$Ru_3(CO)_{12}$-Catalyzed Coupling Reaction of sp^3 C−H Bonds Adjacent to a Nitrogen Atom in Alkylamines with Alkenes

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Abstract: Catalytic reactions which involve the cleavage of an sp^3 C−H bond adjacent to a nitrogen atom in *N*-2-pyridynyl alkylamines are described. The use of $Ru_3(CO)_{12}$ as the catalyst results in the addition of the sp^3 C−H bond across the alkene bond to give the coupling products. A variety of alkenes, including terminal, internal, and cyclic alkenes, can be used for the coupling reaction. The presence of directing groups, such as pyridine, pyrimidine, and an oxazoline ring, on the nitrogen of the amine is critical for a successful reaction. This result indicates the importance of the coordination of the nitrogen atom to the ruthenium catalyst. In addition, the nature of the substituents on the pyridine ring has a significant effect on the efficiency of the reaction. Thus, the substitution of an electron-withdrawing group on the pyridine ring as well as a substitution adjacent to the sp^2 nitrogen in the pyridine ring dramatically retards the reaction. Cyclic amines are more reactive than acyclic ones. The choice of solvent is also very important. Of the solvents examined, 2-propanol is the solvent of choice.

Introduction

Recently, the development of catalytic reactions which involve the cleavage of unreactive C−H bonds has been a subject of considerable interest.[1] For decades, it had been generally believed that the cleavage of a C−H bond *via oxidative addition* was a difficult process because of its strong bond strength. Consequently, the majority of studies focused on the cleavage of C−H bonds via the use of stoichiometric amounts of transition metal complexes. However, since we reported that the addition of the *ortho* C−H bond in aromatic ketones to alkenes can be efficiently attained by the presence of $H_2Ru(CO)(PPh_3)_3$ as the catalyst,[2] in addition to our finding that the C−H bond cleavage step is not as difficult as had been thought and is not a rate-determining step,[3b] a variety of similar C−C bond formations, which involve the cleavage of C−H bonds, have been extended to a wide variety of aromatic and olefinic substrates by a number of research groups.[3−15] In

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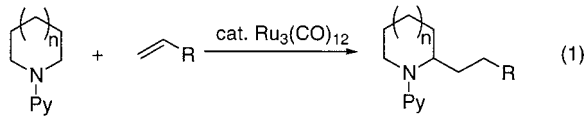
addition, various functional groups were found to promote the site-selective cleavage of C−H bonds as the directing group. The catalytic cleavage of C−H bonds has also been extended to direct carbonylation reactions at C−H bonds in substrates which contain sp^2-nitrogen atoms.[16−21] At present, it has been accepted that the cleavage of C−H bonds is not always a difficult process and that the cleavage of a C−H bond is often not the rate-determining step.[22]

However, essentially all of these reactions reported to date involve the cleavage of sp^2 C−H bonds, and catalytic reactions involving the cleavage of the sp^3 C−H bond are still rare.[1,23,24] Our next project involved the exploration of catalytic reactions which involve the cleavage of *sp^3 C−H bonds*, which is believed to be much more difficult than that of sp^2 C−H bonds. It is known that the cleavage of sp^3 C−H bonds is kinetically and thermodynamically unfavorable. On the basis of a recent literature survey, sp^3 C−H bonds which are adjacent to a heteroatom are, however, more reactive than those surrounded by carbon atoms. A few transition metal catalyzed reactions, which involve the cleavage of sp^3 C−H bonds adjacent to a heteroatom, have recently been reported. The addition of a C−H bond adjacent to an oxygen atom in 1,2-dimethoxytethane across alkenes was achieved via an Ir-catalyzed reaction.[25] The tungsten-catalyzed addition of a C−H bond α to a nitrogen in secondary amines has also been reported.[26] Catalytic alkyl exchange reactions of primary and secondary amines, in the presence of Pd, were reported by Murahashi.[27] Later, Ni,[27c,28] Ru,[27c,29,30] and other transition metal complexes[27c,30] were also reported to be active in the catalytic alkyl exchange reactions. These exchange reactions involve imine or iminium intermediates, which are formed by abstraction of hydrogen α to the nitrogen in amines. Recently, we reported on the $Rh_4(CO)_{12}$-catalyzed carbonylation of a C−H bond in the piperazine ring. Although the reaction involves two cleavages of C−H bonds, carbonylation took place after the initial formation of alkenes via transfer hydrogenation.[20] The results obtained from these papers suggest the possibility of utilizing C−H bonds adjacent to a nitrogen atom for C−H/CO/olefin coupling reactions or C−H/olefin coupling reactions. We then examined the possibility of developing catalytic reactions which involve the cleavage of a C−H bond adjacent to a nitrogen atom in the presence of a wide variety of transition metal complexes as the catalyst. In addition, based on our previous studies we chose substrates with a directing group close to the C−H bond which may react.[3,17−20] Thus, our approach is again based on a chelation-assisted cleavage of C−H bonds, a strategy that has proved to be effective for the development of catalytic reactions involving the cleavage of unreactive bonds, such as sp^2 C−H,[2−21] C−C,[31,32] C−F,[33] and C−O bonds.[34] We now wish to report that the reaction of *N*-2-pyridyldialkylamines with alkenes in the presence of $Ru_3(CO)_{12}$ results in alkylation at the carbon adjacent to the nitrogen atom (eq 1). Recently, Jun reported a similar reaction: the $Ru_3(CO)_{12}$-catalyzed addition of an sp^3 C−H bond adjacent to a nitrogen atom in benzylamine.[35] In his reaction, the substrates were limited to *N*-pyridylbenzylamines, in which only benzylic C−H bonds can add to the alkenes.



(1)

Results and Discussion

The initial aim of the study was the carbonylation at sp^3 C−H bonds. However, it was not possible to explore the direct carbonylation at an sp^3 C−H bond when *N*-pyridyl cyclic amines were used as the substrates with ruthenium complexes as the catalyst.[36] Instead, we found that the addition of a C−H bond to alkenes was achieved by the use of $Ru_3(CO)_{12}$ as a catalyst.[37] Thus, the reaction of 2-(1-pyrrolidinyl)pyridine (**1a**, 1 mmol) with ethylene (initial pressure 10 atm at 25 °C in a 50-mL stainless autoclave) at 1 atm (initial pressure at 25 °C) of CO at 140 °C in toluene (2 mL) in the presence of $Ru_3(CO)_{12}$ (0.08 mmol) for 20 h in a 50-mL stainless steel autoclave gave 2-(2-ethyl-1-pyrrolidinyl)pyridine (**2a**) in 22% isolated yield and 2-(2,5-diethyl-1-pyrrolidinyl)pyridine (**3a**) in 12% isolated yield, along with a 25% yield of the starting material **1a** after column chromatography on silica gel (entry 1 in Table 1). No carbo-

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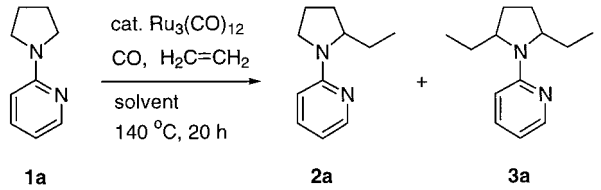
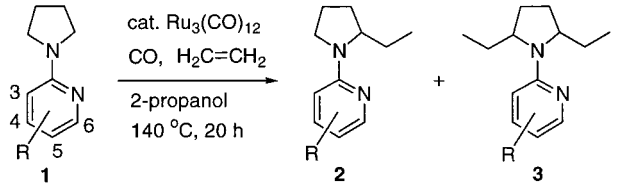
Table 1. The $Ru_3(CO)_{12}$-Catalyzed Reaction of **1a** with Ethylene[a]



entry	solvent	yields, %[b] 2a	3a	recovery of **1a**
1	toluene	22	12	25
2	CH_3CN	27	0	55
3	THF	10	0	86
4	dioxane	0	0	nd[c]
5	DMF	0	0	nd[c]
6	DMSO	0	0	nd[c]
7	MeOH	14	31	9
8	EtOH	8	86	0
9	^{i}PrOH	0	92	0

[a] Reaction conditions: **1a** (1 mmol), $Ru_3(CO)_{12}$ (0.08 mmol), ethylene (initial pressure 10 atm at 25 °C in a 50 mL stainless autoclave), CO (1 atm), solvent (2 mL) at 140 °C for 20 h. [b] Isolated yields based on **1a**. [c] **1a** was recovered, but the amount was not determined.

Table 2. Effect of Substituents on the Pyridine Ring[a]



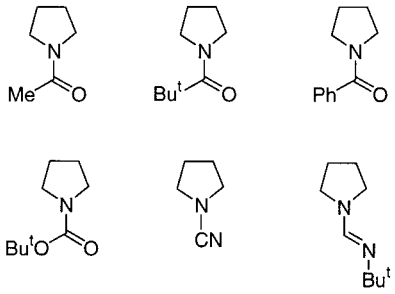
R	yields, %[b,c] 2	3	recovery of **1**
H (**1a**)	0	92 (54:46)	0
3-Me (**1b**)	0	76 (70:30)	0
4-Me (**1c**)	0	90 (66:34)	0
5-Me (**1d**)	0	93 (61:39)	0
6-Me (**1e**)	39	11 (52:48)	35
3-OMe (**1f**)	0	86 (52:48)	0
6-OMe (**1g**)	11	0	77
5-CF_3 (**1h**)	0	94 (63:37)	0
4-COOMe (**1i**)	no reaction		nd

[a] Reaction conditions: **1** (1 mmol), $Ru_3(CO)_{12}$ (0.08 mmol), ethylene (initial pressure 10 atm at 25 °C in a 50 mL stainless autoclave), CO (1 atm) in 2-propanol (2 mL) at 140 °C for 20 h. [b] Isolated yields based on **1**. [c] The numbers in parenthesis are the stereoisomeric ratios.

nylation products were obtained, even when the reaction was carried out at higher CO pressures and at higher reaction temperatures. This finding led us to concentrate on the alkylation at an sp^3 C−H bond adjacent to a nitrogen atom. To optimize the reaction conditions, a variety of solvents were examined. It was found that the nature of solvents significantly affects the efficiency of the coupling reaction. The use of CH_3CN as a solvent gave the mono-ethylation product **2a** as a main product, albeit in low yield (entry 2). Among the solvents examined, 2-propanol was found to be the best. With 2-propanol as the solvent, the yield of **3a** was dramatically increased to 92% (entry 9). Our solvent system enabled the addition of C−H bonds in cyclic amines to alkenes. This result complements the work of Jun, who reported that only the benzylic C−H bond reacted with alkenes.[35] The presence of CO is not essentially required, but it was found to keep the reaction clean, putatively by avoiding the decomposition of the catalyst. In fact, the yield of **3a** was 77% when the reaction of **1a** was carried out under N_2 in place of CO.

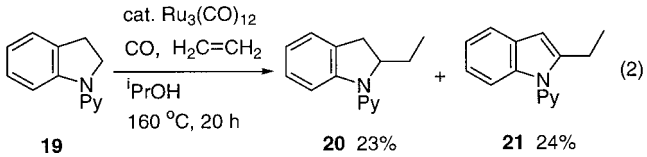
The effect of substituents on the pyridine ring was next examined. The results are shown in Table 2. We have already observed that the electronic nature of the substituents on a pyridine ring has a significant effect on the efficiency of a carbonylation reaction at the C−H bonds reported thus far.[19a] In most cases, the reaction did not stop at the mono-alkylation stage. As expected the nature of the substituents on the pyridine ring had a significant effect on the product yields. The substitution at the 6-position, as in **1e** and **1g**, dramatically decreased the reactivity of the substrates due to steric hindrance around the pyridine ring. The substitution of the electron-withdrawing group at the 4-position, as in **1i**, resulted in no reaction due to an electron deficiency on the pyridine nitrogen. The decreased reactivity of **1e**, **1g**, and **1i** clearly showed that the coordination of the pyridine nitrogen to ruthenium is an important step for the reaction to proceed. The cis/trans ratio in **3** was not affected by either the nature or the position of the substituents.

A variety of functional groups, as shown below, were examined for their ability as directing groups, in place of a pyridine ring, but they were unable to serve as such. This is due to the low coordination ability of these functional groups compared with the sp^2 nitrogen in the pyridine ring.



Various cyclic amines were found to be applicable to the present alkylation. The results are summarized in Table 3. The reaction of 2-(1-piperidinyl)pyridine (**4**) gave 2-(2,6-diethyl-1-piperidinyl)pyridine (**5**) in high yield (entry 1), while the seven-membered amine derivative **8** gave a mixture of mono-ethylation **9** and di-ethylation products **10** (entry 3), indicating that small ring systems are more reactive than larger membered cyclic amines (**1** > **4** > **8**) in the competition between the second ethylene coupling and the dissociation of mono-ethylation product from the metal center. The reaction of **15** gave **16** as a major product and another di-ethylation product, in which two molecules of ethylene had been incorporated; neither were observed at the benzylic position (entry 6). A pyrimidine ring also functioned as a good directing group in place of a pyridine ring (entry 7).

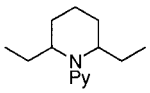
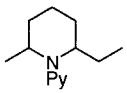
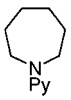
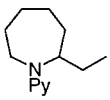
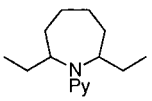
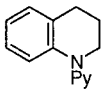
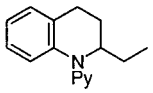
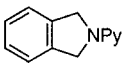
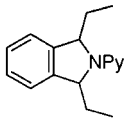
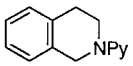
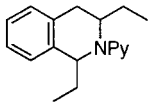
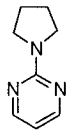
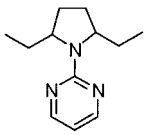
While 2-(2-pyridinyl)-2,3-dihydro-1*H*-isoindole (**13**) gave the corresponding di-ethylation product **14** in high yield (entry 5 in Table 3), the reaction of the dihydroindole derivative **19** gave a mixture of the expected ethylation product **20** and its indole derivative (eq 2). This suggests that compound **21** is formed



(2)

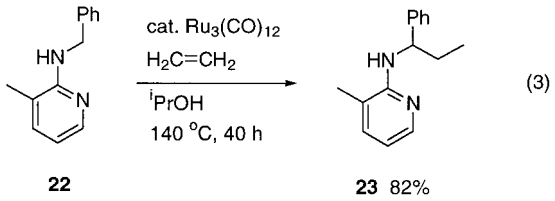
by dehydrogenation of an initial product **20**. An alternative route involving an initial aromatization of **19** to *N*-2-pyridylindole is not likely, since the reaction of *N*-2-pyridylindole under the same reaction conditions as those in eq 2 resulted in no reaction.

Table 3. $Ru_3(CO)_{12}$-Catalyzed Reaction of *N*-2-Pyridylamines with Ethylene[a]

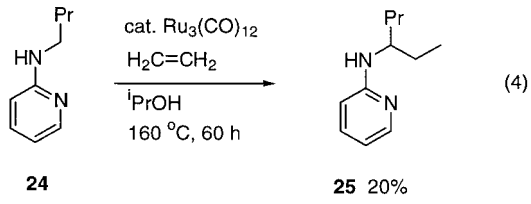
entry	substrate	products [b,c]
1	 **4**	 **5** 73% (60/40)
2	 **6**	 **7** 75% (63/37)
3	 **8**	 **9** 47%  **10** 14% (52:48)
4	 **11**	 **12** 73%
5	 **13**	 **14** 90% (80:20)
6 [d]	 **15**	 **16** 85% (76:24)
7 [d]	 **17**	 **18** 83% (nd)

[a] Reaction conditions: amine (1 mmol), $Ru_3(CO)_{12}$ (0.08 mmol), ethylene (initial pressure 10 atm at 25 °C in a 50 mL stainless autoclave), CO (1 atm) in 2-propanol (2 mL) at 140 °C for 20 h. [b] Isolated yields based on amine. [c] The numbers in parenthesis are the stereoisomeric ratios. [d] For a reaction time of 20 h.

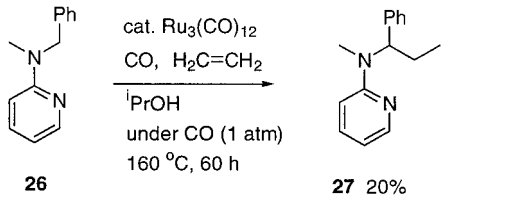
Cyclic amines were found to serve as good substrates for this alkylation reaction, as shown in Table 3. We then examined the reaction of *N*-pyridyl acyclic amines (eqs 3−5). In the case of secondary amines, such as **22** and **24**, the reaction was not carried out under CO, because the reaction of these substrates in the presence of CO resulted in carbonylation at an N−H bond to give formamides as byproducts. Substrate **22**, which was originally reported by Jun to react with alkenes efficiently in the presence of $Ru_3(CO)_{12}$,[35] also reacted with ethylene in 2-propanol to give **23** in high yield (eq 3). The corresponding ether analogue of **22** failed to give an ethylation product,



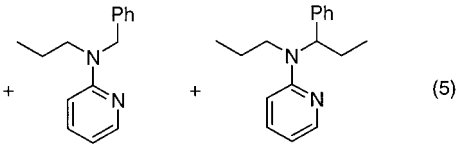
22 **23** 82% (3)



24 **25** 20% (4)



26 **27** 20%

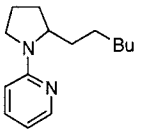
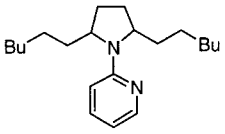
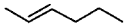
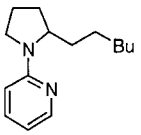
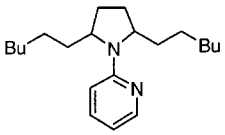
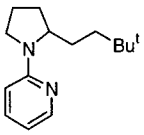
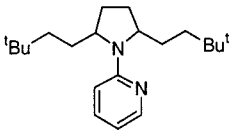
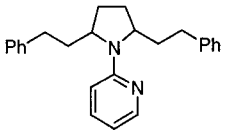
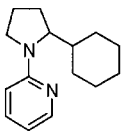
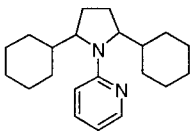


28 8% **29** 12% (5)

indicating that the reaction is limited to amines. Compared with a C−H bond in a benzylic position, a C−H bond in an alkyl group is less reactive. The alkylation of **24** took place to give **25** in 20% yield, along with unreacted **24** (57%) (eq 4). A tertiary amine, such as *N*-benzyl-*N*-methyl-2-pyridylamine (**26**), did not result in a selective alkylation reaction (eq 5). As a result, the scope of this reaction appears to be limited to the addition of C−H bonds in a benzylic position of secondary amines in the case of acyclic amines, as had been reported by Jun.[35]

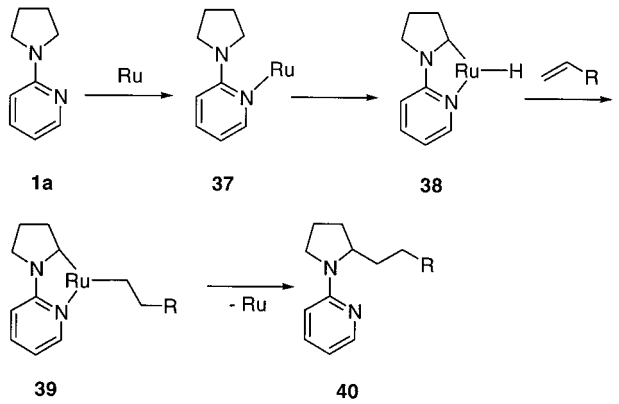
The results on the reaction of **1a** with some alkenes are shown in Table 4. In most cases, mixtures of mono-alkylation products and di-alkylation products were obtained. Mono-alkylation products were not obtained selectively, even when the reactions were carried out for short reaction times with a smaller amount of alkenes. The reaction of **1a** with 1-hexene gave a mixture of the linear products **30** and **31** in a total yield of 91%, and no branched products were observed (entry 1). The similar predominate formation of a linear product was observed when 2-hexene was employed as an alkene. The reaction of **1a** with 2-hexene led to the formation of the corresponding linear alkylation products **30** and **31**, along with a 21% yield of recovered **1a** (entry 2). The reaction of **1a** with hexene under the reaction conditions (in toluene) employed by Jun[35] gave **30** in 8% yield and **31** in 3%, along with 74% of **1a** being recovered after 20 h. This result again demonstrates the efficiency of 2-propanol as the solvent. The reaction of **1a** with styrene gave the di-alkylation product **34** in good yield; however, products formed via hydroesterification and the polymerization of styrene were also produced as contaminants (entry 4). A cyclic olefin, such as cyclohexene, was also applicable to the present alkylation (entry 5). Olefins with an electron-withdrawing group, such as acrylonitrile and butyl vinyl ether, did not function as an alkene partner. Isoprene and 1,5-cyclooctadiene also failed

Table 4. The $Ru_3(CO)_{12}$-Catalyzed Reaction of **1a** with Alkenes[a]

entry	alkene	time, h	products [b,c]	
1		60	 **30** 29%	 **31** 53% (52:48)
2		60	 **30** 36%	 **31** 38% (56:44)
3		60	 **32** 21%	 **33** 73% (51:49)
4		40	 **34** 58% (50:50)	
5		60	 **35** 39%	 **36** 33% (60:40)

[a] Reaction conditions: **1a** (1 mmol), alkene (10 mmol), $Ru_3(CO)_{12}$ (0.08 mmol), in 2-propanol (2 mL) at 140 °C in a 10 mL stainless vial. [b] Isolated yields based on **1a**. [c] The numbers in parentheses are the stereoisomeric ratios.

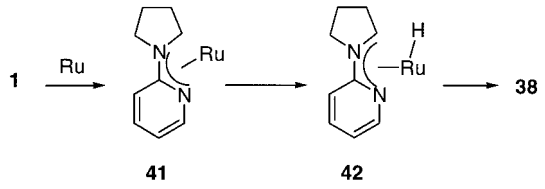
Scheme 1. A Proposed Reaction Mechanism



to react. Alkynes were also tested as a coupling partner instead of alkenes, but none of the alkynes showed any reactivity.

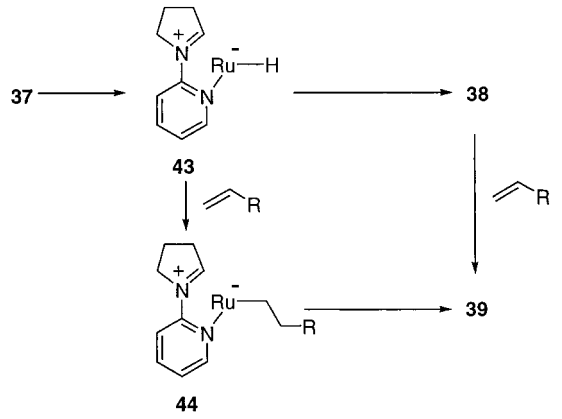
While the precise reaction mechanism is not clear, a proposed reaction mechanism is shown in Scheme 1. Coordination of the nitrogen in **1a** to ruthenium provides complex **37**, in which the C−H bond undergoes cleavage to give the Ru hydride complex **38**. The insertion of an alkene into the H−Ru bond in **38** gives the alkyl Ru complex **39**, from which reductive elimination gives the final product **40**, with the Ru complex being regenerated. Two possibilities for the step in which the C−H bond is cleaved exist in addition to the direct oxidative addition, as has already been shown in Scheme 1. One involves hydride elimination from the 1,3-diaza-π-allyl Ru complex **41** to **42** (Scheme 2). The C−H bond to be cleaved is doubly activated, the C−H bond being next to nitrogen and located at the allylic position.

Scheme 2. An Alternative Mechanism (1) for the Cleavage of a C−H Bond

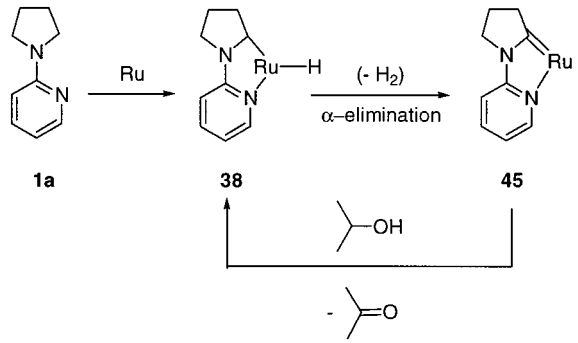


Another alternative mechanism, which involves the participation of an iminium intermediate, cannot be excluded (Scheme 3). Hydride abstraction from **37** gives an iminium intermediate **43**, which undergoes intramolecular nucleophilic attack to give **38**. A related mechanism in which, prior to the formation of **38** from **43**, the insertion of an alkene into the H−Ru bond in **43** followed by intramolecular nucleophilic attack gives **39** is also possible. In the transalkylation of amines, the intermediacy of

Scheme 3. An Alternative Mechanism (2) for the Cleavage of a C−H Bond



Scheme 4

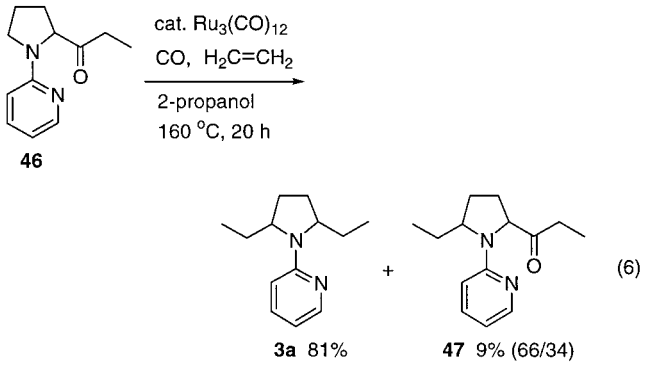


imine or iminium intermediates was invoked.[27−30] Although we have no experimental evidence at present, a direct oxidative addition mechanism seems to be unlikely.

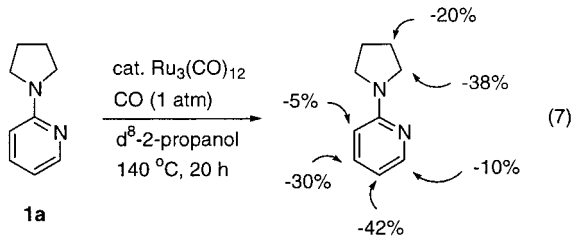
Alcohols were found to be effective solvents for the present reaction. Of the alcohols examined, 2-propanol is the best solvent. The exact role of 2-propanol is not clear at present, but we speculate that its role involves protecting the ruthenium-hydride species **38** from decomposition. If α-elimination from **38** takes place, a carbene complex **45** is formed, which is susceptible to decomposition. However, the ruthenium hydride species **38** can be regenerated by hydrogen donation from 2-propanol to **45**, as shown in Scheme 4. Consequently, **38** has a sufficiently long lifetime to react with alkenes. Recently, Lee, Faller, and Crabtree observed a reversible α-elimination in related iridium complexes.[38]

We have previously reported that the use of a rhodium complex in the reaction of **1a** with CO and ethylene gives carbonylation products and that no alkylation products are obtained.[36] In contrast, carbonylation did not take place in the case of an sp^3 C−H bond when $Ru_3(CO)_{12}$ was used as the catalyst, although $Ru_3(CO)_{12}$ has been found to be an active catalyst for carbonylation at sp^2 C−H bonds.[16−21] While we cannot provide a precise reason, we speculate that a backward reaction exits in the case of the present $Ru_3(CO)_{12}$-catalyzed reaction of alkylamines. In fact, the reaction of **46** under standard reaction conditions gave **3a** in 81% yield along with a small amount of **47** (eq 6). This result shows that decarbonylation of **46** easily took place under these conditions to give **1a**, which then reacted with ethylene to afford **3a**. A similar example of the decarbonylation of ketones has been previously reported by us.[32]

(38) Lee, D.-H.; Chen, J.; Faller, J. W.; Crabtree, R. H. *Chem. Commun.* **2001**, 213.



Next, the H/D exchange reaction was undertaken to obtain information concerning the reaction mechanism. An H/D exchange experiment provided good evidence for the reversibility of C−H bonds between substrates and reactants (alkenes), indicating that the cleavage of C−H bonds is not the rate-determining step.[3b,10] In the present case, however, H/D exchange with the solvent took place even when the reaction was carried out in the absence of ethylene. The treatment of **1a** under catalytic reaction conditions (in the absence of ethylene) in 2-propanol-d_8 showed deuterium incorporation to **1a** at all positions (eq 7). Although this result indicates that C−H bonds in the substrate **1a** can be cleaved in a nonselective manner, it is noteworthy that the cleavage of C−H bonds is a facile process.



Summary

We have demonstrated herein that the addition of an sp^3 C−H bond in alkylamines to alkenes can be achieved via catalysis by a ruthenium complex. The C−H bond next to a nitrogen atom is selectively cleaved and adds to alkenes. The presence of a pyridine ring on the nitrogen in cyclic amines is essential for the reaction to proceed, suggesting the importance of the coordination of pyridine nitrogen to the ruthenium. The use of 2-propanol is also critical for the reaction to proceed.

Experimental Section

Materials. 2-Propanol was distilled over sodium metal and stored over 4 Å molecular sieves. $Ru_3(CO)_{12}$ was prepared according to literature procedures[39] and used after recrystallization from hexane. Alkylamines **1a**,[40] **1b**,[36] **1d**,[36] **1e**,[36] **1f**, **1g**, **4**, **6**, **8**, **11**, **17**, **19**, **22**, **24**, and **26**[41] were obtained from the corresponding substituted 2-bromopyridines and amines according to the Pd-catalyzed amination procedure reported by Buchwald.[41] **1h**,[36] **1i**, and **15** were prepared from the corresponding substituted 2-chloropyridines or 2-chloropyrimidine and pyrrolidine according to literature procedures.[42] And **1c**[36] and **13** were prepared from the corresponding substituted 2-aminopyridines and 1,4-dichlorobutane, with slight modification of the literature procedure.[43]

(39) Bruce, M. I.; Jensen, C. M.; Jones, N. L. *Inorg. Synth.* **1989**, *26*, 259.
(40) Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron* **1999**, *55*, 12829.
(41) Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 7240.
(42) Hassher, A.; Krepski, L. R.; Alexanian, V. *Tetrahedron* **1978**, *34*, 2069.
(43) Craig, L. C.; Hixon, R. M. *J. Am. Chem. Soc.* **1930**, *52*, 804.

Typical Procedure for the Coupling of C−H Bonds α to the Nitrogen Atom in Alkylamines with Ethylene. A 50-mL stainless autoclave was charged with 2-(1-pyrrolidinyl)pyridine (**1a**) (1 mmol, 148 mg), 2-propanol (2 mL), and $Ru_3(CO)_{12}$ (0.08 mmol, 51 mg). After the system was flushed with 10 atm of carbon monoxide three times, it was pressurized with carbon monoxide to 1 atm and then with ethylene to an additional 10 atm. The autoclave was then immersed in an oil bath at 140 °C. After 20 h had elapsed, the autoclave was removed from the oil bath and allowed to cool for ca. 1 h and the gases were then released. The contents were transferred to a round-bottomed flask with toluene, and the volatiles were removed in vacuo. The residue was subjected to column chromatography on silica gel (eluent; hexane/EtOAc = 30/1) to give 2,5-diethyl-1-(2-pyrridinyl)pyrroridine (**3a**) (189 mg, 92% yield, 54/46 stereoisomeric mixture of cis/trans) as a colorless oil. Purification by bulb-to-bulb distillation afforded the analytically pure product.

2-Ethyl-1-(2-pyridinyl)pyrroridine (2a): colorless oil; bp 80 °C (1 mmHg); R_f 0.14 (hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.92 (t, J = 7.6 Hz, 3H), 1.26−1.44 (m, 1H), 1.77−2.04 (c, 5H), 3.33−3.56 (m, 2H), 3.85 (m, 1H), 6.33 (d, J = 7.6 Hz, 1H), 6.48 (dd, J = 6.5 Hz, 5.1 Hz, 1H), 7.39 (ddd, J = 7.6 Hz, 6.5 Hz, 1.9 Hz, 1H), 8.14 (d, J = 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.60, 23.36, 25.66, 29.51, 47.30, 58.98, 106.63, 110.89, 136.66, 148.23, 157.09; IR (neat) 2968 s, 2876 m, 2024 w, 1942 m, 1600 s, 1559 s, 1495 s, 1443 s, 1383 s, 1304 m, 1248 m, 1155 m, 1092 m, 1050 m, 991 s; MS, *m*/*z* (relative intensity, %) 176 (M^+, 11), 147 (100), 119 (10), 78 (36), 51 (15). HRMS Calcd for $C_{11}H_{16}N_2$: 176.1313. Found: 176.1321.

2,5-Diethyl-1-(2-pyridinyl)pyrroridine (3a). Spectral data were obtained from a mixture of cis and trans isomer: colorless oil; bp 95 °C (1 mmHg); R_f 0.26 (hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.86−0.96 (c, 6H), 1.20−1.42 (c, 2H), 1.76−2.05 (c, 6H), 3.81−3.92 (c, 2H), [6.26 (d, J = 8.4 Hz, minor), 6.34 (d, J = 8.6 Hz, major), 1H], 6.43−6.50 (c, 1H), 7.36−7.39 (c, 1H), 8.14 (dd, J = 5.0 Hz, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ [10.67 (major), 10.92 (minor)] [24.34 (minor), 27.74 (major)], [26.95 (minor), 28.94 (major)], [59.02 (minor), 60.09 (major)], [106.66 (minor), 108.21 (minor)], [110.54 (major), 111.10 (minor)], [136.47 (minor), 136.60 (major)], [148.17 (major), 148.42 (minor)], [156.11 (major), 157.66 (minor)]; IR (neat) 3676 w, 3004 m, 2964 s, 2876 s, 1595 s, 1558 s, 1488 s, 1443 s, 1379 s, 1331 m, 1307 s, 1293 m, 1246 m, 1206 m, 1193 m, 1162 s, 1091 m, 1052 m, 1013 m, 989 s, 960 m, 932 w, 897 w, 879 m, 839 w; MS, *m*/*z* (relative intensity, %) 204 (M^+, 12), 176 (11), 175 (100), 147 (15), 121 (20), 119 (15), 107 (11), 95 (19), 79 (13), 78 (40), 55 (25), 51 (15). Anal. Calcd for $C_{13}H_{20}N_2$: C, 76.42; H, 9.87; N, 13.71. Found: C, 76.41; H, 9.92; N, 13.61.

Typical Procedure for the Coupling of C−H Bonds α to the Nitrogen Atom in Alkylamines with Substituted Olefins. A 10-mL stainless vial was charged with 2-(1-pyrrolidinyl)pyridine (**1a**) (1 mmol, 148 mg), 1-hexene (10 mmol, 842 mg), 2-propanol (2 mL), and $Ru_3(CO)_{12}$ (0.08 mmol, 51 mg) under nitrogen. The vial was then immersed in an oil bath at 140 °C. After 60 h had elapsed, the vial was removed from the oil bath and allowed to cool for ca. 1 h and the contents were transferred to a round-bottomed flask with toluene, after which the volatiles were removed in vacuo. The residue was subjected to column chromatography on silica gel (eluent; hexane/EtOAc = 30/1) to give 2-hexyl-1-(2-pyridinyl)pyrrolidine (**30**) (68 mg, 29% yield) and 2,5-dihexyl-1-(2-pyridinyl)pyrrolidine (**31**) (168 mg, 53% yield, 52/48 stereoisomeric mixture of cis/trans) as colorless oils. Purification by bulb-to-bulb distillation afforded analytically pure products.

2-Hexyl-1-(2-pyridinyl)pyrrolidine (30): colorless oil; bp 105 °C (1 mmHg); R_f 0.17 (hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.81−0.89 (m, 3H), 1.20−1.40 (c, 9H), 1.72−2.07 (m, 5H), 3.32−3.42 (m, 1H), 3.46−3.58 (m, 1H), 3.82−3.92 (m, 1H), 6.32 (d, J = 7.6 Hz, 1H), 6.47 (ddd, J = 5.4 Hz, 4.9 Hz, 1.4 Hz, 1H), 7.39 (ddd, J = 7.6 Hz, 5.4 Hz, 1.6 Hz, 1H), 8.15 (dd, J = 4.9 Hz, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.09, 22.61, 23.33, 26.49, 29.44, 30.08, 31.90, 32.99, 47.14, 57.67, 106.96, 110.82, 136.64, 148.25, 157.02; IR (neat) 2928 s, 2856 m, 1599 s, 1559 m, 1494 s, 1443 s, 1381 s, 1297 m, 1155 m, 1092 w, 1050 w, 988 m; MS, *m*/*z* (relative intensity, %) 232 (M^+, 9), 148 (12), 147 (100), 78 (18). HRMS Calcd for $C_{15}H_{24}N_2$: 232.1939. Found: 232.1932.

2,5-Dihexyl-1-(2-pyridinyl)pyrrolidine (31). Spectral data were obtained from a mixture of cis and trans isomer: yellow oil; bp 140 °C (1 mmHg); R_f 0.40 (hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.81−0.94 (c, 6H), 1.06−1.31 (c, 18H), 1.77−2.38 (c, 6H), 3.92 (c, 2H), 6.24−6.34 (c, 1H), 6.41−6.51 (c, 1H), 7.34−7.38 (c, 1H), 8.12−8.15 (c, 1H); ^{13}C NMR ($CDCl_3$) δ 14.11, [22.61 (minor), 22.64 (major)], [26.47 (minor), 26.74 (major)], 27.35, [29.36 (minor), 29.51 (major)], [31.90 (minor), 31.93 (major)], [57.45 (major), 59.18 (minor)], [106.45 (major), 107.96 (minor)], [110.33 (major), 110.87 (minor)], [136.33 (major), 136.48 (minor)], [148.12 (minor), 148.39 (major)], [155.90 (minor), 157.45 (major)]; IR (neat) 2960 s, 2926 s, 2858 s, 1596 s, 1559 m, 1484 s, 1441 s, 1378 s, 1297 m, 1246 w, 1206 w, 1157 m, 1091 w, 1051 w, 978 w; MS, *m*/*z* (relative intensity, %) [316 (M^+, 4), 232 (18), 231 (100), 147 (12), 133 (11), 121 (12), 119 (11), 95 (15), 78 (16), 69 (10), 55 (17), major], [316 (M^+, 6), 232 (17), 231 (100), 147 (19), 133 (17), 121 (13), 119 (17), 95 (18), 78 (20), 64 (12), 55 (20), minor]. Anal. Calcd for $C_{21}H_{36}N_2$: C, 79.69; H, 11.46; N, 8.85. Found: C, 79.77; H, 11.50; N, 8.90.

Procedure for the Backward Reaction from the Carbonylated Product to the Alkylated product. A 50-mL stainless autoclave was charged with 1-[1-(2-pyridinyl)-2-pyrrolidinyl]-1-propanone (**46**) (0.05 mmol, 10 mg), 2-propanol (1 mL), and $Ru_3(CO)_{12}$ (0.008 mmol, 5 mg). After the system was flushed with 10 atm of carbon monoxide three times, it was pressurized with carbon monoxide to 1 atm and then with ethylene to an additional 10 atm. The autoclave was then immersed in an oil bath at 160 °C. After 20 h had elapsed, the autoclave was removed from the oil bath and allowed to cool for ca. 1 h and the gases were then released. The contents were transferred to a round-bottomed flask with toluene, and the volatiles were removed in vacuo. The residue was subjected to column chromatography on silica gel (eluent; hexane/EtOAc = 5/1) to give 2,5-diethyl-1-(2-pyridinyl)pyrroridine (**3a**) and 1-[5-ethyl-1-(2-pyridinyl)-2-pyrrolidinyl]-1-propanone (**47**) as a mixture (8 mg). The yields of **3a** and **47** were determined by comparing the integrations of the 6-H signals on the pyridine for **3a** and **47** in the ^{1}H NMR spectrum of the mixture.

Procedure for the H/D Exchange Experiment in 2-Propanol-d_8. A 50-mL stainless autoclave was charged with 2-(1-pyrrolidinyl)-pyridine (**1a**) (1 mmol, 148 mg), 2-propanol-d_8 (2 mL), and $Ru_3(CO)_{12}$ (0.08 mmol, 51 mg). After the system was flushed with 10 atm of carbon monoxide three times, it was pressurized with carbon monoxide to 1 atm. The autoclave was then immersed in an oil bath at 140 °C. After 20 h had elapsed, the autoclave was removed from the oil bath and allowed to cool for ca. 1 h after which the gases were released. The contents were transferred to a round-bottomed flask with toluene, and the volatiles were removed in vacuo. The residue was subjected to column chromatography on silica gel (eluent; hexane/EtOAc = 5/1) to give deuterized starting material (122 mg, 79% recovered) as a colorless oil. After purification by bulb-to-bulb distillation, D-contents in the recovered starting material were measured by ^{1}H NMR with cyclohexane as an external standard.

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Supporting Information Available: Full characterization data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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