c)**.* Yield: 61% isolated, oil. The product was observed as a mixture of amide rotamers at ambient temperature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, J = 8.8 Hz, 2H, major), 7.18 (d, J = 8.8 Hz, 2H, minor), 6.78 (d, J = 9.6 Hz, 2H, minor), 6.62 (d, J = 9.6 Hz, 2H, major), 5.81−5.61 (m, 1H), 5.24−5.07 (m, 2H), 4.50 (s, 2H, major), 4.41 (s, 2H, minor), 3.96 (d, J = 5.2 Hz, 2H, minor), 3.79 (d, J = 5.2 Hz, 2H, major), 2.78 (s, 3H), 2.32 (s, 3H, minor), 2.21 (s, 3H, major). ^{13}C NMR (126 MHz, $CDCl_3$ 65 °C): δ 171.1, 171.0, 159.2, 159.1, 133.2, 132.7, 129.9, 128.7, 127.8, 127.5, 117.6, 116.9, 114.5, 114.1, 55.5, 55.4, 50.6, 49.9, 47.7, 47.6, 21.9, 21.7. IR (KBr): ν_{CO} 1650 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 70.71; H, 8.15; N, 6.29.

*4-Acetyl-1-(4-methylbenzyl)pyrrolidin-2-one **(11a)**.* Yield: 41% isolated, oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20−7.02 (m, 4H), 4.39 (dd, J = 14.6, 8.3 Hz, 2H), 3.50−3.12 (m, 3H), 2.62 (d, J = 9.8 Hz, 2H), 2.34 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.1, 172.2, 137.7, 133.1, 129.7, 128.4, 47.3, 46.5, 43.5, 33.4, 28.6, 21.3. IR (KBr): ν_{CO} 1699 cm^{-1}. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.44; H, 7.85; N, 6.39.

*4-Acetyl-1-(4-(trifluoromethyl)benzyl)pyrrolidin-2-one **(11b)**.* Yield: 78% isolated, oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, 2H, 8.4 Hz), 7.35 (d, J = 8.4 Hz, 2H), 4.42 (d, J = 11.4 Hz, 2H), 3.45 (m, 1H), 3.40−3.20 (m, 2H), 2.63 (m, 2H), 2.19 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.0, 172.5, 140.3, 128.5, 128.4, 125.9, 125.8, 47.4, 46.3, 43.3, 33.2, 28.7. IR (KBr): ν_{CO} 1699 cm^{-1}. Anal. Calcd for $C_{14}H_{14}F_3NO_2$: C, 58.95; H, 4.95; N, 4.91. Found: C, 58.58; H, 5.21; N, 5.18.

*4-Acetyl-1-(4-methoxybenzyl)pyrrolidin-2-one **(11c)**.* Yield: 21% isolated, oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 4.44 (d, 1H, J = 11.2 Hz, 2H), 4.32 (d, J = 11.2 Hz, 1H), 3.79 (s, 3H), 3.44 (m, 1H), 3.35 (m, 1H), 3.25 (m, 1H), 2.66 (m, 2H), 2.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.15, 171.1, 159.4, 129.7, 128.1, 114.3, 55.5, 47.3, 46.2, 43.5, 33.4, 28.7. IR (KBr): ν_{CO} 1699 cm^{-1}. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.57; H, 7.15; N, 5.29.

*4-Acetyl-1-benzhydrylpyrrolidin-2-one **(11h)**.* Yield: 77% isolated, oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.20 (m, 6H), 7.20−7.08 (m, 4H), 6.57 (s, 1H), m, 3.45−3.35 (m, 1H), 3.33−3.19 (m, 2H), 2.71 (d, J = 11.6 Hz, 2H), 2.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.3, 172.5, 138.5, 138.2, 128.9, 128.8, 128.6, 128.5, 128.0, 127.9, 58.9, 45.3, 43.6, 33.5, 28.8. IR (KBr): ν_{CO} 1699 cm^{-1}. Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 78.20; H, 7.02; N, 4.34. HRMS: m/z calcd for $C_{18}H_{20}NO_2^+$ 294.148 86, found 294.148 75.

*4-Acetyl-1-benzhydrylpiperidin-2-one **(13)**.* Yield: 20% isolated, oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.15 (m, 11H, aromatic and NC(H)Ph_2, as assigned by 2D NMR), 3.19 (m, 1H), 3.00−2.81 (m, 2H), 2.69 (m, 2H), 2.19 (s, 3H), 2.08 (m, 1H), 1.85 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 208.3 (CH_3COC), 168.7 (CON−), 138.7, 138.4, 129.7, 128.7, 128.2, 128.0, 127.5(4), 127.5, 60.0 ($CHPh_2$), 45.7, 42.8, 33.9, 28.3, 25.3.[25] IR (KBr): ν_{CO} 1699 cm^{-1} Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.27; H, 7.20; N, 4.34. HRMS: m/z calcd for $C_{20}H_{22}NO_2^+$ 308.164 51, found 308.164 42.

*1-Benzhydryl-3-(2-oxopropyl)pyrrolidin-2-one **(14)**.* Yield: 60% isolated, oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.20 (m, 6H), 7.20−7.14 (m, H), 6.58 (s, 1H), 3.23−3.02 (m, 3H), 2.90 (m, 1H), 2.59 (m, 1H), 2.35 (m, 1H), 2.19 (s, 3H), 1.7 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$, 65 °C): δ 207.1, 176.0, 138.8, 138.7, 129.1, 128.8, 128.7, 128.2, 127.9, 127.6, 59.1, 44.9, 42.9, 38.2, 30.4, 25.8.[25] IR (KBr): ν_{CO} 1699 cm^{-1}. Anal. Calcd for $C_{20}H_{21}NO_2$: C 78.15; H, 6.89%; N, 4.56. Found: C, 78.27; H, 7.20; N, 4.43. HRMS: m/z calcd for $C_{20}H_{22}NO_2^+$ 308.164 51, found 308.163 99.

*1-Benzhydryl-3-(2-oxopropyl)piperidinone **(15)**.* Yield: 72% isolated, oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.10 (m, 11H, aromatic and NC(H)Ph_2, as assigned by 2D NMR), 3.18−2.84 (m, 4H), 2.65 (m, 1H), 2.19 (s, 3H), 1.95 (m, 1H), 1.80 (m, 2H), 1.58 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.7, 172.4, 139.1, 129.5, 128.9, 128.7, 128.6, 128.5, 127.6, 127.5, 60.3, 45.7, 44.4, 38.4, 30.6, 27.1, 22.7.[25] IR (KBr): ν_{CO} 1699 cm^{-1} Anal. Calcd for $C_{21}H_{23}NO_2$: C, 78.47; H, 7.21; N, 4.36. Found: C, 78.11; H, 7.63; N, 4.22.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR data for compounds **9** and **11** and ^{1}H and ^{13}C NMR and 2D NMR data for compounds **13**−**15**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) While complex **7a** undergoes imine and alkene insertion too rapidly to be isolated, in situ ^{1}H NMR analysis shows it to be analogous to previously generated nickel−acyl complexes:[8]: see the Experimental Section for details.

(17) NMR analysis of the mixture of nickel-chelated amide products in Scheme 3 shows complex **8a** (^{1}H NMR (CD_2Cl_2): δ 4.39 (s, 1H, C(*H*)-*p*-Tol), 2.15 (s, 3H, $COCH_3$)) and two sets of signals for **10a** (^{1}H NMR (CD_2Cl_2): δ 4.10 (s, 1H, C(*H*)-*p*-Tol) and 4.06 (s, 1H C(*H*)-*p*-Tol); 2.11 (s, 3H, $COCH_3$) and 2.07 (s, 3H, $COCH_3$)), in a ca. 1:1 ratio, on the basis of integration of CH_3CO− reasonances. While products **8** and **10** could not be separated for full characterization, these data are similar to those for previously isolated metal-chelated amides,[8,9] and cleavage of the amide ligands with KCN/MeOH was used to confirm the amide ligand structure.

(18) The nickel complex in eq 2 was generated in situ using the general procedure given in Table 1. Before cleavage of the amide ligand with KCN/MeOH, the solvent was removed, the nickel complex was dissolved in CD_3CN, and the solution was heated to 70 °C and monitored by ^{1}H NMR spectroscopy.

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