Transition Metal-Catalyzed Intramolecular C-H/Olefin Coupling

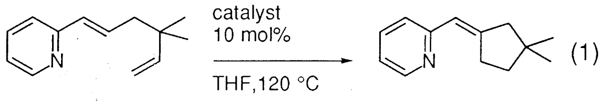
Naoaki Fujii,[†] Fumitoshi Kakiuchi, Naoto Chatani, and Shinji Murai*
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565
[†]*New Drug Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Yodogawa-ku, Osaka 532*

(Received July 22, 1996)

The ruthenium- and rhodium-catalyzed intramolecular C-H/olefin coupling reactions of 1-(2-pyridyl)-1,5- and 1,6-dienes proceeded regio- and stereoselecively to give 5- or 6-membered ring products.

The development of general approaches to carbocycles with carbon-carbon bond formation represents an important ongoing challenge for synthetic organic chemists.[1] Metal-catalyzed cyclization of a 1,n-diene is one of important strategies for ring construction and has been the subject of a number of studies.[2,3] Recentry we have found the transition metal-catalyzed C-H/olefin coupling reactions.[4-9] It seemed important to examine the capability of the new C-H/olefin coupling method in undergoing intramolecular reactions. This is the case. In this communication, we report a selective intramolecular cyclization reaction of 1-(2-pyridyl)-1,5- and 1,6-dienes catalyzed by transition metal catalysts.

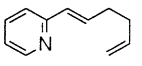
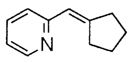
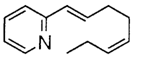
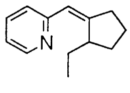
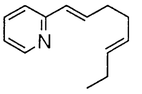
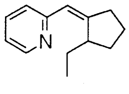
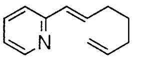
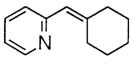
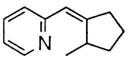
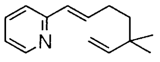
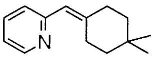
On the basis of the knowledge of successful $Ru(H)_2(CO)(PPh_3)_3$-catalyzed addition of C-H bonds in aromatic ketones[4] and conjugated enones[5] to olefins, we have found that 1-(2-pyridyl)-1,5-diene undergoes desired cyclization in the presence of ruthenium or rhodium catalyst (Eq. 1) after various attempts. Kim and co-workers[10] reported rhodium-catalyzed intermolecular C-H/olefin coupling reactions of 2-vinyl pyridines and olefins.[8] It is found that $RhCl(PPh_3)_3$ has high catalytic activity towards the intramolecular C-H/olefin coupling reactions although some ruthenium complexes are also effective (Eq. 1). When **1** was treated with 10 mol% of $RhCl(PPh_3)_3$ in THF at 120 °C for 3 h under nitrogen, cyclization proceeded smoothly and 5-membered ring product **2** was obtained as a sole product. The (*E*)-stereochemistry of **2** was confirmed by ^{1}H NMR. Irradiation of the vinyl proton in **2** led to a 3% enhancement of the singlet methylene proton at the 2-position.



1 **2**

catalyst	time/h	yield/% (isolated)
$Ru(H)_2(CO)(PPh_3)_3$	15	62
$Ru(CO)_2(PPh_3)_3$	15	86
$Ru(CO)_3(PPh_3)_2$	38	88
$RhCl(PPh_3)_3$	3	89
1/2 $[RhCl(coe)_2]_2$/3PCy_3	1	64

Table 1. $RhCl(PPh_3)_3$-catalyzed cyclization of 1-(2-pyridyl)-1,5- and 1,6-dienes [a]

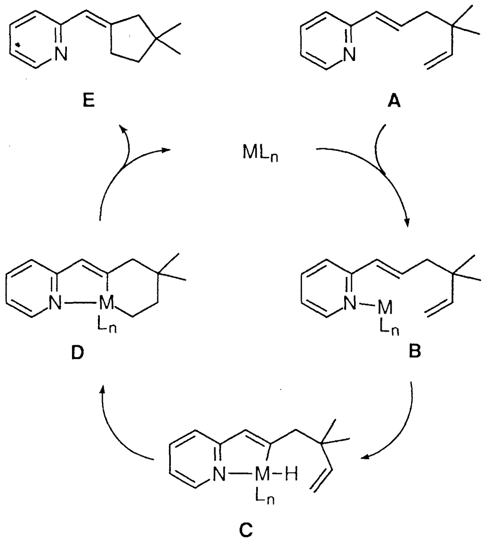
Entry	Substrate	Time/h	Products Yield/%[b]
1	 **3**	4	 **4** 93
2	 **5**	3	 **6** 84
3	 **7**	38	 **6** 86
4	 **8**	48	 **9** 33  **10** 47
5	 **11**	70	 **12** 60

[a]Reactions conditions ; 10 mol% $RhCl(PPh_3)_3$,THF, substrarc (0.2 M), 120 °C (oil bath temp.) under nitrogen. [b] Isolated yield by silica gel column chromatography.

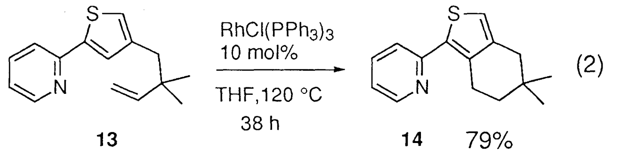
The reactions of various pyridyl dienes were carried out. Selected results are shown in Table 1. Although terminal olefins tend to isomerize to internal ones in the presence of transition metal complexes, such isomerization did not occur under the present reaction conditions (entries 1 and 4). Isomerization of *exo* double bond of products to *endo* one did not occur also. Internal olefins could cyclize. *Z*-Olefin **5** reacted faster than *E*-olefin **7** probably according to the well known tendency[11] (entries 2 and 3). Both of 5- and 6-membered rings were produced from 1,6-diene (entry 4), but the steric crowdness on allyl carbon strongly supresses the 5-membered ring formation (entry 5).

A proposed mechanism is shown in Scheme 1. The reaction appears to be initiated *via* the formation of a metal hydride complex **C** by cleavage of a vinylic C-H bond assisted by coordination[12] of nitrogen atom of the pyridine ring. The intramolecular insertion of the olefin into a metal-hydrogen bond in **C** would give an intermediate **D**, which then would afford the product **E**. An alternative mechanism involving initial hydrometalation of the terminal unsaturated bond followed by carbometalation and dehydrometalation seems less likely since the stereochemistry of the double bond in the product is only *E*.

Another observation favoring the C-H bond cleavage mechanism (Scheme 1) is that **13** reacts under the present reaction conditions to give only one regioisomer **14** (Eq. 2).



Scheme 1. A proposed mechanism.



In conclusion, $RhCl(PPh_3)_3$ catalyzed the cyclization of 1-(2-pyridyl)-1,5- and 1,6-dienes. The reaction is likely to involve regioselective cleavage of a C-H bond on sp^2 carbon and insertion of olefinic moiety. Internal olefins also can react and *Z*-olefins react faster than *E*-olefins. 5-Membered ring was formed faster than 6-membered ring, but actual selectivity was also influenced by steric factor. Further investigation of this study are now in progress.

Supplementary Material (10 pages) including synthetic procedures and spectral data of new compounds are available on request to the author by telefax (+81-6-879-7396).

References

1 For representative reviews, see "*Comprehensive Organometallic Chemistry II, Vol 12,*" ed by E. W. Abel, F. G. A. Stone, and G. Wilkinson, Pergamon press, Oxford, U. K. (1995); I. Ojima, M. Tzamarioudaki, Z. Li, and R. J. Donovan, *Chem. Rev.*, **96**, 635(1996).

2 B. Bogdanovic, *Adv. Organomet. Chem*, **17**, 105(1979); R. Grigg, J. F. Malone, T. R. B. Mitchell, A. Ramasubbu, and R. M. Scott, *J. Chem. Soc., Perkin Trans. I*, **1984**, 1745; W. E. Piers, P. J. Shapiro, E. E. Bunel, and J. E. Bercaw, *Synlett,* **1990**, 74; G. A. Molander and J. O. Hoberg, *J. Am. Chem. Soc.*, **114**, 3123(1992); K. H. Shaughnessy and R. M. Waymouth, *J. Am. Chem. Soc.*, **117**, 5873(1995).

3 For a short review on the catalytic ring-closing metathesis of dienes, see: H-G. Schmalz, *Angew. Chem., Int. Ed. Engl.*, **34**, 1833(1995).

4 S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, and N. Chatani, *Nature (London),* **366**, 529(1993); S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, and N. Chatani, *Pure Appl. Chem.*, **66**, 1257(1994); F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, and S. Murai, *Bull. Chem. Soc. Jpn.*, **68**, 62(1995); M. Sonoda, F. Kakiuchi, N. Chatani, and S. Murai, *J. Organomet. Chem.*, **504**, 151(1995).

5 F. Kakiuchi, Y. Tanaka, T. Sato, N. Chatani, and S. Murai, *Chem. Lett.*, **1995**, 679.

6 F, Kakiuchi, Y. Yamamoto, N. Chatani, and S. Murai, *Chem. Lett.*, **1995**, 681.

7 M. Sonoda, F. Kakiuchi, A. Kamatani, N. Chatani, and S. Murai, *Chem. Lett.*, **1996**, 109.

8 We also described briefly the reaction of 2-phenylpyridine undergoing C-H/CO/olefin coupling by $Ru_3(CO)_{12}$ as the catalyst. S. Murai, *J. Synth. Org. Chem. Jpn.*, **54**, 992 (1994) (in English).

9 Recently, we have reported $Ru_3(CO)_{12}$-catalyzed addition of aromatic imines at the *ortho* C-H bonds to olefins. F. Kakiuchi, M. Yamauchi, N. Chatani, and S. Murai, *Chem. Lett.*, **1996**, 111.

10 Y.-G. Lim, Y. H. Kim, and J.-B. Kang, *J. Chem. Soc., Chem. Commun.*, **1994**, 2267; Y.-G. Lim, J.-B. Kang, and Y. H. Kim, *J. Chem. Soc., Chem. Commun.*, **1996**, 585.

11 For example, see: J. P. Collman, L. S. Hegedus, J. R. Norton, and R. G. Finke, *"Principle and Applications of Organotransition Metal Chemistry,"* University Science Books, Mill Valley, U.S.A. (1987), pp 530 and 698.

12 For the C-H cleavage using stoichiometric amount of catalyst, see: I. Omae, "*Organometallic Intramoleculer-coordination Compounds,*" Elsevier, Amsterdam, Netherlands (1986).