JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

COMMUNICATION

pubs.acs.org/JACS

Rare-Earth-Catalyzed C−H Bond Addition of Pyridines to Olefins

Bing-Tao Guan and Zhaomin Hou*

Organometallic Chemistry Laboratory and Advanced Catalyst Research Team, RIKEN Advanced Science Institute, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan

Supporting Information

ABSTRACT: An efficient and general protocol for the *ortho*-alkylation of pyridines via C−H addition to olefins has been developed, using cationic half-sandwich rare-earth catalysts, which provides an atom-economical method for the synthesis of alkylated pyridine derivatives. A wide range of pyridine and olefin substrates including α-olefins, styrenes, and conjugated dienes are compatible with the catalysts.

Pyridine moieties are among the most important heterocyclic structural motifs and exist widely in a large number of natural products, pharmaceuticals, ligands, and functional materials.[1] Therefore, the development of efficient, atom-economical processes for the synthesis of pyridine-containing compounds through direct C−H functionalization of pyridine has received intensive attention.[2−6] Among possible approaches to the functionalization of pyridines, catalytic C−H bond addition to olefins is the most atom-economical way for the synthesis of alkylated pyridine derivatives. However, direct C−H alkylation of pyridines has met with limited success to date, partly because of the low activity of pyridyl species and easy β-H elimination of transition metal alkyl species.

Pioneering work reported in 1989 by Jordan and co-workers showed that cationic zirconium metallocenes, which are active olefin polymerization catalysts, could effect the catalytic C−H addition of α-picoline to propylene in the presence of H_2.[7] Recently, Bergman and Ellman reported that Rh(I)−phosphine complexes could catalyze the *ortho*-alkylation of pyridines at high temperatures (165 °C).[8] Nakao and Hiyama found that, in the presence of Lewis acids, N-heterocyclic carbene nickel complexes catalyzed the alkylation of pyridines with unprecedented C-4-selectivity.[9] In most of these reactions, aliphatic alkenes were applicable, but styrenes and conjugated dienes seemed not suitable for the catalytic transformation.[10]

Various rare-earth alkyl complexes have been reported previously to undergo *ortho*-metalation of pyridine through C−H bond activation.[11] However, reports on the insertion of olefins into a rare-earth pyridyl bond remain scarce.[11d,f] Teuben and co-workers reported in 1994 that yttrium metallocene complexes catalyzed the ethylation of pyridine under high temperature (110 °C) and high ethylene pressure (40 bar).[11d] This is the only precedent of rare-earth-catalyzed alkylation of pyridine. Unfortunately, this catalyst was active only for ethylene, whereas the insertion of a higher olefin was much slower and could not be achieved catalytically.

We recently demonstrated that cationic half-sandwich rare-earth alkyl complexes can serve as excellent catalysts for the polymerization and copolymerization of a variety of olefins.[12,13] However, the use of the cationic rare-earth alkyls in the C−H addition of pyridines to olefins has remained unexplored to date.[14] Herein, we report the first highly efficient, *ortho*-selective C−H addition of pyridines to olefins catalyzed by cationic half-sandwich rare-earth alkyl complexes. The selectivity and functional group tolerance of the present rare-earth catalysts are complementary to those of late transition metal catalysts. A wide range of pyridine and olefin substrates, including α-olefins, styrenes, and conjugated dienes, are applicable to afford a new family of functionalized pyridine derivatives.

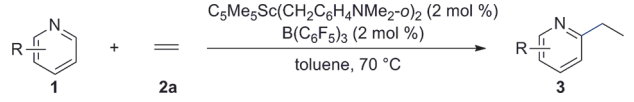
On the basis of catalyst screening for the reaction of α-picoline with norbornene (see Supporting Information, Table S1), we first chose the combination of the half-sandwich scandium bis(benzyl) complex $(C_5Me_5)Sc(CH_2C_6H_4NMe_2\text{-}o)_2$[13e] and $B(C_6F_5)_3$ as catalyst to examine the ethylation of various pyridine derivatives. Some representative results are summarized in Table 1. The *o*-C−H ethylation of α-picoline took place easily under 3 atm of ethylene at 70 °C to give 2-methyl-6-ethylpyridine (**3aa**) almost quantitatively (entry 1). Ethylene polymerization did not take place until α-picoline was completely consumed. Ethylation of 2-ethylpyridine and 2-isopropylpyridine also took place selectively (entries 2 and 3), while reaction of the bulkier 2-*tert*-butylpyridine with ethylene yielded a mixture of oligomers under the same conditions, possibly owing to the steric hindrance of the *t*-Bu group, which could retard the abstraction of hydrogen from 2-*t*-Bu-pyridine by a 2-*t*-Bu-pyridylethyl−Sc species and thus lead to continuous insertion of ethylene into the pyridylethyl−Sc bond. However, when the yttrium complex $(C_5Me_5)Y(CH_2C_6H_4NMe_2\text{-}o)_2$ was used in place of the Sc analogue, the ethylation reaction of 2-*t*-Bu-pyridine took place selectively and quantitatively (entry 4), probably because the larger Y ion in the pyridylethyl yttrium intermediate could promote more efficiently the coordination and subsequent deprotonation of 2-*t*-Bu-pyridine rather than the insertion of another molecule of ethylene.

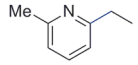
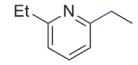
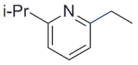
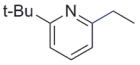
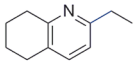
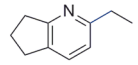
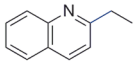
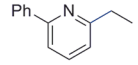
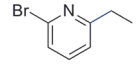
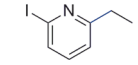
Tetrahydroquinoline (**1e**), 2,3-cyclopentenopyridine (**1f**), quinoline (**1g**), and 2-phenylpyridine (**1h**) could also be *o*-ethylated selectively by the scandium catalyst (Table 1, entries 5−8). It is noteworthy that the ethylation of 2-phenylpyridine took place selectively at the *ortho* position of the pyridine unit (rather than the phenyl group) (entry 8), in contrast with late transition metal-catalyzed reactions, in which the pyridine unit usually serves as a directing group to lead the C−H activation taking place at the phenyl ring.[15] Remarkably, 2-bromopyridine (**1i**) and 2-iodopyridine (**1j**) could also undergo selective C−H ethylation to give the corresponding Br- and I-containing

Received: August 29, 2011
Published: October 14, 2011

ACS Publications © 2011 American Chemical Society

Table 1. Catalytic C−H Addition of Pyridine Derivatives to Ethylene[a]



Entry	Pyridine	time (h)	Product	yield (%)[b]
1	 (**1a**)	22		**3aa** 98[c]
2	 (**1b**)	8		**3ba** 99[c]
3	 (**1c**)	14		**3ca** 96[c]
4[d]	 (**1d**)	3		**3da** 97
5	 (**1e**)	36		**3ea** 96
6[e]	 (**1f**)	24		**3fa** 94
7[f]	 (**1g**)	12		**3ga** 86
8	 (**1h**)	48		**3ha** 98
9	 (**1i**)	48		**3ia** 91
10	 (**1j**)	48		**3ja** 97

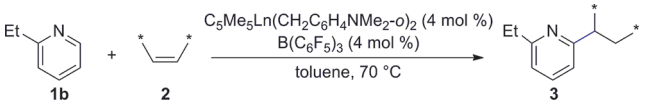
[a] Reactions were carried out with 1 mmol of pyridine in 3 mL of toluene under 3 atm of ethylene, unless otherwise noted. [b] Isolated yield. [c] Yield obtained by converting the product to its hydrochloride salt. [d] $C_5Me_5Y(CH_2C_6H_4NMe_2\text{-}o)_2$ was used. [e] 0.5 mmol of pyridine **1f**, 4% catalyst. [f] 0.5 mmol of quinoline **1g**, 8% catalyst.

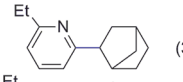
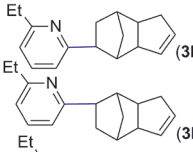
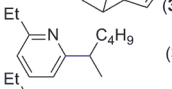
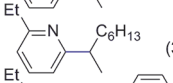
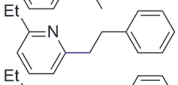
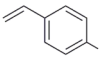
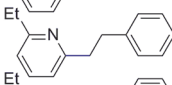
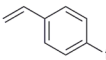
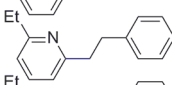
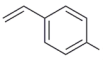
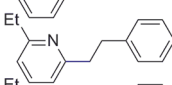
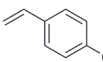
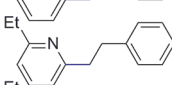
ethylpyridine derivatives (entries 9, 10); no dehalogenation was observed.

To examine the scope of olefin substrates, 2-ethylpyridine was then used to react with various olefins (Table 2). The *o*-C−H addition of 2-ethylpyridine to norbornene took place smoothly in the presence of 2 mol % of the Sc catalyst to afford the corresponding alkylation product **3bb** quantitatively (entry 1). In the case of dicyclopentadiene (**2c**), the reaction took place selectively at the norbornene unit, leaving the cyclopentene unit unchanged.[16] Two regioisomer products (**3bc** and **3bc′**) due to the asymmetry of the norbornene unit in dicyclopentadiene were obtained in a ca. 2:1 ratio (entry 2). In the alkylation with α-olefins such as 1-hexene and 1-octene, branched isomer products were obtained exclusively (entries 3 and 4), in contrast with late transition metal-catalyzed reactions, which always gave the linear isomers as a predominant product. [8a,9]

The scandium catalyst showed rather poor activity for the reaction of 2-ethylpyridine with styrene, although it was extremely active for the polymerization of styrene in the absence of a pyridine compound.[13k] However, the larger yttrium catalyst, though less active for the polymerization of styrene,[13a] showed excellent catalytic activity for *o*-alkylation of 2-ethylpyridine with styrene to give selectively the corresponding linear product (Table 2, entry 5). This reaction is also in contrast with the Ni-catalyzed

Table 2. Catalytic C−H Addition of 2-Ethylpyridine to Various Olefins[a]



Entry	Olefin	Ln	time (h)	Product	yield (%)[b]
1[c]	 (**2b**)	Sc	4	 (**3bb**)	98
2[c]	 (**2c**)	Sc	12	 (**3bc**) (**3bc′**)	99[e]
3[d]	 (**2d**)	Sc	32	 (**3bd**)	95
4[d]	(**2e**)	Sc	48	 (**3be**)	96
5	 (**2f**)	Y	32	 (**3bf**)	94
6	 (**2g**)	Y	16	 (**3bg**)	99
7	 (**2h**)	Y	12	 (**3bh**)	98
8	 (**2i**)	Y	48	 (**3bi**)	90
9	 (**2j**)	Y	48	 (**3bj**)	94
10	(**2k**)	Y	48	(**3bk**)	96
11	(**2l**)	Y	12	(**3bl**)	74
12	(**2m**)	Y	12	(**3bm**) n = 1 (**3bm′**) n = 2	62[f]

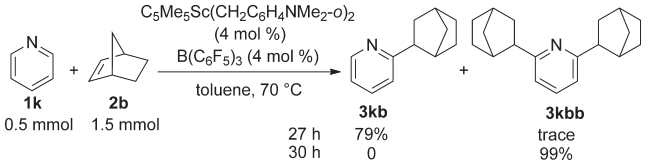
[a] Reactions were carried out with 0.5 mmol of pyridine and 1 mmol of an olefin in 2 mL of toluene, unless otherwise noted. [b] Isolated yield. [c] 1 mmol pyridine, 1.5 mmol olefin and 2% catalyst. [d] 1 mL toluene and 1 mL olefin. [e] **3bc**/**3bc′** = 2:1, determined by ^{1}H NMR. [f] **3bm**/**3bm′** = 1.2:1, determined by ^{1}H NMR. A small amount of 3,4-isoprene insertion products was also observed.

alkylation of pyridine with styrene, in which the branched isomer was formed as a major product and C−C bond formation took place at the C-4 position of pyridine.[9] Alkyl-, fluoro-, chloro-, and methoxy-substituted styrenes are also compatible with the yttrium catalyst to afford selectively the corresponding linear alkylation products (entries 6−10). To the best of our knowledge, this is the first example of catalytic *o*-selective alkylation of a pyridine compound with styrenes.[10]

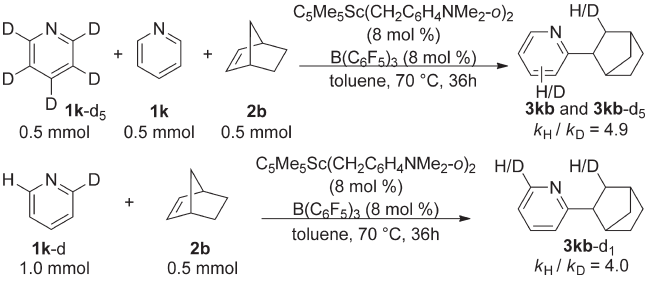
The yttrium catalyst is also suitable for C−H addition of 2-ethylpyridine to 1,3-cyclohexadiene to afford the corresponding allylated pyridine product **3bl** (entry 11). In the case of isoprene, both mono- and double-insertion products were obtained, even when an equimolar amount of isoprene was used (entry 12). These reactions represent the first example of catalytic C−H addition of a pyridine compound to a conjugated diene.[10]

dx.doi.org/10.1021/ja208129t |*J. Am. Chem. Soc.* 2011, 133, 18086–18089

Scheme 1. Mono- and Dialkylation of Pyridine with Norbornene



Scheme 2. C−H vs C−D Addition of Pyridine to Norbornene: Kinetic Isotope Effect



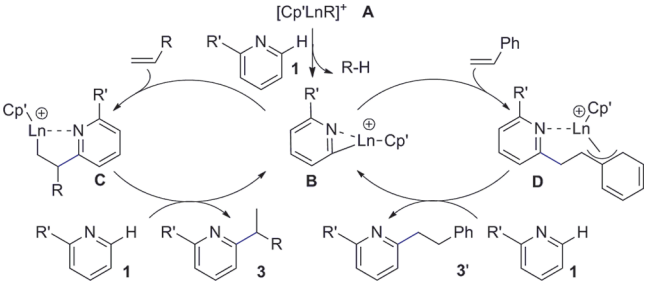
Similar to Zr catalysts,[7a] no alkylation was observed in the reaction of pyridine with ethylene and styrene, probably because of the formation of a relatively stable pyridine-coordinated metal species. However, the reaction between pyridine and norbornene took place smoothly in the presence of scandium catalyst (Scheme 1). Double *o*-alkylation of pyridine could also be achieved after most of the pyridine was consumed, but no dialkylation product was observed at the early stage. If the reaction was quenched after the first 27 h, the monoalkylation product **3kb** was isolated in 79% yield. Further alkylation of the monoalkylation product took place rapidly to afford the dialkylation product **3kbb** in 99% isolated yield in ca. 3 h (Scheme 1).

The reaction of a 1:1 mixture of pyridine and pyridine-d_5 with norbornene and the reaction of 2-D-pyridine with norbornene showed significant kinetic isotope effects (k_H/k_D = 4.9 and 4.0, respectively, Scheme 2), suggesting that C−H bond activation (deprotonation) could be involved in the rate-determining step of the present catalytic reaction.

On the basis of the observations described above and reported previously,[7,11d,f,13a,h,i,m] a possible mechanism for the present catalytic alkylation of pyridines can be proposed as shown in Scheme 3. Coordination of a pyridine compound **1** to the metal center of the cationic alkyl species **A**, generated from its neutral dialkyl precursor and an activator such as $B(C_6F_5)_3$, would promote *o*-C−H activation (deprotonation) of **1** to give pyridyl species **B**.[17] The 2,1-insertion of a 1-alkene into the metal−pyridyl bond in **B** would be sterically favored to afford **C**, which on subsequent deprotonation of another molecule of pyridine **1** should yield the branched alkylation product **3** and regenerate **B**. In the case of styrene, 1,2-insertion would be preferred because of possible formation of a stable benzallylic species such as **D**, which after protonation with a pyridine compound should give the linear alkylation product **3′**.

In summary, we have demonstrated that half-sandwich rare-earth dialkyl complexes such as $(C_5Me_5)Ln(CH_2C_6H_4NMe_2\text{-}o)_2$ (Ln = Sc, Y) in combination with an activator such as $B(C_6F_5)_3$ can serve as an excellent catalyst for *ortho*-selective C−H addition of

Scheme 3. A Possible Mechanism for Catalytic C−H Addition of Pyridines to Olefins



pyridines to a variety of olefins such as 1-alkenes, styrenes, and 1,3-conjugated dienes to afford straightforwardly a series of alkylated pyridine derivatives in an atom-economical way. The present rare-earth catalysts are complementary to late transition metal catalysts in terms of selectivity, functional group tolerance, and substrate scope. Further studies on rare-earth-catalyzed C−H functionalizations with other substrates are in progress.

■ ASSOCIATED CONTENT

Supporting Information. Detailed experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
houz@riken.jp

■ ACKNOWLEDGMENT

This work was partly supported by a Grant-in-Aid for Scientific Research (S) (21225004) from JSPS and the Key Project of International Cooperation of NSFC (20920102030). Dr. Jia-Rui Wang and Dr. Hao Zhang are gratefully appreciated for conducting initial studies of the related work.

■ REFERENCES

(1) (a) Michael, J. P. *Nat. Prod. Rep.* **2005**, *22*, 627–646. (b) Henry, G. D. *Tetrahedron* **2004**, *60*, 6043–6061. (c) Bagley, M. C.; Glover, C.; Merritt, E. A. *Synlett* **2007**, 2459–2482. (d) Arena, C. G.; Arico, G. *Curr. Org. Chem.* **2010**, *14*, 546–580. (e) Bianchini, C.; Giambastiani, G.; Luconi, L.; Meli, A. *Coord. Chem. Rev.* **2010**, *254*, 431–455. (f) Holliday, B. J.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2022–2043. (g) Kurth, D. G.; Higuchi, M. *Soft Matter* **2006**, *2*, 915–927.

(2) A recent review: Nakao, Y. *Synthesis* 2011, *20*, 3209–3219.

(3) For examples of borylation, see: (a) Cho, J.; Iverson, C. N.; Smith, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 12868–12869. (b) Takagi, J.; Sato, K.; Hartwig, J. F.; Ishiyama, T.; Miyaura, N. *Tetrahedron Lett.* **2002**, *43*, 5649–5651. (c) Mkhalid, I. A. I.; Coventry, D. N.; Albesa-Jove, D.; Batsanov, A. S.; Howard, J. A. K.; Perutz, R. N.; Marder, T. B. *Angew. Chem., Int. Ed.* **2006**, *45*, 489–491. (d) Murphy, J. M.; Liao, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 15434–15435. (e) Fischer, D. F.; Sarpong, R. *J. Am. Chem. Soc.* **2010**, *132*, 5926–5927. (f) Hurst, T. E.; Macklin, T. K.; Becker, M.; Hartmann, E.; Gel, W. K.; Salle, J. P.; Batsanov, A. S.; Marder, T. B.; Snieckus, V. *Chem.—Eur. J.* **2010**, *16*, 8155–8161.

(4) For examples of arylation, see: (a) Godula, K.; Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 3648–3649. (b) Berman, A. M.; Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 14926–14927. (c) Tobisu, M.; Hyodo, I.; Chatani, N. *J. Am. Chem. Soc.* **2009**, *131*, 12070–12071. (d) Yanagisawa, S.; Ueda, K.; Taniguchi, T.; Itami, K. *Org. Lett.* **2008**, *10*, 4673–4676. (e) Kobayashi, O.; Uraguchi, D.; Yamakawa, T. *Org. Lett.* **2009**, *11*, 2679–2682. (f) Li, M.; Hua, R. *Tetrahedron Lett.* **2009**, *50*, 1478–1481. (g) Seiple, I. B.; Su, S.; Rodriguez, R. A.; Gianatassio, R.; Fujiwara, Y.; Sobel, A. L.; Baran, P. S. *J. Am. Chem. Soc.* **2010**, *132*, 13194–13196.

(5) For examples of olefination, see: (a) Murakami, M.; Hori, S. *J. Am. Chem. Soc.* **2003**, *125*, 4720–4721. (b) Nakao, Y.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2008**, *130*, 2448–2449. (c) Tsai, C.; Shih, W.; Fang, C.; Li, C.; Ong, T.; Yap, G. P. A. *J. Am. Chem. Soc.* **2010**, *132*, 11887–11889. (d) Ye, M.; Gao, G.; Yu, J. *J. Am. Chem. Soc.* **2011**, *133*, 6964–6967.

(6) For some other examples, see: (a) Moore, E. J.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888–5890. (b) Kawashima, T.; Takao, T.; Suzuki, H. *J. Am. Chem. Soc.* **2007**, *129*, 11006–11007. (c) Beveridge, R. E.; Arndtsen, B. A. *Synthesis* **2010**, 1000–1008. (d) Tran, L. D.; Daugulis, O. *Org. Lett.* **2010**, *12*, 4277–4279. (e) Li, B.; Shi, Z. *Chem. Sci.* **2011**, *2*, 488–493. (f) Correia, C. A.; Yang, L.; Li, C. *Org. Lett.* **2011**, *13*, 4581–4583.

(7) (a) Jordan, R. F.; Taylor, D. F. *J. Am. Chem. Soc.* **1989**, *111*, 778–779. (b) Jordan, R. F.; Taylor, D. F.; Baenziger, N. C. *Organometallics* **1990**, *9*, 1546–1557. (c) Rodewald, S.; Jordan, R. F. *J. Am. Chem. Soc.* **1994**, *116*, 4491–4492. (d) Guram, A. S.; Jordan, R. F. *Organometallics* **1991**, *10*, 3470–3479.

(8) (a) Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 5332–5333. (b) Yotphan, S.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2010**, *12*, 2978–2981.

(9) Nakao, Y.; Yamada, Y.; Kashihara, N.; Hiyama, T. *J. Am. Chem. Soc.* **2010**, *132*, 13666–13668.

(10) Stoichiometric addition of zirconium−pyridyl species to styrene and conjugated dienes was reported; see refs 7c and 7d. Ni-catalyzed C-4-alkylation of pyridine with styrene was reported recently; see ref 9.

(11) Selected examples: (a) Watson, P. L. *J. Chem. Soc., Chem. Commun.* **1983**, 276–277. (b) Thompson, M. E.; Baxter, S. M.; Bulls, A. R.; Burger, B. J.; Nolan, M. C.; Santarsiero, B. D.; Schaefer, W. P.; Bercaw, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 203–219. (c) Den Haan, K. H.; Wielstra, Y.; Teuben, J. H. *Organometallics* **1987**, *6*, 2053–2060. (d) Deelman, B.; Stevels, W. M.; Teuben, J. H.; Lakin, M. T.; Spek, A. L. *Organometallics* **1994**, *13*, 3881–3891. (e) Duchateau, R.; van Wee, C. T.; Teuben, J. H. *Organometallics* **1996**, *15*, 2291–2302. (f) Duchateau, R.; Brussee, E. A. C.; Meetsma, A.; Teuben, J. H. *Organometallics* **1997**, *16*, 5506–5516. (g) Jantunen, K. C.; Scott, B. L.; Gordon, J. C.; Kiplinger, J. L. *Organometallics* **2007**, *26*, 2777–2781. (h) Carver, C. T.; Diaconescu, P. L. *J. Am. Chem. Soc.* **2008**, *130*, 7558–7559. (i) Arndt, S.; Elvidge, B. R.; Zeimentz, P. M.; Spaniol, T. P.; Okuda, J. *Organometallics* **2006**, *25*, 793–795. (j) Yahia, A.; Kramer, M. U.; Okuda, J.; Maron, L. *J. Organomet. Chem.* **2010**, *695*, 2789–2793. (k) Kramer, M. U.; Yahia, A.; Maron, L.; Okuda, J. *C. R. Chim.* **2010**, *13*, 626–632.

(12) Recent reviews: (a) Hou, Z. M.; Luo, Y. J.; Li, X. F. *J. Organomet. Chem.* **2006**, *691*, 3114–3121. (b) Nishiura, M.; Hou, Z. M. *Nature Chem.* **2010**, *2*, 257–268.

(13) For examples, see: (a) Luo, Y.; Baldamus, J.; Hou, Z. *J. Am. Chem. Soc.* **2004**, *126*, 13910–13911. (b) Zhang, L.; Luo, Y.; Hou, Z. *J. Am. Chem. Soc.* **2005**, *127*, 14562–14563. (c) Li, X.; Hou, Z. *Macromolecules* **2005**, *38*, 6767–6769. (d) Li, X. F.; Baldamus, J.; Nishiura, M.; Tardif, O.; Hou, Z. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 8184–8188. (e) Li, X. F.; Nishiura, M.; Mori, K.; Mashiko, T.; Hou, Z. M. *Chem. Commun.* **2007**, 4137–4139. (f) Yu, N.; Nishiura, M.; Li, X. F.; Xi, Z. F.; Hou, Z. M. *Chem.—Asian J.* **2008**, *3*, 1406–1414. (g) Zhang, H.; Luo, Y.; Hou, Z. *Macromolecules* **2008**, *41*, 1064–1066. (h) Li, X.; Nishiura, M.; Hu, L.; Mori, K.; Hou, Z. *J. Am. Chem. Soc.* **2009**, *131*, 13870–13882. (i) Li, X.; Hou, Z. *Macromolecules* **2010**, *43*, 8904–8909. (j) Pan, L.; Zhang, K.; Nishiura, M.; Hou, Z. *Macromolecules* **2010**, *43*, 9591–9593. (k) Guo, F.; Nishiura, M.; Koshino, H.; Hou, Z. *Macromolecules* **2011**, *44*, 6335–6344. (l) Guo, F.; Nishiura, M.; Koshino, H.; Hou, Z. *Macromolecules* **2011**, *44*, 2400–2403. (m) Luo, Y.; Luo, Y.; Qu, J.; Hou, Z. *Organometallics* **2011**, *30*, 2908–2919. (n) Pan, L.; Zhang, K.; Nishiura, M.; Hou, Z. *Angew. Chem., Int. Ed.* **2011** in press. DOI: 10.1002/anie.201104011.

(14) For stoichiometric *o*-metalation of pyridine by cationic rare-earth alkyls, see refs 11i−11k. For examples of the use of cationic rare-earth catalysts in organic synthesis, see: (a) Lauterwasser, F.; Hayes, P. G.; Bräse, S.; Piers, W. E.; Schafer, L. L. *Organometallics* **2004**, *23*, 2234–2237. (b) Tazelaar, C. G. J.; Bambirra, S.; van Leusen, D.; Meetsma, A.; Hessen, B.; Teuben, J. H. *Organometallics* **2004**, *23*, 936–939. (c) Ge, S.; Meetsma, A.; Hessen, B. *Organometallics* **2009**, *28*, 719–726. (d) Takimoto, M.; Usami, S.; Hou, Z. *J. Am. Chem. Soc.* **2009**, *131*, 18266–18268.

(15) Similar regioselectivity was observed in the Zr-mediated stoichiometric reaction of 2-phenylpyridine with propylene; see ref 7c. For examples of the use of a pyridine unit as a directing group in late transition metal-catalyzed aromatic C−H activation, see: (a) Lim, Y.; Kim, Y. H.; Kang, J. *J. Chem. Soc., Chem. Commun.* **1994**, 2267–2268. (b) Hull, K. L.; Anani, W. Q.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 7134–7135. (c) Tsai, A. S.; Tauchert, M. E.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 1248–1250.

(16) No reaction between 2-ethylpyridine and cyclopentene or cyclohexene was observed under the same conditions. For the Rh-catalyzed alkylation of quinoline with cyclohexene, see ref 8a. For stoichiometric addition of Zr-pyridyl species to 2-butene, see ref 7c.

(17) Alkylation of 2-Me-6-D-pyridine with ethylene or styrene in the presence of $(C_5Me_5)Ln(CH_2C_6H_4NMe_2\text{-}o)_2$ (Ln = Sc or Y)/$B(C_6F_5)_3$ in toluene at 70 °C gave the corresponding *o*-alkylation products with partial deuteration at both the *o*-methyl group and the β-carbon atom. In the absence of an olefin, H/D exchange between the methyl C−H and the pyridyl C−D units was observed. This is under further investigation and will be reported in due course.