$Ru_3(CO)_{12}$- and $Rh_4(CO)_{12}$-Catalyzed Reactions of Pyridylolefins or *N*-(2-Pyridyl)enamines with CO and Olefins. Carbonylation at Olefinic C−H Bonds

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This paper describes a study of the $Ru_3(CO)_{12}$-catalyzed carbonylation at an olefinic C−H bond. The reaction of pyridylolefins with CO and ethylene in the presence of a catalytic amount of $Ru_3(CO)_{12}$ in toluene results in propionylation at an olefinic C−H bond in pyridylolefins. The carbonylation occurs regioselectively at a position γ to the pyridine nitrogen. Transition-metal complexes other than $Ru_3(CO)_{12}$, that have thus far been examined exhibit no catalytic activity, and ethylene serves as the only olefin. A similar tendency has been noted in the previously reported carbonylation at a C−H bond in the benzene ring of pyridylbenzenes. This reaction can be also applied to *N*-(2-pyridyl)enamines, in which an olefin unit is separated from the pyridine ring by an sp^3-nitrogen atom. The reaction of *N*-(2-pyridyl)enamines with CO and ethylene gives the corresponding ethyl ketones as the coupling products. Interestingly, $Rh_4(CO)_{12}$ also shows high catalytic activity in the case of *N*-(2-pyridyl)enamines. In addition, olefins such as propene, 1-hexene, 3,3-dimethyl-1-butene, styrene, cyclopentene, acryl acid methyl ester, ethyl vinyl ether, and trimethylvinylsilane can also be used. This is in sharp contrast to the case of the carbonylation at a C−H bond in pyridylbenzenes reported previously and to the results of pyridylolefins as mentioned above, where $Ru_3(CO)_{12}$ is the only active catalyst and hexene cannot substitute for ethylene.

Introduction

The development of transition-metal-catalyzed reactions involving cleavage of a C−H bond represents a challenging project in organic synthesis.[1] The catalytic addition of a C−H bond of benzene derivatives to olefins has been extensively studied, and many papers on the subject have appeared in the literature.[2−6] It has also been found that an olefinic C−H bond can be added to olefins[7−9] and that this reaction can be utilized for additions to acetylenic bonds.[10,11] In contrast, a comparatively small effort has been made relative to the effective, catalytic carbonylation of a C−H bond, although the reaction represents a direct method for the introduction of a carbonyl functionality to readily available, simple starting materials, such as hydrocarbons. The $Ru_3(CO)_{12}$-catalyzed carbonylation at a C−H bond α to the nitrogen atom in pyridine derivatives was reported by Moore in 1992.[12] This represents the first effective carbonylation at a C−H bond, to the best of our knowledge. We have reported the $Ru_3(CO)_{12}$-catalyzed reaction of imidazoles with CO and olefins, in which carbonylation also occurs at the C−H bond α to the sp^2-nitrogen atom.[13]

(1) For recent reviews, see: Jones, W. D. In *Selective Hydrocarbon Activation Principles and Progress*; Davies, J. A.; Watson, P. L.; Greenberg, A.; Liebman, J. F.; Eds.; VCH Publishers: New York, 1990; p 113. Ryabov, A. D. *Chem. Rev.* **1990**, *90*, 403.

(2) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529. Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Pure Appl. Chem.* **1994**, *66*, 1527. Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62. Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *J. Organomet. Chem.* **1995**, *504*, 151. Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Chem. Lett.* **1996**, 109. Murai, S.; Chatani, N.; Kakiuchi, F. *Pure Appl. Chem.* **1997**, *69*, 589. Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117.

(3) Lim, Y.-G.; Kim, Y. H.; Kang, J.-B. *J. Chem. Soc., Chem. Commun.* **1994**, 2267. Lim, Y.-G.; Kim, Y. H.; Kang, J.-B. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2201.

(4) Guo, H.; Weber, W. P. *Polym. Bull.* **1994**, *32*, 525. Guo, H.; Tapsak, M. A.; Weber, W. P. *Polym. Bull.* **1994**, *33*, 417. Guo, H.; Tapsak, M. A.; Weber, W. P. *Polym. Bull.* **1995**, *34*, 49. Guo, H.; Weber, W. P. *Polym. Bull.* **1995**, *35*, 259. Tapsak, M. A.; Guo, H.; Weber, W. P. *Polym. Prep.* **1995**, *36*, 451. Guo, H.; Tapsak, M. A.; Weber, W. P. *Polym. Prep.* **1995**, *36*, 705. Guo, H.; Tapsak, M. A.; Weber, W. P. *Macromolecules* **1995**, *28*, 4714. Guo, H.; Wang, G.; Tapsak, M. A.; Weber, W. P. *Macromolecules* **1995**, *28*, 5686. Wang, G.; Guo, H.; Weber, W. P. *J. Organomet. Chem.* **1996**, *521*, 351. Lu, P.; Paulasaari, J. K.; Weber, W. P. *Macromolecules* **1996**, *29*, 8583. Wang, G.; Guo, H.; Weber, W. P. *Polym. Bull.* **1996**, *37*, 169. Guo, H.; Wang, G.; Weber, W. P. *Polym. Bull.* **1996**, *37*, 423. Guo, H.; Tapsak, M. A.; Wang, G.; Weber, W. P. *ACS Symp. Ser.* **1996**, *624*, 99. Wang, G.; Tongco, E.; Guo, H.; Prakash, G. K. S.; Weber, W. P. *Polym. Prep.* **1996**, *37*, 329. Lu, P.; Paulasaari, J.; Weber, W. P. *Polym. Prep.* **1996**, *37*, 342. Guo, H.; Weber, W. P. *Polym. Prep.* **1996**, *37*, 344. Londergan, T. M.; Weber, W. P. *Macromol. Rapid Commun.* **1997**, *18*, 207. Londergan, T. M.; Weber, W. P. *Polym. Prep.* **1997**, *38*, 184.

(5) Harris, P. W. R.; Woodgate, P. D. *J. Organomet. Chem.* **1996**, *506*, 339. Harris, P. W. R.; Woodgate, P. D. *J. Organomet. Chem.* **1997**, *530*, 211.

(6) Grigg, R.; Savic, V. *Tetrahedron Lett.* **1997**, *38*, 5737.

(7) (a) Kakiuchi, F.; Tanaka, Y.; Sato, T.; Chatani, N.; Murai, S. *Chem. Lett.* **1995**, 679. (b) Fujii, N.; Kakiuchi, F.; Chatani, N.; Murai, S. *Chem. Lett.* **1996**, 939. (c) Fujii, N.; Kakiuchi, F.; Yamada, A.; Chatani, N.; Murai, S. *Chem. Lett.* **1997**, 425. (d) Fujii, N.; Kakiuchi, F.; Yamada, A.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 285.

(8) Trost, B. M.; Imi, K.; Davies, I. W. *J. Am. Chem. Soc.* **1995**, *117*, 5371.

(9) Lim, Y.-G.; Kang, J.-B.; Kim, Y. H. *J. Chem. Soc., Chem. Commun.* **1996**, 585.

(10) Kakiuchi, F.; Yamamoto, Y.; Chatani, N.; Murai, S. *Chem. Lett.* **1995**, 681.

(11) Halbritter, G.; Knoch, F.; Wolski, A.; Kisch, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1603. Halbritter, G.; Konch, F.; Kisch, H. *J. Organomet. Chem.* **1995**, *492*, 87. Aulwurm, U. R.; Melchinger, J. U.; Kisch, H. *Organometallics* **1995**, *14*, 3385. Dürr, U.; Heinemann, F. W.; Kisch, H. *J. Organomet. Chem.* **1997**, *541*, 307. Review: Dürr, U.; Kisch, H. *Synlett* **1997**, 1335.

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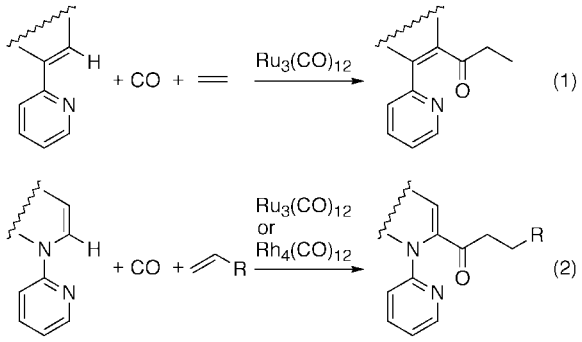
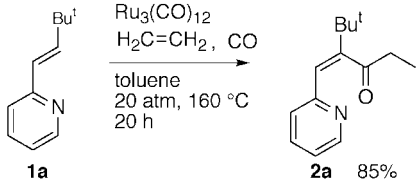
In these two reactions, carbonylation occurred at a C−H bond in the heteroaromatic ring. It is also noteworthy that we recently reported on the carbonylation at a C−H bond in the benzene ring. Thus, the $Ru_3(CO)_{12}$-catalyzed reaction of pyridylbenzenes with CO (20 atm) and ethylene in toluene at 160 °C gave rise to site selective carbonylation at an ortho C−H bond in the benzene ring.[14] The pyridine ring is necessary as a directing group to promote the reaction.[15] An imino group was also found to be a good directing group for carbonylation at an ortho C−H bond in aromatic imines.[16] Since these discoveries, we have been examining the carbonylation of a variety of sp^2 C−H bond systems, such as heteroaromatic, olefinic, and functionalized olefinic C−H bonds, as well as related structures. Herein, we report our results on the carbonylation of pyridylolefins (eq 1) and *N*-(2-pyridyl)enamines (eq 2) catalyzed by $Ru_3(CO)_{12}$ and, in the latter cases, by $Ru_3(CO)_{12}$ and $Rh_4(CO)_{12}$ as well. Such coupling of an olefinic C−H bond with CO and an olefin provides an efficient new route to α,*β*-unsaturated ketones. It is interesting to note that, for the case of coupling with *N*-(2-pyridyl)enamines and CO, a variety of substituted olefins can be used.



Results and Discussion

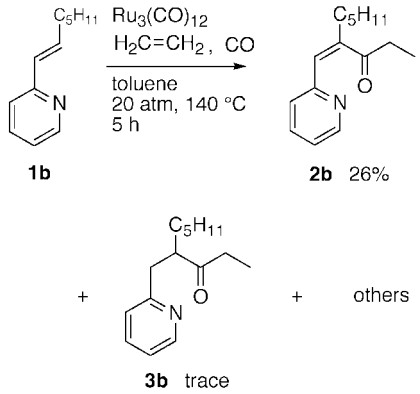
The reaction of 2-pyridylethylene (2 mmol) with CO (initial pressure 20 atm at 25 °C in a 50-mL stainless steel autoclave) and ethylene (7 atm) in toluene (6 mL) in the presence of a catalytic amount of $Ru_3(CO)_{12}$ (0.10 mmol) at 160 °C for 20 h, under reaction conditions that are as the same as those used for the $Ru_3(CO)_{12}$-catalyzed reaction of pyridylbenzenes,[14] gave a complex mixture in which the corresponding coupling product cannot clearly be observed. This may be due to polymerization of 2-pyridylethylene. Lower reaction temperature (140 °C) and shorter reaction times did not improve on this reaction.

Next, we examined the reaction of pyridylolefins having a substituent at the olefinic portion. The reaction of 2-[(*E*)-3,3-dimethyl-1-butenyl]pyridine (**1a**) with CO and ethylene resulted in the carbonylation at a C−H bond to give (*Z*)-5,5-dimethyl-4-[(2-pyridyl)methylene]hexan-3-one (**2a**) as the sole product in 85% yield (eq 3). The



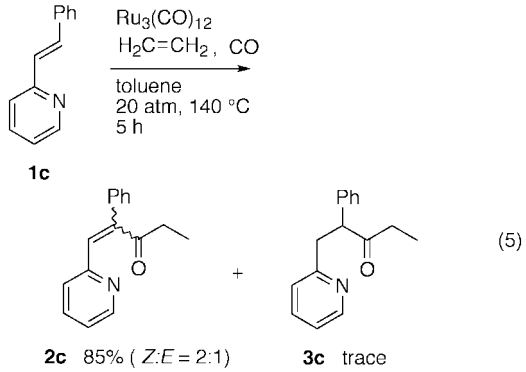
coupling was highly siteselective at a C−H bond which was *γ* to the pyridine nitrogen, and no other isomers were detected by ^1H and ^{13}C NMR spectroscopy or GC−MS of the reaction mixture. The regiochemistry and stereochemistry of **2a** was established by long-range C−H COSY and H−H NOESY spectroscopy. The long-range C−H COSY spectrum exhibited third-order coupling for the 3-position in the pyridine ring and the vinyl hydrogen, indicating that the carbonylation occurred at an olefinic C−H bond *γ* to the pyridine nitrogen. The assignment of the olefin geometry was deduced from the H−H NOESY spectrum, which showed that the vinyl hydrogen signal was within NOE distance of the methyl hydrogen one in the *tert*-butyl group, indicating a cis configuration of the vinyl hydrogen and *tert*-butyl group. Other transition-metal carbonyl complexes, such as $Rh_4(CO)_{12}$, $Co_2(CO)_8$, and $Os_3(CO)_{12}$, were not effective for the reaction in eq 3. Olefins, such as hexene and 3,3-dimethyl-1-butene did not work, and only starting material **1a** was recovered. These observations are nearly the same as the results of carbonylation at a C−H bond in the benzene ring reported previously.[14]

The success of the reaction of **1a** prompted us to examine the reaction of a variety of pyridylolefins with ethylene in the presence of $Ru_3(CO)_{12}$. The replacement of the *tert*-butyl group by a pentyl group, as in **1b**, gave a complex mixture which included the expected carbonylation product (**2b**, 26%) and a trace amount of its saturated ketone **3b** (detected by GC-MS, but not isolated). Other products are the stereosiomer of **2b** and olefin−isomerization products of **2b**, and these could not be isolated in pure form (eq 4).

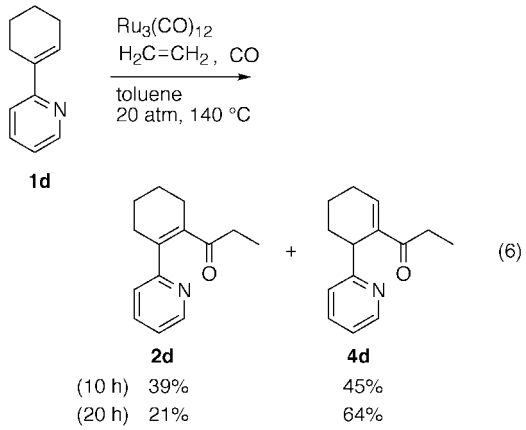


The reaction of the *γ*-phenyl-substituted compound **1c** with CO and ethylene at 140 °C for 5 h gave the corresponding ketone **2c** in 85% total yield with a *Z*/*E* ratio of 2:1, along with a trace amount of saturated ketone **3c** (eq 5). Longer reaction times (10 h) or more rigorous conditions (160 °C) increased the yield of the saturated ketone **3c**, which the expected primary product

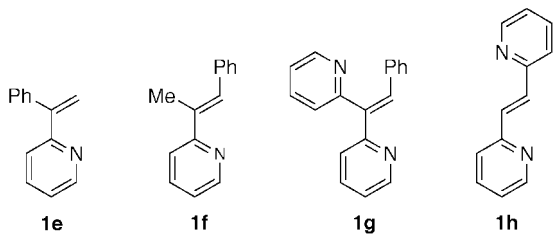
(12) Moore, E.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888.
(13) Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 493.
(14) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 2604.
(15) A related carbonylation promoted by a pyridine ring as a directing group was reported. Ishii, Y.; Chatani, N.; Kakiuchi, F.; Murai, S. *Organometallics* **1997**, *16*, 3615.
(16) Fukuyama, T.; Chatani, N.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 5647.



2c produced via the ruthenium-catalyzed water gas shift reaction with in situ water.[17] The carbonylation also proceeds smoothly for a cyclic pyridylolefin **1d** to give a mixture of isomers **2d** and **4d** in 84% yield, along with a trace amount of saturated ketone (eq 6). A longer

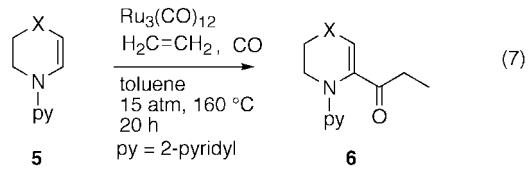


reaction time (20 h) led to the predominant formation of **4d**. Compound **4d** would be produced by olefin isomerization of **2d** because of steric congestion in **2d**.[18] In contrast to pyridylbenzenes,[14] side reactions, such as olefin isomerization and further hydrogenation, cannot be suppressed in the reaction of pyridylolefins. In addition, the reaction suffers from limitations regarding the structure of the substrates. The pyridylolefins, **1e**−**h**, shown below gave complex mixtures.



We propose that the reaction mechanism is similar to that which operates for pyridylbenzenes,[14] as shown in Scheme 1. Coordination of the pyridine nitrogen to ruthenium complex brings the metal in close proximity to a C−H bond, which can then be cleaved. The cleavage of an olefinic C−H bond of **1** gives a five-membered metallacycle such as **I**. Although the stoichiometric reaction of $Ru_3(CO)_{12}$ with pyridylolefins is not known, Deeming reported that $Os_3(CO)_{10}(CH_3CN)_2$ reacts with 2-pyridylethylene to give a five-membered metallacyclic complex related to **I** via the cleavage of an olefinic C−H bond.[19] Insertion of ethylene into H−Ru bond of **I** gives the ethyl complex **II**, which undergoes CO insertion,[20] followed by reductive elimination to give the final product **2**.

Carbonylation of pyridylolefins is less efficient than that of pyridylbenzenes because of side reactions, such as olefin isomerization and hydrogenation of the C=C double bond. To extend the carbonylation at an olefinic C−H bond, we investigated the reaction using a variety of olefins, such as cyclic, acyclic, terminal, internal, and functionalized olefins. Among these, we found that cyclic olefins involving a nitrogen atom in the ring gave high yields of carbonylation products. The reaction of 1,2,3,4-tetrahydro-1-methyl-4-(2-pyridyl)pyrazine (**5a**; 1 mmol) with CO (15 atm) and ethylene (10 atm) in toluene (3 mL) in the presence of $Ru_3(CO)_{12}$ (0.04 mmol) at 160 °C for 20 h gave 1-[1,4,5,6-tetrahydro-4-methyl-1-(2-pyridyl)-pyrazyl]-1-propanone (**6a**)[21] in 95% isolated yield after column chromatography (eq 7). Carbonylation takes



place regioselectively at an olefinic C−H bond α to the nitrogen atom substituted by the pyridine ring. The reaction of morpholine derivative **5b** also afforded the corresponding α,β-unsaturated ketone **6b** in a high yield. In contrast to **5a** and **5b**, 1,2,3,4-tetrahydro-1-(2-pyridyl)-pyridine (**5c**; X = CH_2) did not work well. The reaction of **5c** gave the corresponding coupling product **6c** and its saturated ketone **7c** (structure not shown) in somewhat lower yield (total 28%), along with 50% of unreacted **5c**. The reactivity decreased in the order of **5a** ∼ **5b** > **5c**. A similar high reactivity of cyclic olefins bearing an oxygen atom in the ring was reported for the Ru-catalyzed addition of an olefinic C−H bond in α,β-unsaturated ketones to olefins.[7a]

The catalytic activity of other transition-metal carbonyl complexes for the reaction of **5b** with CO and ethylene was then examined. It had been anticipated that only $Ru_3(CO)_{12}$ had catalytic activity because it is the only active catalyst for carbonylation at a C−H bond in benzene ring of pyridylbenzenes[14] and pyridylolefins

(17) Recent reviews on water gas shift reaction, see: Laine, R. M.; Crawford, E. J. *J. Mol. Catal.* **1988**, *44*, 357. Ford, R. C.; Rokicki, A. *Adv. Organomet. Chem.* **1988**, *28*, 139. Kalck, P.; Monteil, F. *Adv. Organomet. Chem.* **1992**, *34*, 219.

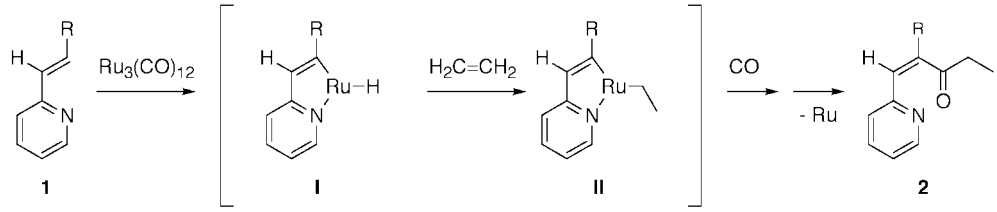
(18) $Ru_3(CO)_{12}$-catalyzed olefin isomerization is known: Castiglioni, M.; Milone, L.; Osella, D.; Vaglio, G. A.; Valle, M. *Inorg. Chem.* **1976**, *15*, 394. Castiglioni, M.; Giordano, R.; Sappa, E. *J. Organomet. Chem.* **1987**, *319*, 167. Kaspar, J.; Graziani, M.; Trovarelli, A. Dolcetti, G. *J. Mol. Cat.* **1989**, *55*, 229.

(19) Burgess, K.; Holden, H. D.; Johnson, B. F. G.; Lewis, J.; Hursthouse, M. B.; Walker, N. P. C.; Deeming, A. J.; Manning, P. J.; Peters, R. *J. Chem. Soc., Dalton Trans.* **1985**, 85.

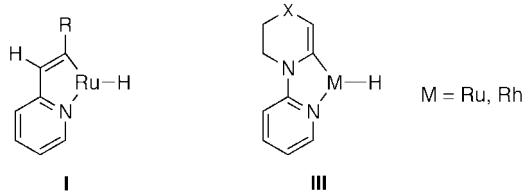
(20) Insertion may occur either into the Et−Ru bond or, more likely, into the sp^2-C−Ru bond.

(21) The structure of **6a** was confirmed by X-ray analysis. See ref 15.

Scheme 1



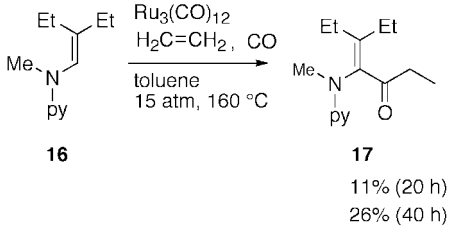
described above. Complexes such as $W(CO)_6$, $Mn_2(CO)_{10}$, $Re_2(CO)_{10}$, $Fe_3(CO)_{12}$, $Os_3(CO)_{12}$, and $Ir_4(CO)_{12}$ proved to be totally inactive, as expected. Interestingly, however, $Rh_4(CO)_{12}$ showed highly catalytic activity for the reaction of **5b** to give **6b** in 93% yield, while no carbonylation of pyridylbenzenes[14] and pyridylolefins was observed when $Rh_4(CO)_{12}$ was used as a catalyst. $Rh_4(CO)_{12}$ was also active for the production of **6a** (93%). The hydride complex **III**, analogous to **I**, is likely to play a key role in



the formation of **6**. The cyclometalated complex **III** structurally differs from **I** in that it has no conjugated unsaturated bonds in the five-membered metallacyclic ring. The subtle changes in the intermediate framework seem to be largely responsible for the phenomena that $Rh_4(CO)_{12}$ also catalyzes this carbonylation and a variety of olefins can be used (vide infra) in *N*-(2-pyridyl)-enamines such as **5**.[22]

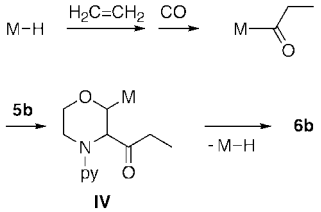
In contrast to the reaction of pyridylbenzenes[14] and pyridylolefins such as **1**, the scope of the reaction of *N*-(2-pyridyl)enamines with respect to applicable olefins is not limited to ethylene or 3,3-dimethyl-1-butene. Typical results are shown in Table 1. In most cases, a mixture of the linear and branched coupling products were obtained in favor of a linear isomer. The reaction of **5b** with CO and propene gave a mixture of 1-[3,4-dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-1-butanone (**8a**) and its branched isomer **8b** in high yields (entry 1). Carbonylation of **5b** with 1-hexene afforded 1-[3,4-dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-1-heptanone (**9a**) and its branched isomers **9b** and **9c** in 38, 21, and 7% yields, respectively (entry 2). The reaction of 2-hexene (cis/trans mixture) also gave the same three regioisomers in 31% combined yield in exactly the same ratio as that found for the reaction of 1-hexene.[24] The use of 3,3-dimethyl-1-butene gave only a linear isomer (entry 3). Aryl-substituted and cyclic olefin also react with **5b** (entries 4 and 5). In the case of an electron-deficient olefin, such as methyl acrylate, only the linear coupling compound **13** was obtained, with no branched isomer being detected (entry 6). An olefin with an electron-donating group, such as ethyl vinyl ether, can also be used, and the corresponding ketones **14a** and **14b** were obtained, along with **6b**[25] (entry 7). A reaction with trimethylvinylsilane gave the corresponding ketone **15a** (30%) and enol silyl ether **15b** (33%), along with **6b** in 18% yield (entry 8). The branched isomer, α-silyl ketone, may have isomerized to the enol silyl ether **15b** by 1,3-silyl migration in situ.[26] It is likely that the byproduct **6b** arises from the reaction of **5b** with CO and ethylene, which is generated in situ from the vinylsilane.[27] Alternatively, it could be produced by in situ hydrolysis of **15b**. The rhodium catalyst, $Rh_4(CO)_{12}$, showed a reactivity and selectivity similar to those of $Ru_3(CO)_{12}$ (entries 1 and 3−6). It is noteworthy that a variety of olefins can be applied in *N*-(2-pyridyl)enamines, which is in contrast to the cases of pyridylbenzenes[14] and pyridylolefins.

We next examined the reaction of acyclic enamines (eq 8). The reaction of *N*-(2-ethyl-1-butenyl)-*N*-methyl-2-pyridinamine (**16**) with CO and ethylene gave the corresponding ethyl ketone (**17**), albeit in low yield (11%). That the recovered starting material **16** contains *N*-allylamine isomer indicates that partial isomerization of the double bond in the starting material **16** occurs. The yield of **17** was improved to 26% when the reaction was carried out for 40 h.



(8)

(22) Considerable differences between the results for pyridylolefins and those of *N*-(2-pyridyl)enamines cannot rule out an alternative mechanism. An alternative one is shown below, which does not contain an oxidative addition−reductive elimination process in a catalytic cycle.[23] It is also necessary to allow for the inversion on the carbon α to metal of intermediate **IV** or anti elimination from the intermediate **IV** in order to cause *β*-hydride elimination in this mechanism.



(23) The insertion of an olefin into a transition metal-acyl bond and the following *β*-hydride elimination have been reported. Brumbaugh, J. S.; Whittle, R. R.; Parvez, M. A.; Sen, A. *Organometallics* **1990**, *9*, 1735. Dekker: G. P. C. M.; Elsevier: C. J.; Vrieze, K.; van Leeuwen, P. W. N. M.; Roobeek, C. F. *J. Organomet. Chem.* **1992**, *430*, 357.

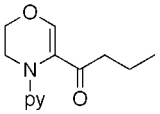
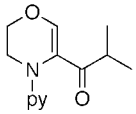
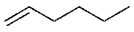
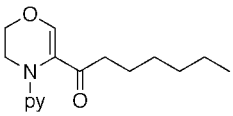
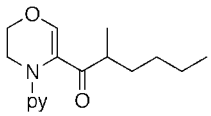
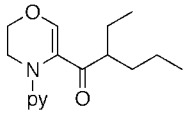
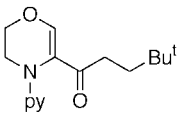
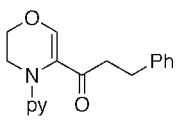
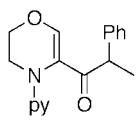
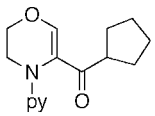
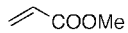
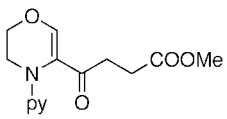
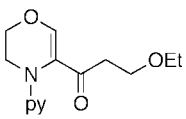
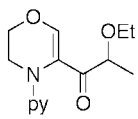
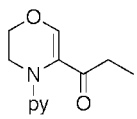
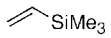
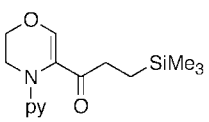
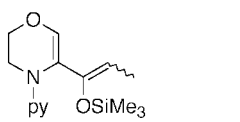
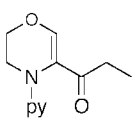
(24) We also observed that the ratio of the linear and branched coupling products was the same, irrespective of whether 1-hexene or 2-hexene as an olefin was used in the reaction of $Ru_3(CO)_{12}$-catalyzed coupling of heteroaromatic C−H/CO/olefins. See ref 13.

(25) In the case of pyridylbenzenes, only the ethyl ketone derivatives, such as **6b**, were obtained, albeit in low yield.[14]

(26) MacRae studied the thermal isomerization of α-silyl ketones to enol silyl ethers in detail. Brook, A. G.; MacRae, D. M.; Bassindale, A. R. *J. Organomet. Chem.* **1975**, *86*, 185.

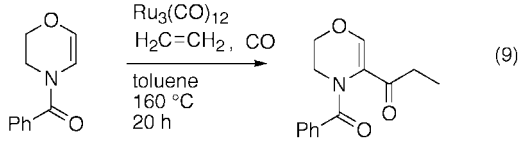
(27) The ruthenium-catalyzed conversion of vinylsilanes to ethylene and disilylethylene is known; see: Wakatsuki, Y.; Yamazaki, H.; Nakano, M.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 703. Marciniec, B.; Pietraszuk, C. *J. Organomet. Chem.* **1991**, *412*, C1. See also: Seki, Y.; Takeshita, K.; Kawamoto, K. *J. Organomet. Chem.* **1989**, *369*, 117.

Table 1. $Ru_3(CO)_{12}$- and $Rh_4(CO)_{12}$-Catalyzed Coupling of 5b with CO and Olefins[a]

entry	olefin	products[b] *n*-isomer	products[b] *i*-isomer	products[b] others
1		 **8a** 49% (51%)[c]	 **8b** 32% (29%)[c]	
2		 **9a** 38%	 **9b** 21%	 **9c** 7%
3		 **10** 87% (80%)[c]		
4[d]		 **11a** 56% (32%)[c]	 **11b** 14% (13%)[c]	
5[d]		 **12** 61% (65%)[c]		
6		 **13** 39% (34%)[c]		
7		 **14a** 12%	 **14b** 3%	 **6b** 18%
8		 **15a** 30%	 **15b** 33% (one isomer)[e]	 **6b** 18%

[a] Reaction conditions: **5b** (1 mmol), CO (15 atm), olefin (10 mmol), $Ru_3(CO)_{12}$ (0.04 mmol), toluene (3 mL), 160 °C, 20 h unless otherwise noted. [b] Isolated yields. [c] $Rh_4(CO)_{12}$ (0.04 mmol) was used as a catalyst. [d] 40 h reaction time. [e] Stereochemistry was not determined.

The presence of the pyridyl group is necessary as a directing group. However, the pyridine ring is undesirable from the organic chemical standpoint because of the difficulty in removing it. To make the reaction more practical, other functional groups which are easier to remove[28] and also capable of promoting cleavage of a C−H bond were examined. As a result, we found that an *N*-acyl group also promotes the reaction.[29] The reaction of 4-benzoyl-3,4-dihydro-2*H*-1,4-oxazine (**18**) with CO (15 atm) and ethylene (10 atm) gave 1-(4-benzoyl-3,4-dihydro-2*H*-1,4-oxazin-5-yl)-1-propanone (**19**) in 31% yield, which is less efficient than a pyridyl group (eq 9). When the reaction was carried out under lower



18 **19** 31% (CO 15 atm) 47% (CO 5 atm) (9)

CO pressure (5 atm), the yield of **19** increased to 47%, along with 42% of unreacted starting material **18**. $Rh_4(CO)_{12}$ was a less effective catalyst for eq 9. The reaction of **18** using $Rh_4(CO)_{12}$ as catalyst under 15 atm of CO

(28) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley-Interscience: New York, 1991.

(29) For catalytic carbonylation involving the cleavage of C−H bond promoted by amido as a directing group, see: Ishii, Y.; Chatani, N.; Kakiuchi, F.; Murai, S. *Tetrahedron Lett.* **1997**, *38*, 7565.

gave **19** in 12% yield. The search for other functional groups for this reactions is now in progress.

Conclusions

$Ru_3(CO)_{12}$ catalyzes carbonylation reactions involving the cleavage of a variety of sp^2 C−H bond in pyridylolefins and *N*-(2-pyridyl)enamines. In these systems, the carbonylation takes place selectively at the olefinic C−H bond γ to the pyridine nitrogen. In pyridylolefins, nearly the same reactivity as that of pyridylbenzenes is observed, while the reaction gives more complex results than pyridylbenzenes due to the isomerization and hydrogenation of C=C double bond. In addition, *N*-(2-pyridyl)enamines show a somewhat different reactivity rather than pyridylbenzenes and pyridylolefins in various points: (i) $Rh_4(CO)_{12}$ also showed catalytic activity for this transformation, (ii) a variety of functionalized olefins can be applied, and (iii) carbonylation is also promoted by a carbonyl group as a directing group.[30] Further studies are currently underway in our laboratory to expand the scope of this carbonylation.

Experimental Section

Materials. Toluene was distilled over CaH_2. $Ru_3(CO)_{12}$ was purchased from Aldrich Chemical Co. and used after recrystallization from hexane. $Rh_4(CO)_{12}$ was purchased from Strem Chemicals, Inc. and used without any purification. 2-[(*E*)-3,3-Dimethyl-1-butenyl]pyridine (**1a**), 2-[(*E*)-1-hexenyl]-pyridine (**1b**), and 2-[(*E*)-2-phenylethenyl]pyridine (**1c**) were obtained by acid-catalyzed dehydration of the corresponding (2-pyridyl)methyl alcohol. 2-(1-Cyclohexenyl)pyridine (**1d**) was synthesized from 2-(tributylstannyl)pyridine and 1-cyclohexenyltriflate according to general procedure of the Pd-catalyzed coupling reaction. 1,2,3,4-Tetrahydro-1-methyl-4-(2-pyridyl)-pyrazine (**5a**), 3,4-dihydro-4-(2-pyridyl)-2*H*-1,4-oxazine (**5b**), 1,2,3,4-tetrahydro-1-(2-pyridyl)pyridine (**5c**), and 4-benzoyl-3,4-dihydro-2*H*-1,4-oxazine (**18**) were prepared according to a previously reported procedure.[15] The synthesis of *N*-(2-ethyl-1-butenyl)-*N*-methyl-2-pyridinamine (**16**) was performed from *N*-methyl-2-pyridinamine and 2-ethylbutanal by acid-catalyzed condensation.

General Procedures. In a 50-mL stainless autoclave were placed $Ru_3(CO)_{12}$ (64 mg, 0.10 mmol), 2-[(*E*)-3,3-dimethyl-1-butenyl]pyridine (**1a**; 322 mg, 2 mmol), and toluene (6 mL). The autoclave was charged with ethylene to 7 atm and carbon monoxide to 20 atm at 25 °C and then heated in an oil bath at 160 °C for 20 h. The autoclave was cooled and depressured. The solvent was removed in vacuo, and the coupling product was isolated by column chromatography on silica gel with hexane/EtOAc as eluant. Purification by bulb-to-bulb distillation or recrystallization afforded the analytically pure product.

(*Z*)-5,5-Dimethyl-4-[(2-pyridyl)methylene]hexan-3-one (2a): colorless solid; mp 54−55 °C (hexane/EtOAc = 30/1); R_f = 0.20 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.14 (t, J = 7.1 Hz, 3H), 1.24 (s, 9H), 2.43 (q, J = 7.1 Hz, 2H), 6.45 (s, 1H), 7.07 (dd, J = 7.6, 5.0 Hz, 1H), 7.16 (d, J = 7.9 Hz, 1H), 7.59 (ddd, J = 7.9, 7.6, 2.0 Hz, 1H), 8.48 (dd, J = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.9, 29.7, 35.6, 38.3, 122.9, 123.3, 136.4, 148.9, 154.4, 157.2, 210.7; IR (neat) 2972, 1696, 1586, 1477, 1432 cm^{-1}; MS, *m*/*z* (rel intensity) 217 (M^+, 1), 188 (M^+ − CH_2CH_3, 100). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.24; H, 8.79; N, 6.52.

(*Z*)-4-[(2-Pyridyl)methylene]nonan-3-one (2b): colorless oil; bp 140 °C (2 mmHg); R_f = 0.20 (hexane/EtOAc = 6/1); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, J = 6.9 Hz, 3H), 1.15 (t, J = 7.3 Hz, 3H), 1.20−1.37 (c, 4H), 1.30−1.50 (c, 2H), 2.74 (t, J = 6.9 Hz, 2H), 2.82 (q, J = 7.3 Hz, 2H), 7.19 (dd, J = 7.6, 4.6 Hz, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.38 (s, 1H), 7.70 (ddd, J = 8.3, 7.6, 2.0 Hz, 1H), 8.66 (dd, J = 4.6, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.7, 14.0, 22.3, 26.4, 28.8, 31.2, 32.0, 122.5, 125.0, 135.8, 136.2, 145.4, 149.7, 155.2, 203.5; IR (neat) 2960, 2936, 1674 cm^{-1}; MS, *m*/*z* (rel intensity) 231 (M^+, 12), 57 (100); exact mass calcd for $C_{15}H_{21}NO$ 231.1623, found 231.1616.

2-Phenyl-1-(2-pyridyl)-1-penten-3-one (2c). The stereochemistry of the *E*/*Z* isomers was determined by H−H NOESY spectroscopy. **(*Z*)-form:** colorless oil; R_f = 0.11 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.3 Hz, 3H), 2.68 (q, J = 7.3 Hz, 2H), 6.79 (s, 1H), 7.11 (dd, J = 7.5, 5.0 Hz, 1H), 7.27 (d, J = 6.9 Hz, 1H), 7.30−7.45 (c, 3H), 7.46−7.55 (c, 2H), 7.64 (ddd, J = 7.5, 6.9, 2.0 Hz, 1H), 8.53 (dd, J = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.9, 36.7, 121.9, 123.9, 125.2, 126.3, 128.6, 128.8, 135.9, 136.5, 147.0, 149.0, 153.6, 209.0; IR (neat) 1699, 1586, 778 cm^{-1}; MS, *m*/*z* (rel intensity) 237 (M^+, 8), 208 (M^+ − CH_2CH_3, 100); exact mass calcd for $C_{16}H_{15}NO$ 237.1153, found 237.1173. **(*E*)-form:** colorless soild; mp 79−81 °C (hexane/EtOAc = 30/1); R_f = 0.21 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.14 (t, J = 7.3 Hz, 3H), 2.74 (q, J = 7.3 Hz, 2H), 6.68 (d, J = 7.9 Hz, 1H), 7.08 (dd, J = 7.6, 4.6 Hz, 1H), 7.12−7.20 (c, 2H), 7.33 (ddd, J = 7.9, 7.6, 2.0 Hz, 1H), 7.34−7.42 (c, 3H), 7.70 (s, 1H), 8.60 (dd, J = 4.6, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.4, 32.9, 122.8, 125.0, 128.1, 128.9, 129.4, 135.6, 136.0, 138.0, 143.5, 149.7, 154.5, 202.2; IR (neat) 1693, 1679, 1462, 1126, 702 cm^{-1}; MS, *m*/*z* (rel intensity) 237 (M^+, 16), 180 (M^+ − $C(O)CH_2CH_3$, 100); exact mass calcd for $C_{16}H_{15}NO$ 237.1154, found 237.1150.

1-[2-(2-Pyridyl)-1-cyclohexenyl]-1-propanone (2d): colorless oil; bp 160 °C (2 mmHg); R_f = 0.02 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 0.98 (t, J = 7.3 Hz, 3H), 1.69−1.78 (c, 4H), 2.19 (q, J = 7.3 Hz, 2H), 2.30−2.35 (m, 2H), 2.44−2.47 (m, 2H), 7.08 (dd, J = 7.6, 5.0 Hz, 1H), 7.19 (d, J = 7.9 Hz, 1H), 7.60 (ddd, J = 7.9, 7.6, 2.0 Hz, 1H), 8.47 (dd, J = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.2, 21.8, 22.2, 27.5, 27.7, 35.3, 120.8, 121.8, 134.5, 136.3, 141.4, 148.4, 157.6, 210.5; IR (neat) 2936, 1688, 1585 cm^{-1}; MS, *m*/*z* (rel intensity) 215 (M^+, 2), 186 (M^+ − CH_2CH_3, 100). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.84; H, 7.98; N, 6.59.

1-[6-(2-Pyridyl)-1-cyclohexenyl]-1-propanone (4d): colorless oil; bp 160 °C (2 mmHg); R_f = 0.13 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, J = 7.4 Hz, 3H), 1.47−1.60 (m, 2H), 1.80−1.91(m, 2H), 2.19−2.45 (m, 2H), 2.51−2.69 (m, 2H), 4.04 (td, J = 4.6, 1.0 Hz, 1H), 6.99 (dd, J = 7.6, 5.0 Hz, 1H), 7.05 (d, J = 7.9 Hz, 1H), 7.12 (td, J = 4.3, 1.0 Hz, 1H), 7.50 (ddd, J = 7.9, 7.6, 2.0 Hz, 1H), 8.42 (dd, J = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.2, 17.9, 26.0, 30.1, 30.3, 41.4, 120.7, 122.2, 136.0, 140.1, 140.8, 148.9, 164.4, 201.4; IR (neat) 1671, 1591, 1435, 1195 cm^{-1}; MS, *m*/*z* (rel intensity) 215 (M^+, 3), 158 (M^+ − $C(O)CH_2CH_3$, 100). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.13; H, 7.88; N, 6.68.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-1-propanone (6b): colorless oil; bp 160 °C (2 mmHg); R_f = 0.14 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.06 (t, J = 7.4 Hz, 3H), 2.46 (q, J = 7.4 Hz, 2H), 3.98 (t, J = 4.6 Hz, 2H), 4.08 (t, J = 4.6 Hz, 2H), 6.51 (d, J = 8.3 Hz, 1H), 6.78 (dd, J = 6.9, 5.0 Hz, 1H), 7.31 (s, 1H), 7.51 (ddd, J = 8.3, 6.9, 2.0 Hz, 1H), 8.24 (dd, J = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.5, 30.8, 43.7, 66.1, 111.6, 115.9, 123.2, 137.5, 143.6, 148.1, 157.3, 198.4; IR (neat) 1593, 1475, 1434 cm^{-1}; MS, *m*/*z* (rel intensity) 218 (M^+, 9), 78 (100). Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 65.95; H, 6.51; N, 13.05.

1-[1,4,5,6-Tetrahydro-1-(2-pyridyl)pyridinyl]-1-propanone (6c) and 1-[1-(2-Pyridyl)piperidinyl]-1-propanone (7c). Spectral data were obtained from a mixture of **6c** and **7c:** colorless oil; R_f = 0.03 (MeOH); ^{1}H NMR ($CDCl_3$), **6c**, δ 1.03 (t, J = 7.4 Hz, 3H), 1.70−1.90 (m, 2H), 2.24−2.32 (m, 2H), 2.38−2.60 (m, 2H), 3.74−3.79 (m, 2H), 5.96 (t, J = 4.0 Hz, 1H), 6.67−6.73 (c, 2H), 7.44−7.55 (c, 1H), 8.14 (dd, J = 5.0, 2.0 Hz, 1H); **7c**, δ 1.04 (t, J = 7.3 Hz, 3H), 1.40−1.85 (c, 5H), 2.09−2.16 (m, 1H), 2.35−2.61 (m, 2H), 3.28 (ddd, J = 13.5, 10.1, 3.5 Hz, 1H), 3.69 (ddd, J = 13.5, 8.3, 4.1 Hz, 1H), 5.12 (t, J = 5.3 Hz, 1H), 6.59 (dd, J = 6.6, 5.0 Hz, 1H), 6.69 (d, J = 8.6 Hz, 1H), 7.47 (ddd, J = 8.6, 6.6, 2.0 Hz, 1H), 8.09 (dd, J = 5.0, 2.0

(30) For a review on substrate-directable chemical reactions, see: Hoveyda, A. H.; Evans, D. A.; Fu, G. *Chem. Rev.* **1993**, *93*, 1307.

Hz, 1H); ^{13}C NMR ($CDCl_3$), **6c**, δ 8.6, 22.3, 23.1, 31.9, 46.8, 110.3, 115.3, 118.3, 137.8, 142.6, 147.8, 157.5, 193.4; **7c**, δ 7.8, 21.0, 24.9, 25.7, 32.4, 44.2, 61.4, 107.0, 113.1, 137.5, 147.4, 159.1, 212.3; IR (neat) 1594, 1478, 1441 cm^{-1}; MS, *m*/*z* (rel intensity), **6c**, 216 (M^+, 1), 187 ($M^+ - CH_2CH_3$, 100); exact mass calcd for $C_{13}H_{16}N_2O$ 216.1263, found 216.1279; **7c**, 218 (M^+, 2), 161 ($M^+ - C(O)CH_2CH_3$, 100); exact mass calcd for $C_{13}H_{18}N_2O$ 218.1419, found 218.1404.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-1-butanone (8a): colorless oil; R_f = 0.13 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 7.4 Hz, 3H), 1.62 (sext, *J* = 7.4 Hz, 2H), 2.41 (t, *J* = 7.4 Hz, 2H), 3.98 (t, *J* = 4.0 Hz, 2H), 4.08 (t, *J* = 4.0 Hz, 2H), 6.51 (d, *J* = 8.3 Hz, 1H), 6.78 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.31 (s, 1H), 7.51 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 8.24 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 18.0, 39.6, 43.8, 66.2, 111.8, 116.0, 123.7, 138.0, 143.9, 148.1, 157.4, 197.8; IR (neat) 1594, 1569, 1476, 1435, 1239, 1152, 776 cm^{-1}; MS, *m*/*z* (rel intensity) 232 (M^+, 10), 189 ($M^+ - CH_2CH_2CH_3$, 100); exact mass calcd for $C_{13}H_{16}N_2O_2$ 232.1211, found 232.1218.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-2-methyl-1-propanone (8b): colorless oil; R_f = 0.14 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.06 (d, *J* = 6.9 Hz, 6H), 2.80 (sept, *J* = 6.9 Hz, 1H), 3.99 (t, *J* = 4.1 Hz, 2H), 4.09 (t, *J* = 4.1 Hz, 2H), 6.49 (d, *J* = 8.6 Hz, 1H), 6.78 (dd, *J* = 7.0, 5.0 Hz, 1H), 7.26 (s, 1H), 7.51 (ddd, *J* = 8.6, 7.0, 2.0 Hz, 1H), 8.24 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 19.0, 35.1, 43.5, 66.3, 111.3, 115.9, 122.4, 137.7, 143.3, 148.2, 157.4, 202.5; IR (neat) 1596, 1477, 1437, 1241 cm^{-1}; MS, *m*/*z* (rel intensity) 232 (M^+, 4), 189 ($M^+ - CH(CH_3)_2$, 100); exact mass calcd for $C_{13}H_{16}N_2O_2$ 232.1211, found 232.1196.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-1-heptanone (9a): colorless oil; bp 200 °C (2 mmHg); R_f = 0.13 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, *J* = 6.6 Hz, 3H), 1.20−1.33 (c, 6H), 1.59 (quint, *J* = 7.3 Hz, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 3.97 (t, *J* = 4.1 Hz, 2H), 4.08 (t, *J* = 4.1 Hz, 2H), 6.51 (d, *J* = 8.3 Hz, 1H), 6.78 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.30 (s, 1H), 7.50 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 8.24 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.4, 24.6, 28.8, 31.5, 37.7, 43.7, 66.1, 111.7, 115.9, 123.6, 137.5, 143.8, 148.1, 157.4, 198.0; IR (neat) 2932, 1682, 1593, 1569, 1476, 1435, 1241, 1207, 1152, 983, 775 cm^{-1}; MS, *m*/*z* (rel intensity) 274 (M^+, 3), 189 (M^+ − hexyl, 100). Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.97; H, 8.16; N, 10.28.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-2-methyl-1-hexanone (9b) and 1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-2-ethyl-1-pentanone (9c). Spectral data were obtained from a mixture of **9b** and **9c:** colorless oil; bp 190 °C (2 mmHg); R_f = 0.14 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$), **9b**, δ 0.85 (t, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.20−1.40 (c, 4H), 1.40−1.48 (m, 1H), 1.53−1.70 (m, 1H), 2.66−2.75 (m, 1H), 3.92−4.00 (m, 1H), 4.00−4.05 (m, 1H), 4.05−4.12 (m, 2H), 6.51 (d, *J* = 8.3 Hz, 1H), 6.78 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.27 (s, 1H), 7.50 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 8.23 (dd, *J* = 5.0, 2.0 Hz, 1H); **9c**, δ 0.78−0.89 (c, 6H), 1.20−1.80 (c, 6H), 2.56−2.65 (m, 1H), 3.50 (t, *J* = 5.0 Hz, 2H), 3.82 (t, *J* = 5.0 Hz, 2H), 6.54 (d, *J* = 8.3 Hz, 1H), 6.78 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.31 (s, 1H), 7.50 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 8.23 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$), **9b**, δ 13.9, 17.2, 22.6, 29.3, 33.3, 40.1, 43.6, 66.2, 111.4, 115.9, 123.0, 137.5, 143.4, 148.1, 157.5, 202.2; **9c**, δ 11.7, 14.2, 20.4, 24.8, 33.7, 45.6, 46.8, 66.7, 111.9, 116.0, 123.9, 137.5, 143.9, 147.9, 157.6, 201.2; IR (neat) 2962, 2934, 1683, 1601, 1569, 1475, 1436, 1380, 1241, 1206, 1156, 985, 955, 775 cm^{-1}; MS, *m*/*z* (rel intensity), **9b**, 274 (M^+, 2), 189 (M^+ − 2-hexyl, 100); **9c**, 274 (M^+, 3), 189 (M^+ − 3-hexyl, 100). Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.84; H, 7.98; N, 10.14.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-4,4-dimethyl-1-pentanone (10): colorless oil; bp 190 °C (2 mmHg); R_f = 0.09 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.80 (s, 9H), 1.44−1.52 (m, 2H), 2.33−2.46 (m, 2H), 3.97 (t, *J* = 4.3 Hz, 2H), 4.07 (t, *J* = 4.3 Hz, 2H), 6.52 (d, *J* = 8.6 Hz, 1H), 6.77 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.28 (s, 1H), 7.50 (ddd, *J* = 8.6, 7.3, 2.0 Hz, 1H), 8.23 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.9, 29.9, 33.4, 38.3, 43.6, 66.0, 111.5, 115.8, 123.3, 137.5, 143.5, 148.0, 157.3, 198.4; IR (neat) 1593, 1476, 1435, 1238, 1205 cm^{-1}; MS, *m*/*z* (rel intensity) 274 (M^+, 3), 189 ($M^+ - CH_2CH_2C(CH_3)_3$, 100). Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.74; H, 7.98; N, 10.43.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-3-phenyl-1-propanone (11a): colorless oil; R_f = 0.19 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 2.75 (t, *J* = 7.3 Hz, 2H), 2.92 (t, *J* = 7.3 Hz, 2H), 3.91 (t, *J* = 4.1 Hz, 2H), 4.05 (t, *J* = 4.1 Hz, 2H), 6.42 (d, *J* = 8.3 Hz, 1H), 6.76 (dd, *J* = 7.3, 4.9 Hz, 1H), 7.10−7.30 (c, 5H), 7.27 (s, 1H), 7.44 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 8.21 (dd, *J* = 4.9, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 30.5, 39.3, 43.7, 66.2, 111.6, 116.0, 123.6, 125.9, 128.3, 128.4, 137.7, 141.2, 144.0, 148.1, 157.3, 196.8; IR (neat) 1594, 1475, 1436 cm^{-1}; MS, *m*/*z* (rel intensity) 294 (M^+, 27), 189 ($M^+ - CH_2CH_2Ph$, 100); exact mass calcd for $C_{18}H_{18}N_2O_2$ 294.1369, found 294.1378.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-2-phenyl-1-propanone (11b): colorless oil; R_f = 0.26 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.36 (d, *J* = 7.3 Hz, 3H), 3.14 (ddd, *J* = 13.5, 8.6, 2.3 Hz, 1H), 3.83−3.94 (c, 2H), 4.12 (dt, *J* = 9.9, 2.3 Hz, 1H), 4.28 (dt, *J* = 13.5, 3.0 Hz, 1H), 6.43 (d, *J* = 8.6 Hz, 1H), 6.78 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.13−7.31 (c, 5H), 7.15 (s, 1H), 7.48 (ddd, *J* = 8.6, 7.3, 2.0 Hz, 1H), 8.25 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.0, 42.8, 47.2, 66.4, 110.9, 115.9, 122.5, 126.7, 127.8, 128.5, 137.8, 141.1, 143.9, 148.4, 157.3, 198.8; IR (neat) 1594, 1476, 1434 cm^{-1}; MS, *m*/*z* (rel intensity) 294 (M^+, 5), 189 ($M^+ - CH(Ph)CH_3$, 100); exact mass calcd for $C_{18}H_{18}N_2O_2$ 294.1369, found 294.1371.

Cyclopentyl[3,4-dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]methanone (12): colorless oil; bp 200 °C (2 mmHg); R_f = 0.09 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.45−1.60 (c, 2H), 1.50−1.80 (c, 6H), 3.04 (quint, *J* = 7.6 Hz, 1H), 3.99 (t, *J* = 4.1 Hz, 2H), 4.09 (t, *J* = 4.1 Hz, 2H), 6.49 (d, *J* = 8.6 Hz, 1H), 6.77 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.29 (s, 1H), 7.50 (ddd, *J* = 8.6, 7.3, 2.0 Hz, 1H), 8.24 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.2, 30.2, 43.5, 45.8, 66.3, 111.6, 115.9, 123.3, 137.6, 143.7, 148.1, 157.4, 201.1; IR (neat) 1593, 1476, 1435, 1240 cm^{-1}; MS, *m*/*z* (rel intensity) 258 (M^+, 3), 189 (M^+ − cyclopentyl, 100). Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.36; H, 7.06; N, 10.97.

4-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-4-oxobutanoic acid methyl ester (13): colorless oil; R_f = 0.13 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 2.61 (t, *J* = 7.0 Hz, 2H), 2.80 (t, *J* = 7.0 Hz, 2H), 3.66 (s, 3H), 3.98 (t, *J* = 4.0 Hz, 2H), 4.09 (t, *J* = 4.0 Hz, 2H), 6.56 (d, *J* = 8.3 Hz, 1H), 6.79 (dd, *J* = 7.3, 4.9 Hz, 1H), 7.37 (s, 1H), 7.53 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 8.24 (dd, *J* = 4.9, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.0, 32.4, 43.8, 51.7, 66.3, 111.9, 116.1, 123.3, 137.7, 144.5, 148.1, 157.4, 173.4, 195.3; IR (neat) 1738, 1594, 1477, 1437, 1244, 1206 cm^{-1}; MS, *m*/*z* (rel intensity) 276 (M^+, 8), 189 ($M^+ - CH_2CH_2C(O)OCH_3$, 100). Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.63; H, 5.88; N, 9.97.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-3-ethoxy-1-propanone (14a): colorless oil; R_f = 0.10 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.17 (t, *J* = 6.9 Hz, 3H), 2.74 (t, *J* = 6.6 Hz, 2H), 3.46 (q, *J* = 6.9 Hz, 2H), 3.72 (t, *J* = 6.6 Hz, 2H), 3.98 (t, *J* = 4.1 Hz, 2H), 4.09 (t, *J* = 4.1 Hz, 2H), 6.54 (d, *J* = 8.3 Hz, 1H), 6.77 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.37 (s, 1H), 7.50 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 8.23 (dd, *J* = 5.0, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.1, 38.0, 43.6, 66.1, 66.3, 66.4, 111.9, 115.9, 124.0, 137.5, 144.9, 148.1, 157.2, 195.3; IR (neat) 1594, 1477, 1436, 1241, 1212, 1151, 1106 cm^{-1}; MS, *m*/*z* (rel intensity) 262 (M^+, 20), 189 ($M^+ - CH_2CH_2OCH_2CH_3$, 100); exact mass calcd for $C_{14}H_{18}N_2O_3$ 262.1317, found 262.1315.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-2-ethoxy-1-propanone (14b): colorless oil; R_f = 0.10 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.1 Hz, 3H), 1.37 (d, *J* = 6.9 Hz, 3H), 3.30−3.37 (m, 1H), 3.55−3.74 (c, 2H), 3.97−4.31 (c, 4H), 6.56 (d, *J* = 8.3 Hz, 1H), 6.79 (dd, *J* = 7.2, 4.9 Hz, 1H), 7.52 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.57 (s, 1H), 8.23 (dd, *J* = 4.9, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.3, 19.0, 43.8, 65.0, 66.5, 78.0, 111.5, 116.1, 121.7, 137.7, 145.4, 148.2, 157.3, 197.6; IR (neat) 1594, 1569, 1476, 1437, 1244, 1202, 1154, 1122, 776 cm^{-1}; MS, *m*/*z* (rel intensity) 262 (M^+, 1), 189

($M^+ - CH(CH_3)OCH_2CH_3$, 100); exact mass calcd for $C_{14}H_{18}N_2O_3$ 262.1317, found 262.1307.

1-[3,4-Dihydro-4-(2-pyridyl)-2*H*-1,4-oxazin-5-yl]-3-(trimethylsilyl)-1-propanone (15a): colorless oil; bp 180 °C (2 mmHg); $R_f = 0.09$ (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ −0.09 (s, 9H), 0.72−0.79 (m, 2H), 2.32−2.39 (m, 2H), 3.96 (t, $J = 4.1$ Hz, 2H), 4.06 (t, $J = 4.1$ Hz, 2H), 6.50 (d, $J = 8.6$ Hz, 1H), 6.76 (dd, $J = 7.3$, 5.0 Hz, 1H), 7.27 (s, 1H), 7.49 (ddd, $J = 8.6$, 7.3, 2.0 Hz, 1H), 8.22 (dd, $J = 5.0$, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −1.9, 11.2, 32.3, 43.8, 66.2, 111.8, 116.0, 123.1, 137.6, 143.6, 148.2, 157.5, 199.1; IR (neat) 1594, 1476, 1436, 1245, 860, 838 cm^{-1}; MS, *m*/*z* (rel intensity) 290 (M^+, 1), 189 ($M^+ - CH_2CH_2SiMe_3$, 100). Anal. Calcd for $C_{15}H_{22}N_2O_2Si$: C, 62.03; H, 7.64; N, 9.65. Found: C, 61.94; H, 7.54; N, 9.78.

3,4-Dihydro-4-(2-pyridyl)-5-[1-[(trimethylsilyl)oxy]-1-propenyl]-2*H*-1,4-oxazine (15b): colorless oil; $R_f = 0.31$ (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 9H), 1.72 (d, $J = 7.3$ Hz, 3H), 4.00−4.04 (m, 2H), 4.06−4.09 (m, 2H), 4.86 (q, $J = 7.3$ Hz, 1H), 6.34 (s, 1H), 6.68 (dd, $J = 7.0$, 5.0 Hz, 1H), 6.80 (d, $J = 8.3$ Hz, 1H), 7.43 (ddd, $J = 8.3$, 7.0, 2.0 Hz, 1H), 8.18 (dd, $J = 5.0$, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.1, 12.9, 42.9, 66.3, 105.2, 111.8, 114.8, 116.3, 135.8, 137.1, 145.1, 147.6, 156.5; IR (neat) 1593, 1478, 1437, 1251, 1232, 1139, 901, 870, 845 cm^{-1}; MS, *m*/*z* (rel intensity) 290 (M^+, 12), 73 ($SiMe_3$+, 100). Anal. Calcd for $C_{15}H_{22}N_2O_2Si$: C, 62.03; H, 7.64; N, 9.65. Found: C, 61.72; H, 7.77; N, 9.48.

5-Ethyl-4-[methyl(2-pyridyl)amino]-4-hepten-3-one (17): colorless oil; bp 130 °C (2 mmHg); $R_f = 0.14$ (hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, $J = 7.1$ Hz, 3H), 1.01 (t, $J = 7.6$ Hz, 3H), 1.15 (t, $J = 7.4$ Hz, 3H), 2.11 (q, $J = 7.6$ Hz, 2H), 2.30 (br s, 2H), 2.56 (br s, 2H), 3.27 (s, 3H), 6.34 (d, $J = 8.6$ Hz, 1H), 6.59 (dd, $J = 7.3$, 5.0 Hz, 1H), 7.38 (ddd, $J = 8.6$, 7.3, 2.0 Hz, 1H), 8.21 (dd, $J = 5.0$, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.8, 11.8, 13.2, 24.2, 25.6, 33.3, 37.8, 106.9, 112.6, 136.8, 137.3, 148.2, 157.8, 157.9, 203.1; IR (neat) 1595, 1488 cm^{-1}; MS, *m*/*z* (rel intensity) 246 (M^+, 2), 217 ($M^+ - CH_2CH_3$, 100). Anal. Calcd for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37. Found: C, 72.85; H, 8.92; N, 11.32.

1-[4-Benzoyl-3,4-dihydro-2*H*-1,4-oxazin-5-yl]-1-propanone (19): colorless solid; mp 139−141 °C (hexane/EtOAc = 20/1); $R_f = 0.04$ (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.89 (t, $J = 7.3$ Hz, 3H), 2.34 (q, $J = 7.3$ Hz, 2H), 3.81 (br s, 2H), 4.27 (t, $J = 4.5$ Hz, 2H), 7.13 (s, 1H), 7.34−7.50 (c, 3H), 7.57−7.62 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 8.4, 30.9, 41.6, 68.0, 122.16, 128.3, 128.4, 128.6, 131.0, 143.0, 169.2, 195.1; IR (neat) 1650, 1620, 1391, 1369, 1242, 1165, 993, 709 cm^{-1}; MS, *m*/*z* (rel intensity) 245 (M^+, 5), 105 ($PhC(O)^+$, 100). Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.51; H, 6.26; N, 5.70.

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Supporting Information Available: Copies of the ^{1}H and ^{13}C NMR spectra for compounds **2b**, **2c**, **8a**, **8b**, **11a**, **11b**, **14a**, and **14b** (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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