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# Selective Preparation of Pyridines, Pyridones, and Iminopyridines from Two Different Alkynes via Azazirconacycles

Tamotsu Takahashi,* Fu-Yu Tsai, Yanzhong Li, Hui Wang, Yoshihiko Kondo, Masamichi Yamanaka, Kiyohiko Nakajima,† and Martin Kotora

*Contribution from the Catalysis Research Center and Graduate School of Pharmaceutical Sciences, Hokkaido University, and CREST, Science and Technology Corporation (JST), Sapporo 060-0811, Japan, and Department of Chemistry, Aichi University of Education, Igaya, Kariya, Aichi 448-8542, Japan*

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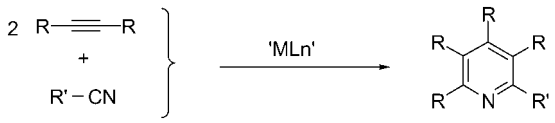
***Abstract:*** Selective preparation of pyridine derivatives from two different alkynes and a nitrile was achieved by a novel procedure in which an alkyne and a nitrile couple first to give an azazirconacyclopentadiene followed by reaction with the second alkyne in the presence of 1 equiv of $NiCl_2(PPh_3)_2$. This procedure gives only single products of pyridine derivatives from two different symmetrical alkynes and a nitrile. Our novel procedure can be used even with two similar alkyl-substituted alkynes such as 3-hexyne and 4-octyne. Two possible pyridine isomers from 3-hexyne, 4-octyne, and acetonitrile could be completely and independently prepared as single products by this method. The origin of the selectivity comes from the addition order of two different alkynes. This method was applied for the formation of pyridones and iminopyridines using isocyanate and carbodiimide derivatives instead of nitriles, respectively. Reaction of an alkyne with $Cp_2ZrEt_2$ and an isocyanate or a carbodiimide gives an azazirconacycle. Treatment of the azazirconacycle with the second alkyne in the presence of 1 equiv of $NiCl_2(PPh_3)_2$ gave a pyridone or an iminopyridine derivative. The use of two different unsymmetrical alkynes afforded the pyridine with five different substituents when the first alkyne has a trialkylsilyl group and the second alkyne has a phenyl group as functional groups. On the other hand, azazirconacyclopentadienes reacted with propargyl bromide in the presence of CuCl with excellent regioselectivity to give tetrasubstituted pyridine derivatives as single products. With the assistance of the trialkylsilyl groups, pyridines with all different substituents including H were also prepared.

## Introduction

Transition metal catalyzed or mediated formation of heterocycles has always received considerable synthetic attention.[1−13] Among them the preparation of pyridines directly from alkynes and nitriles is especially attractive methodology, because it enables the construction of compounds with a high degree of complexity from a rather simple starting material (Scheme 1). A great deal of work has been done in this area with regard to mechanistic and synthetic aspects of this reaction and the most effective reagents for this type of cycloaddition are those based on Co complexes.[2,3] The pyridine formation from two alkynes and a nitrile with Co complexes was originated by Wakatsuki and Yamazaki.[2a] Although this method is very effective, there is a critical problem for the selective intermolecular coupling of two different alkynes with a nitrile. In a few cases, a single product of the pyridines was obtained with the assistance of a functional group such as an alkoxy carbonyl group.[2d] However, in most cases a mixture of two regioisomers is obtained. The major reason can be attributed to the reaction mechanism.[14]

***Scheme 1***




Studies on pyridine formation have shown that the first step is the intermolecular coupling of two alkynes forming a cobaltacyclopentadiene (Scheme 2; M = Co).[3d] Then a nitrile reacts with the cobaltacyclopentadiene to give a pyridine compound. In the case of a cobaltacyclopentadiene prepared from two different alkynes, there are two possible orientations for the nitrile as shown in Scheme 2 (M = Co). Therefore, pyridines are usually obtained as a mixture of two regioisomers. In some cases the ratio of the regioisomers can be controlled

* Address correspondence to this author at Hokkaido University. E-mail: tamotsu@cat.hokudai.ac.jp.
† Present address: Aichi University of Education.

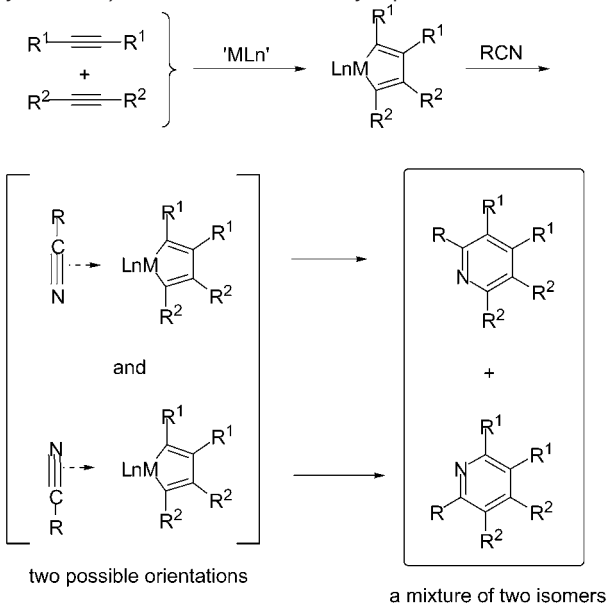
(1) For reviews, see: (a) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92. (b) Grotjahn, D. B. *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier Science Ltd: Oxford, 1995; Vol. 12; pp 741−770. (c) Schore, N. E. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon Press Ltd: Oxford, 1991; Vol. 5, pp 1129−1162. (d) Harrington, P. J. *Transition Metals in Total Synthesis*; John Wiley & Sons: New York, 1990; pp 200−240. (e) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081−1119. (f) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539−556. (g) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901−2915.

due to the substituents or sometimes a single isomer can be obtained. This selectivity is completely dependent on the substituents of alkynes.

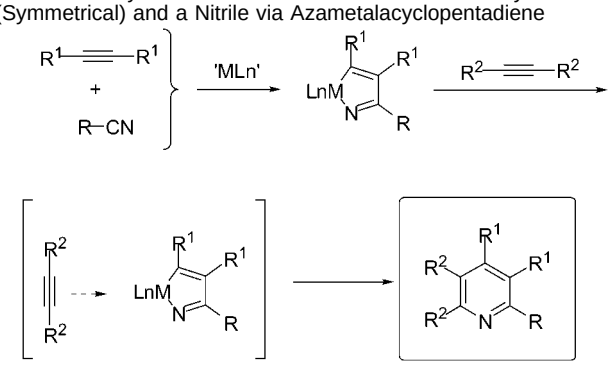
However, to develop a useful procedure for the formation of a single isomer of pyridine derivatives from two different alkynes and a nitrile, a novel procedure via azametalacyclopentadienes as shown in Scheme 3 has an advantage. This procedure always affords a single isomer of pyridine derivatives from two symmetrical alkynes.

We have recently reported the formation of azazirconacyclopentadienes from one alkyne and a nitrile.[13] This preparative method of azazirconacyclopentadienes could be used for our novel procedure. Very recently we have preliminarily reported the selective formation of pyridine derivatives from two different alkynes and a nitrile.[16] In this paper we report the details of the strategy and extension of this method to selective formation of pyridones and iminopyridines via azazirconacycles in the presence of $NiCl_2(PPh_3)_2$. We also report the formation of pyridine derivatives with five different substituents from two different unsymmetrical alkynes and a nitrile with assistance from functional groups. Furthermore, we report here the selective formation of pyridine derivatives by the reaction of azazirconacyclopentadienes with propargyl halides with excellent regioselectivity in the presence of CuCl.

***Scheme 2.*** Pyridine Formation from Two Different Alkynes (Symmetrical) and a Nitrile via Metalacyclopentadiene




***Scheme 3.*** Pyridine Formation from Two Different Alkynes (Symmetrical) and a Nitrile via Azametalacyclopentadiene




## Results and Discussion

**Selective Pyridine Formation from Two Different Symmetrical Alkynes and a Nitrile.** To develop the substituent-independent procedure for the formation of pyridine derivatives

(2) Pyridine formation for Co: (a) Wakatsuki, Y.; Yamazaki, H. *J. Chem. Soc., Chem. Commun.* **1973**, 280−281. (b) Wakatsuki, Y.; Yamazaki, H. *Tetrahedron Lett.* **1973**, 3383−3384. (c) Wakatsuki, Y.; Yamazaki, H. *Synthesis* **1976**, 26−28. (d) Wakatsuki, Y.; Yamazaki, H. *J. Chem. Soc., Dalton Trans* **1978**, 1278−1282. (e) Wakatsuki, Y.; Yamazaki, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2715−2716. (f) Vollhardt, K. P. C.; Bergman, R. G. *J. Am. Chem. Soc.* **1974**, *96*, 4996−4998. (g) Naiman, A.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 708−709. (h) Brien, D. J.; Naiman, A.; Vollhardt, K. P. C. *J. Chem. Soc., Chem. Commun.* **1982**, 133−134. (i) Bonnemann, H.; Brinkmann, R.; Schenkluhn, H. *Synthesis* **1974**, 575−577. (j) Bonnemann, H.; Brinkmann, R. *Synthesis* **1975**, 600−602. (k) Bonnemann, H.; Brijoux, W.; Brinkmann, R.; Meuers, W.; Mynott, R.; von Phillipsborn, W.; Egolf, T. *J. Organomet. Chem.* **1984**, *272*, 231−249. (l) Vitulli, G.; Bertozzi, S.; Lazzaroni, R.; Salvadori, P. *J. Organomet. Chem.* **1986**, *307*, C35−C37. (m) Vitulli, G.; Bertozzi, S.; Vignali, M.; Lazzaroni, R.; Salvadori, P. *J. Organomet. Chem.* **1987**, *326*, C33−C36. (n) Chiusoli, G. P.; Pallini, L.; Terenghi, G. *Transition Met. Chem.* **1983**, *8*, 250−252. (o) Chiusoli, G. P.; Pallini, L.; Terenghi, G. *Transition Met. Chem.* **1984**, *9*, 360. (p) Battaglia, L. P.; Delledonne, D.; Nardelli, M.; Predieri, G.; Chiusoli, G. P.; Costa, M.; Pelizzi, C. *J. Organomet. Chem.* **1989**, *363*, 209−222. (q) Zhou, Z.; Battaglia, L. P.; Chiusoli, G. P.; Costa, M.; Nardelli, M.; Pelizzi, C.; Predieri, G. *J. Organomet. Chem.* **1991**, *417*, 51−63. (r) Jerome, K. S.; Parsons, E. J. *Organometallics* **1993**, *12*, 2991−2993. (s) Viljoen, J. S.; du Plessis, J. A. K. *J. Mol. Catal.* **1993**, *79*, 75−84. (t) Heller, B.; Oehme, G. *J. Chem. Soc., Chem. Commun.* **1995**, 179−180. (u) Varela, A.; Castedo, L.; Saá, C. *J. Org. Chem.* **1997**, *62*, 4189−4192. (v) Varela, A.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **1998**, *120*, 12147−12148. (w) Varela, A.; Castedo, L.; Saá, C. *Org. Lett.* **1999**, *1*, 2141−2143. (x) Eaton, B. E.; Fatland, A. W *Org. Lett.* **2000**, *2*, 3131−3133.
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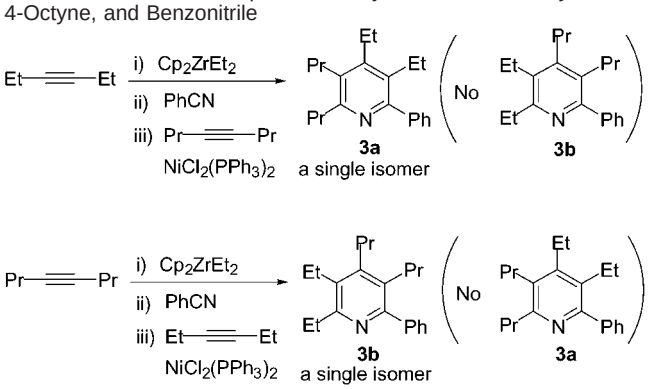
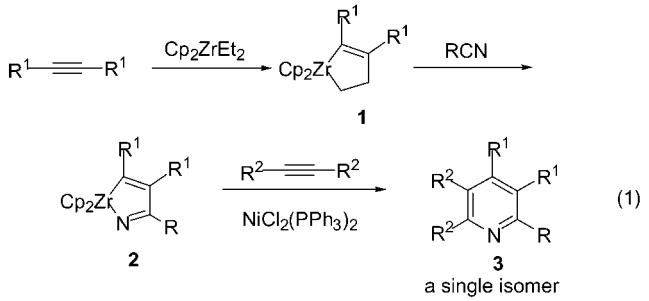
(5) Pyridine formation for Ru: (a) Yamamoto, Y.; Ogawa, R.; Itoh, K. *J. Am. Chem. Soc.* **2001**, *123*, 6189−6190. (b) Yamamoto, Y.; Okuda, S.; Itoh, K. *Chem. Commun.* **2001**, 1102−1103.
(6) Pyridine formation for Ti: (a) Hill, J. E.; Balaich, G.; Fanwick, P. E.; Rothwell, I. P. *Organometallics* **1993**, *12*, 2911−2924.
(7) Pyridine formation for Ta: (a) Strickler, J. R.; Bruck, M. A.; Wigley, D. E. *J. Am. Chem. Soc.* **1990**, *112*, 2814−2816. (b) Smith, D. P.; Strickler, J. R.; Gray, S. D.; Bruck, M. A.; Holmes, R. S.; Wigley, D. E. *Organometallics* **1992**, *11*, 1275−1288. (c) Takai, K.; Yamada, M.; Utimoto, K. *Chem. Lett.* **1995**, 851−852.
(8) Pyridone formation for Co: (a) Hong, P.; Yamazaki, H. *Tetrahedron Lett.* **1977**, 1333−1336. (b) Hong, P.; Yamazaki, H. *Synthesis* **1977**, 50−52. (c) Earl, R. A.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 4786−4800. (d) Diversi, P.; Ingrosso, G.; Luchering, A.; Malquori, S. *J. Mol. Catal.* **1987**, *40*, 267.
(9) Pyridone formation for Ni: (a) Hoberg, H.; Oster, B. W. *J. Organomet. Chem.* **1982**, *234*, C35−C38. (b) Hoberg, H.; Oster, B. W. *Synthesis* **1982**, 324−325. (c) Hoberg, H.; Oster, B. W. *J. Organomet. Chem.* **1983**, *252*, 359−364.
(10) Pyridone formation for Rh: Flynn, S. T.; Hasso-enderson, S. E.; Parkins, A. W. *J. Mol. Catal.* **1985**, *32*, 101−105.
(11) Pyridone formation for Ru: Yamamoto, Y.; Takagishi, H.; Itoh, K. *Org. Lett.* **2001**, *3*, 2117−2119.
(12) Iminopyridine formation for Co: see refs 8a,b.
(13) Iminopyridine formation for Ni: Hoberg, H.; Burkhart, G. *Synthesis* **1979**, 525−526.
(14) (a) Wakatsuki, Y.; Kuramitsu, T.; Yamazaki, H. *Tetrahedron Lett.* **1974**, 4549−4552. (b) Yamazaki, H.; Wakatsuki, Y. *J. Organomet. Chem.* **1977**, *139*, 157−167. (c) Wakatsuki, Y.; Nomura, O.; Kitaura, K.; Morokuma, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1983**, *105*, 1907−1912.
(15) (a) Takahashi, T.; Xi, C.; Xi, Z.; Kageyama, M.; Fischer, R.; Nakajima, K.; Negishi, E. *J. Org. Chem.* **1998**, *63*, 6802−6806. (b) For a preliminary report, see: Takahashi, T.; Kageyama, M.; Denisov, V.; Hara, R.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 687−690.
(16) Takahashi, T.; Tsai, F.-Y.; Kotora, M. *J. Am. Chem. Soc.* **2000**, *122*, 4994−4995.

***Scheme 4.*** Selective Preparation of Pyridines from 3-Hexyne, 4-Octyne, and Benzonitrile



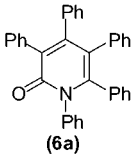
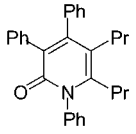
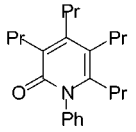
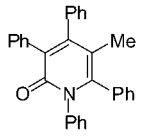
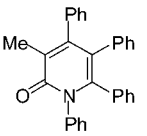
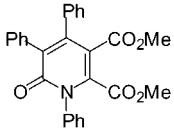
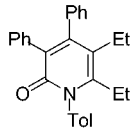
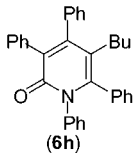

from two different alkynes and a nitrile, the preparation of pyridines via azametalacyclopentadienes has been investigated. As shown in Scheme 3, by this method via azazirconacyclopentadienes there is only one possible orientation for the second symmetric alkynes. Therefore, this procedure always gives a single isomer of the pyridines. It is independent from the substituents of the alkynes. The orientation of two different symmetrical alkynes is dependent on the order of addition of those two alkynes. The first alkyne always couples with the carbon of the nitrile and the second alkyne makes the bond with the nitrogen of the nitrile. This selectivity can be completely controlled by this method.




In the case of cobalt complexes, coupling of an alkyne and a nitrile is not convenient. As Saá and co-workers showed in the mechanism, it is believed that two alkynes couple first but not the coupling of an alkyne and a nitrile.[2u−w] Recently, we have reported the formation of azazirconacyclopentadienes from one alkyne and a nitrile via C−C bond cleavage of zirconacyclopentenes. We found that the azazirconacyclopentadienes did not directly react with the second alkyne, but in the presence of Ni(II) complexes, they reacted to give pyridine derivatives.[17] As shown in Scheme 3, when two different symmetrical alkynes were used, always only one isomer among two possible isomers was obtained. Usually, the recognition of the difference between 3-hexyne and 4-octyne is quite difficult. By this method two isomers of pyridines from 3-hexyne and 4-octyne and a nitrile could be completely controlled as shown in Scheme 4.

**Formation of Pyridones and Iminopyridines via Azazirconacycles.** Our novel addition-order-dependent selective coupling reactions can be applied for other heterocycle formations such as pyridones[3−11] and iminopyridines.[12,13] Recently we have reported the formation of azazirconacyclopentenones **4** from zirconacyclopentenes and isocyanates.[18] The structure of **4** is not clear yet. It might be in equilibrium between **4a** and oxazirconacycle **4b**. Fortunately, this problem is of no importance for further steps in the preparation of pyridones. The reaction of **4** with the second alkyne in the presence of $NiCl_2(PPh_3)_2$ gave the corresponding pyridone **6** as a single isomer. Results are shown in Table 1. It is noteworthy that when unsymmetrically substituted alkynes were used as the first alkyne or as the second alkyne, only one regioisomer was obtained for **6e**, **6d**, and **6h**. This could be achieved either by

***Table 1.*** Formation of Pyridone Derivatives

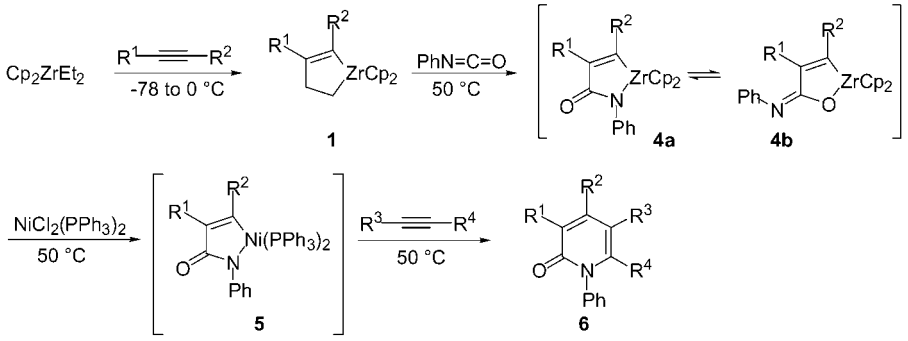
| 1 st Alkyne | 2 nd Alkyne | Product | Yield /(%)[a] |
|---|---|---|---|
| Ph—≡—Ph | Ph—≡—Ph |  (**6a**) | (67) |
| Ph—≡—Ph | Pr—≡—Pr |  (**6b**) | 72 (61) |
| Pr—≡—Pr | Pr—≡—Pr |  (**6c**) | 46(40) |
| Ph—≡—Ph | Ph—≡—Me |  (**6d**) | (56) |
| Ph—≡—Me | Ph—≡—Ph |  (**6e**) | (65) |
| Ph—≡—Ph | MeO2C—≡—CO2Me |  (**6f**) | (20) |
| Ph—≡—Ph[b] | Et—≡—Et |  (**6g**) | (49) |
| Ph—≡—Ph | Ph—≡—Bu |  (**6h**) | (61) |

[a] NMR or GC yields are given in parentheses. [b] The reaction was carried out with (4-methylphenyl)isocyanate.

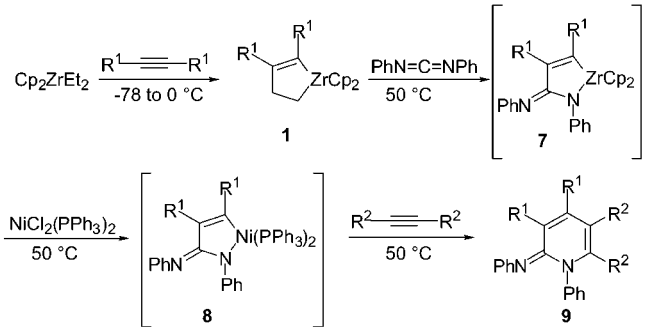
(17) For a detailed discussion concerning the reaction mechanism with transmetalation to Ni, see: (a) Reference 16. (b) Takahashi, T.; Tsai, F.-Y.; Li, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1999**, *121*, 11093−11100.

(18) Takahashi, T.; Li, Y.; Tsai, F.-Y.; Nakajima, K. *Organomatallics* **2001**, *20*, 595−597.

***Scheme 5***



***Scheme 6***



***Scheme 7***

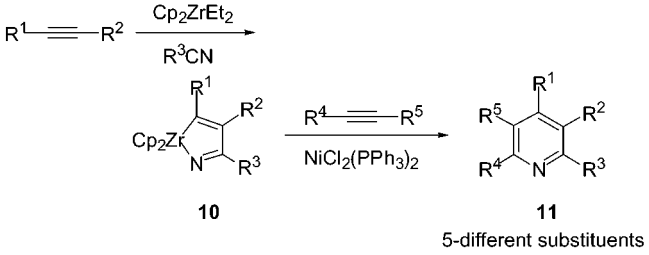
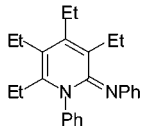
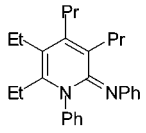
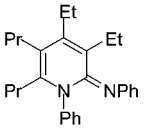
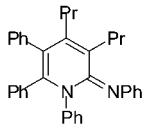
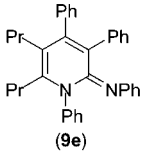


***Table 2.*** Formation of Iminopyridines

| 1 st Alkyne | 2 nd Alkyne | Product | Isolated yield (%) |
|---|---|---|---|
| Et—≡—Et | Et—≡—Et |  (**9a**) | 61 |
| Pr—≡—Pr | Et—≡—Et |  (**9b**) | 56 |
| Et—≡—Et | Pr—≡—Pr |  (**9c**) | 69 |
| Pr—≡—Pr | Ph—≡—Ph |  (**9d**) | 35 |
| Ph—≡—Ph | Pr—≡—Pr |  (**9e**) | 78 |

the regioselective preparation of an unsymmetrically substituted zirconacyclopentene or by regioselective insertion of the second alkyne. Note that compounds **6d** and **6e** are regioisomers. Preparation of these isomers can be controlled by this method. The reaction also may be carried out with electron-deficient alkynes such as DMAD to give **6f**, although the yield of the product was rather low.

A plausible reaction mechanism involves the formation of azanickelacyclopetenone **5** by transmetalation of **4** to Ni and the subsequent insertion of the second alkyne to give **6**. In fact, it has been reported that azanickelacyclopentenone **5** with a TMEDA ligand instead of $PPh_3$ ($R^1 = R^2 =$ Ph) reacted with DMAD to give **6f**.[9c]

The formation of iminopyridines is similar to that of pyridones and it proceeds through the same reaction mechanism and under the identical reaction conditions, except for the use of a carbodiimide instead of an isocyanate (Scheme 6). The reaction proceeds through intermediates **7** and **8**. Some typical examples are given in Table 2. The reaction proceeded as expected, affording the corresponding iminopyridines in good yields. Once again the selective formation of regioisomers is illustrated by the synthesis of **9d** and **9e.** The structure of **9a** was confirmed by X-ray analysis.

**Selective Pyridine Formation from Two Different Unsymmetrical Alkynes and a Nitrile.** As mentioned above, we have developed a novel procedure for the selective preparation of pyridine derivatives, pyridones, and iminopyridines from two different symmetrical alkynes. This procedure was independent from the substituents of the alkynes. To develop a selective method using unsymmetrical alkynes, the procedure should be dependent on the functional groups of the alkynes. Here we would like to demonstrate a novel combination of our new method described above (the addition-order-dependent selective coupling reaction) and the functional-group-dependent selective coupling of unsymmetrical alkynes.

As we reported, silyl-substituted unsymmetrical alkynes and nitriles can provide azazirconacyclopentadienes with complete regioselectivity.[19] It is noteworthy that when phenyl- and alkyl-

(19) (a) Takahashi, T.; Xi, Z.; Nishihara, Y.; Huo, S.; Kasai, K.; Aoyagi, K.; Denisov, V.; Negishi, E. *Tetrahedron* **1997**, *53*, 9123−9134. (b) Xi, Z.; Hara, R.; Takahashi, T. *J. Org. Chem.* **1995**, *60*, 4444−4446. (c) See also ref 15a. (d) Takahashi, T.; Xi, Z.; Rousset, C. J.; Suzuki, N. *Chem. Lett.* **1993**, 1001−1002.

***Scheme 8***

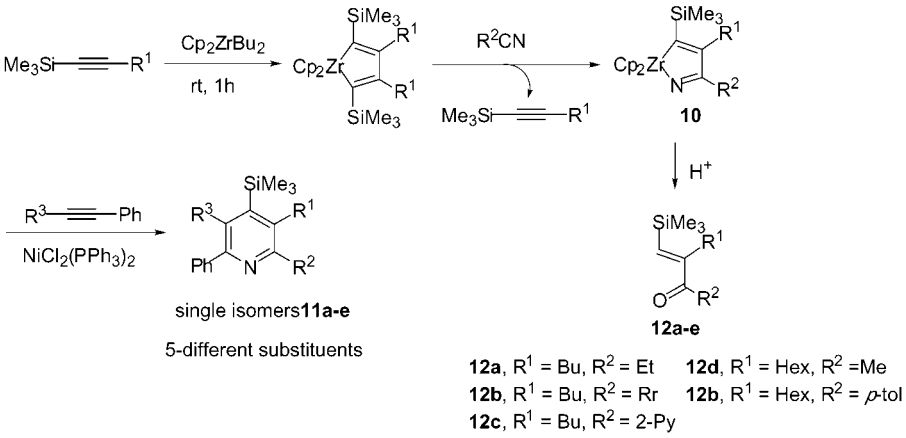
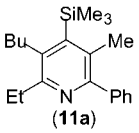
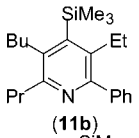
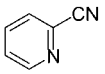
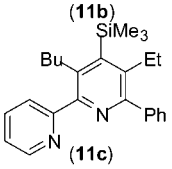
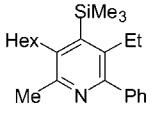
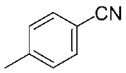
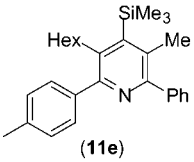



***Table 3.*** Regioselective Formation of Pentasubstituted Pyridines from Two Different Unsymmetrical Alkynes

| 1st Alkyne | Nitrile | 2nd Alkyne | Product | Yield (%)[a] |
|---|---|---|---|---|
| Me$_3$Si—≡—Bu | CN | Ph—≡—Me |  (**11a**) | 77 (52) |
| Me$_3$Si—≡—Bu | CN | Ph—≡—Et |  (**11b**) | 75 (53) |
| Me$_3$Si—≡—Bu |  | Ph—≡—Et |  (**11c**) | 62 (49) |
| Me$_3$Si—≡—Hex | MeCN | Ph—≡—Et |  (**11d**) | 69 (59) |
| Me$_3$Si—≡—Hex |  | Ph—≡—Me |  (**11e**) | 58 (45) |

[a] GC yields. Isolated yileds are given in parentheses.

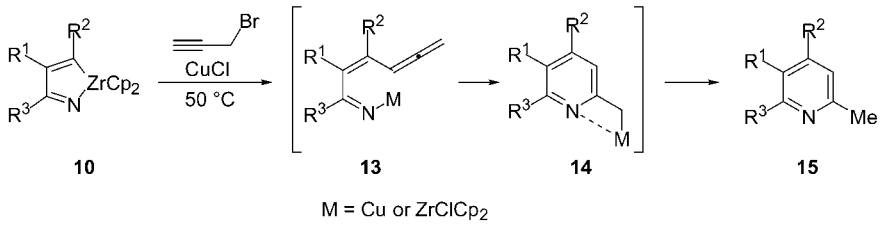
substituted alkynes were used as the second alkynes, the coupling reaction proceeded selectively and only a single product was obtained as reported. Phenyl group-substituted carbon in the C−C triple bond always makes a bond with the nitrogen atom of the azametalacyclopentadienes. Those two selective reactions could be combined as shown to give pyridine derivatives from two different unsymmetrical alkynes as shown in Scheme 8.

We have previously shown that such α,α′-trimethylsilyl-substituted zirconacycles, prepared by the reaction of $Cp_2ZrBu_2$ (Negishi reagent) with 2 equiv of a trimethylsilylalkyne, undergo substitution of one of the alkyne moieties via β,β′-carbon−carbon cleavage with a number of unsaturated compounds including a nitrile. Moreover, the remaining trimethylsilyl group always occupies an α-position to the zirconium atom.[20] Therefore by using this method the reaction of Negishi reagent with 2 equiv of trimethylsilylalkyne afforded zirconacyclopentadiene, which was followed by the subsequent substitution with the nitrile resulting in the formation of an azazirconacyclopentadiene **10**. As far as the reaction with the nitrile is concerned, the nitrogen atom of azazirconacyclopentadiene is always bonded to the zirconium atom. Results are shown in Table 3.

The regiochemistry of the trimethylsilyl group and an $R^1$ group was determined in the hydrolysis products **12a**−**e**. In all cases, only single isomers were obtained with complete regioselectivity. The regiochemistry of a phenyl group and an alkyl group ($R^3$) in **11a**−**e** were determined by observation of the NOEs between the trimethylsilyl group and the alkyl group ($R^3$) in their NMR spectra.

(20) Hara, R.; Xi, Z.; Kotora, M.; Xi, C.; Takahashi, T. *Chem. Lett.* **1996**, 1003−1004.

***Scheme 9***




In all cases, we obtained the pyridines with five different groups as single products. No traces of regioisomers were found. The trimethylsilyl group always occupied a $\gamma$-position and the phenyl group from the second alkyne was at an $\alpha$-position in the pyridine ring.

Although the intermediate after transmetalation of azazirconacyclopentadienes to Ni(II) is still unclear, we believe that azanickelacyclopentadienes are formed, since the nickelacyclopentadiene has been isolated in the case of the reaction of bis(cyclopentadienyl)tetraphenylzirconacyclopentadiene with $NiCl_2$(dppe). The regiochemistry of the second alkyne was controlled by the difference between a phenyl group and an alkyl group.[16]

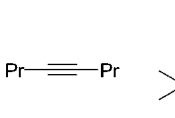
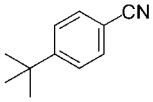
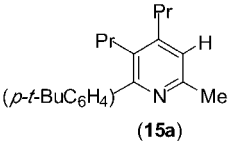
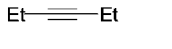
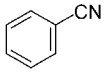
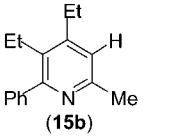
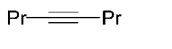
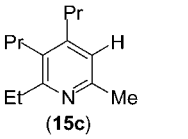
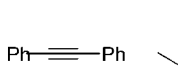
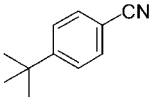
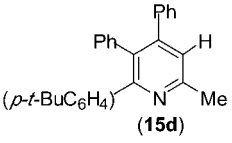
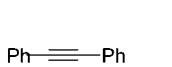
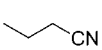
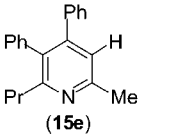
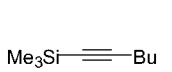
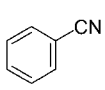
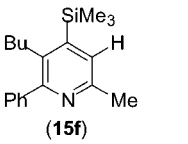
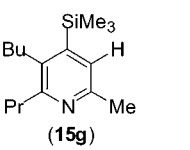
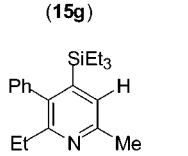
**Reaction of Azazirconacyclopentadienes with Propargyl Halides in the Presence of CuCl.** Azazirconacyclopentadienes have two different bonds such as the Zr−C and the Zr−N bonds. This difference can be used for the regioselective coupling of the second alkynes. We found that in the presence of CuCl, propargyl bromides reacted with azazirconacyclopentadienes to afford tetrasubstituted pyridine derivatives with excellent regioselecitvity on the propargyl compounds as shown in Scheme 9.[21] It is well-known that the $sp^2$-C in the zirconacycles readily transmetalates from Zr to Cu. Therefore, in this case the selective transmetalation of the $sp^2$-C from Zr to Cu is the first step. Successive addition of the alkenyl copper moiety to the allene moiety leads to the formation of pyridine derivatives.

In Table 4 are given some characteristic examples. It is important to stress that as the result of the reaction mechanism in all cases this approach furnishes selectively 2,3,4,6-substituted pyridines **15**. Once again no other isomers were detected in any of the reaction mixtures. Alkyl- and aryl-tetrasubstituted pyridines prepared from symmetrical alkynes through the azazirconacyclopentadiene pathway were obtained in good yields. The pyridines with five different substituents including H also could be prepared by this method with assistance from the trimethylsilyl group or triethylsilylphenylethyne, where an almost quantitative yield of the pyridine was obtained.

## Conclusion

We have presented a general strategy for the regioselective preparation of nitrogen-containing heterocycles such as pyridines, pyridones, and iminopyridines by the reaction of azazirconacycles with alkyne derivatives. Selective formation of pyridines, pyridones, and iminopyridines could be achieved via azazirconacycles. The selectivity is not dependent on the substituents of alkynes. The orientation of two different alkynes and a nitrile is dependent on the order of addition of alkynes. When two different unsymmetrical alkynes were used, the assistance of the functional groups was required. Two regioselective reactions were combined for the selective formation of five different substituted pyridines. For the first alkyne, the complete selectivity was given by the role of trialkylsilyl groups. The trialkylsilyl groups always occupy the $\alpha$-position of the azazirconacycles. The excellent regioselectivity of the second alkynes can be attributed to the selective coupling of phenyla-

***Table 4.*** Regioselective Formation of Tetrasubstituted Pyridines from the Reaction of Azazirconacyclopentadienes with Propargyl Bromide

| Alkyne | Nitrile | Product | Yield (%)[a] |
|---|---|---|---|
|  |  |  (**15a**) | 93 (81) |
|  |  |  (**15b**) | 98 (77) |
|  |  |  (**15c**) | 57 (43) |
|  |  |  (**15d**) | 73 (50) |
|  |  |  (**15e**) | 66 (57) |
|  |  |  (**15f**) | 54 (46) |
|  |  |  (**15g**) | 34 (27) |
|  |  |  (**15h**) | 94 (81) |

[a] GC yields. Isolated yields are given in parentheses.

(21) The similar reaction mechanism accounts for the formation of benzenes by the reaction of zirconacyclopentadienes with propargyl chloride. Kotora, M.; Noguchi, Y.; Takahashi, T. *Collect. Czech. Chem. Commun.* **1999**, *64*, 1119−1124.

lkylethynes in the presence of Ni(II) complexes. Selective transmetalation of the Zr−C bond in the azazirconacycles to Cu led to excellent regioselectivity for the reaction with propargyl bromide.

## Experimental Section

**General Information.** All reactions involving air or moisture sensitive organometallic reactions were carried out under dry nitrogen. THF was distilled over sodium and benzophenone. Zirconocene dichloride was purchased from Nichia Chemical Co., Inc. Alkynes were purchased from Aldrich Chemical Co., Inc. *n*-BuLi (1.6 M solution in hexane) and EtMgBr (1.0 M solution in THF) were purchased from Kanto Chemical Co., Ltd. $^1$H and $^{13}$C NMR spectra were recorded for $CDCl_3$ (containing 1% TMS) solution at 25 °C on a Bruker ARX-400 or a JEOL JNM-AL300 NMR spectrometer. GC analysis was performed on a Shimadzu GC-14A equipped with the fused silica capillary column Shimadzu CBP1-M25-O25 and Shimadzu C-R6A-Chromatopac integrator.

**A Typical Procedure for the Preparation of Pyridones (6).** To a solution of $Cp_2ZrCl_2$ (365 mg, 1.25 mmol) in THF (5 mL) was added EtMgBr (2.5 mmol) at −78 °C. After the mixture was stirred for 1 h at the same temperature an alkyne (1.0 mmol) was added and the reaction mixture was allowed to warm to 0 °C. After this mixture was stirred for 3 h, phenylisocyanate (1.5 mmol) was added to the reaction mixture and stirring was continued at 50 °C for 3 h. After cooling to room temperature an alkyne (2.0 mmol) and $NiCl_2(PPh_3)_2$ (1.2 mmol) were added to the reaction mixture and stirring was continued at 50 °C for 3 h. Then the reaction mixture was quenched with $NH_4OH$ and extracted with ether. The extract was washed with water and dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by chromatography on silica gel.

**1,3,4,5,6-Pentaphenylpyrid-2-one (6a):** isolated yield 67%; white solid, mp 239−240 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 6.80−7.40 (m, 25H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 121.26, 125.71, 126.38, 126.46, 126.91, 126.97, 127.06, 127.11, 127.30, 127.52, 128.40, 129.04, 129.90, 130.32, 130.59, 131.05, 131.60, 134.48, 135.69, 136.98, 137.90, 139.27, 145.79, 151.29, 162.07; IR (Nujol) 2953, 2930, 2926, 1649, 1489, 1458, 1444, 742, 694 cm$^{-1}$. Anal. Calcd for $C_{35}H_{25}NO$: C, 88.39; H, 5.30; N, 2.95. Found: C, 88.41; H, 5.41; N 2.90.

**1,3,4-Triphenyl-5,6-dipropylpyrid-2-one (6b):** isolated yield 61%; $^1$H NMR yield 72%; yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.65 (t, $J$ = 7.3 Hz, 3H), 0.68 (t, $J$ = 7.2 Hz, 3H), 1.20−1.35 (m, 2H), 1.40−1.55 (m, 2H), 2.20−2.30 (m, 2H), 2.30−2.45 (m, 2H), 6.90−7.60 (m, 15H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.24, 22.73, 24.22, 31.06, 32.60, 117.07, 126.03, 126.79, 126.93, 127.43, 128.23, 128.47, 129.06, 129.13, 129.39, 130.83, 136.03, 138.28, 139.46, 145.67, 152.56, 162.26; IR (neat) 2961, 2872, 1632, 1578, 1532, 1491, 733, 702 cm$^{-1}$; HRMS calcd for $C_{29}H_{29}NO$ 407.2249, found 407.2242.

**1-Phenyl-3,4,5,6-tetrapropylpyrid-2-one (6c):** isolated yield 40%; GC yield 46%; yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.66 (t, $J$ = 7.3 Hz, 3H), 0.96 (t, $J$ = 7.4 Hz, 3H), 1.03 (t, $J$ = 7.3 Hz, 3H), 1.07 (t, $J$ = 7.3 Hz, 3H), 1.30−1.40 (m, 2H), 1.45−1.60 (m, 6H), 2.20−2.30 (m, 2H), 2.30−2.40 (m, 2H), 2.45−2.60 (m, 4H), 7.10−7.50 (m, 5H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.18, 14.61, 14.64, 14.82, 22.32, 22.76, 23.95, 24.90, 29.84, 30.47, 32.05, 32.24, 116.81, 128.00, 128.50, 128.65, 129.12, 139.90, 142.98, 150.43, 162.96; IR (neat) 2932, 2872, 1682, 1640, 1599, 1527, 1466, 754, 696 cm$^{-1}$; HRMS calcd for $C_{23}H_{33}NO$ 339.2560, found 339.2575.

**5-Methyl-1,3,4,6-tetraphenylpyrid-2-one (6d):** isolated yield 56%; white solid: mp >300 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 1.62 (s, 3H), 6.90−7.30 (m, 20H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 17.35, 112.95, 126.38, 127.03, 127.13, 127.42, 127.84, 127.95, 127.98, 128.40, 128.98, 129.18, 129.95, 130.85, 130.93, 135.14, 135.88, 138.51, 139.64, 144.90, 152.47, 161.86; IR (Nujol) 2884, 2866, 2847, 1643, 1583, 1524, 1491, 748, 706 cm$^{-1}$. Anal. Calcd for $C_{30}H_{23}NO$: C, 87.14; H, 5.61; N, 3.39. Found: C, 87.05; H, 5.81; N 3.29.

**3-Methyl-1,4,5,6-tetraphenylpyrid-2-one (6e):** isolated yield 65%; white solid, mp 245−247 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 2.07 (s, 3H), 6.70−7.40 (m, 20H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.94, 120.97, 125.59, 126.44, 126.73, 126.78, 126.93, 127.09, 127.41, 127.56, 128.39, 128.70, 129.02, 130.73, 131.49, 134.53, 137.15, 138.42, 139.52, 143.53, 150.65, 162.88; IR (Nujol) 2970, 2847, 1649, 1608, 1527, 1487, 1443, 745, 698 cm$^{-1}$; HRMS calcd for $C_{30}H_{23}NO$ 413.1780, found 413.1794.

**5,6-Dicarbomethoxy-1,3,4-triphenylpyrid-2-one (6f):** isolated yield 20%; yellow solid, mp 238.5−239 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 3.41 (s, 3H), 3.50 (s, 3H), 6.90−7.60 (m, 15H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 52.28, 52.95, 113.09, 127.29, 127.43, 127.69, 127.76, 128.02, 128.45, 129.10, 129.30, 130.69, 133.19, 134.01, 137.03, 137.66, 141.24, 148.21, 160.93, 162.03, 165.77; IR (Nujol) 2961, 2957, 2857, 1746, 1715, 1669, 1589, 1491, 1456, 1433, 1319, 1263, 1240, 1219, 723, 698 cm$^{-1}$; HRMS calcd for $C_{27}H_{21}NO_5$ 439.1420, found 439.1413.

**5,6-Diethyl-1-(4-methylphenyl)-3,4-diphenylpyrid-2-one (6g):** isolated yield 49%; yellow solid, mp 155−156 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.89 (t, $J$ = 7.3 Hz, 3H), 1.04 (t, $J$ = 7.3 Hz, 3H), 2.33 (q, $J$ = 7.3 Hz, 2H), 2.38 (s, 3H), 2.49 (q, $J$ = 7.3 Hz, 2H), 7.00−7.30 (m, 14H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 13.66, 15.22, 21.02, 21.69, 23.42, 117.79, 125.91, 126.70, 126.80, 127.38, 128.09, 128.98, 129.29, 129.73, 130.77, 136.00, 136.63, 137.98, 138.18, 146.85, 152.39, 162.27; IR (Nujol) 2957, 2951, 2945, 1649, 1574, 1508, 1460, 799, 696 cm$^{-1}$; HRMS calcd for $C_{28}H_{27}NO$ 393.2093, found 393.2086.

**5-Butyl-1,3,4,6-tetraphenylpyrid-2-one (6h):** isolated yield 58%; yellow solid, mp 176−178 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.38 (t, $J$ = 7.3 Hz, 3H), 0.65−0.80 (m, 2H), 0.95−1.10 (m, 2H), 2.00−2.10 (m, 2H), 7.10−7.30 (m, 20H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 12.99, 22.23, 28.99, 32.51, 118.37, 126.31, 126.96, 127.07, 127.40, 127.51, 127.70, 127.95, 128.39, 129.13, 129.24, 130.08, 130.88, 131.18, 134.64, 135.89, 137.95, 139.58, 145.18, 152.33, 161.68; IR (Nujol) 2995, 2968, 1649, 1643, 1526, 1491, 746, 696 cm$^{-1}$; HRMS calcd for $C_{33}H_{29}NO$ 455.2249, found 455.2257.

**Typical Experimental Procedure for the Preparation of Iminopyridines (9).** To a solution of zirconacyclopentene (1.0 mmol), prepared from diethylzirconocene and an alkyne (1.0 mmol), was added diphenylcarbodiimide (1.0 mmol). The mixture was allowed to warm to 50 °C for 3 h, then alkyne (2.5 mmol) and $NiCl_2(PPh_3)_2$ (1.0 mmol) were added. After this mixture was stirred for an additional 3 h at 50 °C the solution was quenched with saturated aquous $NaHCO_3$ and extracted with EtOAc. Column chromatography on silica gel afforded products.

**3,4,5,6-Tetraethyl-1-phenyl-2-phenylimino-1,2-dihydropyridine (9a):** isolated yield 61%; yellow solid, mp 134−135 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.86 (t, $J$ = 7.4 Hz, 3H), 1.07−1.25 (m, 9H), 2.32 (q, $J$ = 7.3 Hz, 2H), 2.48−2.66 (m, 6H), 6.34−6.36 (m, 2H), 6.57−6.60 (m, 1H), 6.87−6.91 (m, 2H), 7.06−7.20 (m, 5H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 13.48, 13.70, 14.73, 15.54, 21.19, 21.28, 22.62, 23.31, 118.54, 119.11, 121.79, 127.81, 128.20, 128.45, 129.12, 133.25, 140.88, 146.98, 150.30, 150.82, 151.38. IR (KBr) 2971, 2932, 2903, 2872, 1612, 1591, 1553, 1514, 1489, 766, 746, 694 cm$^{-1}$; HRMS calcd for $C_{25}H_{30}N_2$ 358.2409, found 358.2405.

**5,6-Diethyl-1-phenyl-2-phenylimino-3,4-dipropyl-1,2-dihydropyridine (9b):** isolated yield 56%; yellow solid, mp 100−101 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.75 (t, $J$ = 7.4 Hz, 3H), 0.82 (t, $J$ = 7.5 Hz, 3H), 1.05 (t, $J$ = 7.4 Hz, 3H), 1.14 (t, $J$ = 7.4 Hz, 3H), 1.43−1.57 (m, 4H), 2.16−2.22 (m, 2H), 2.35−2.45 (m, 6H), 6.30−6.31 (m, 2H), 6.55−6.57 (m, 1H), 6.85−7.15 (m, 7H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 13.12, 14.23, 14.77, 15.84, 21.05, 22.06, 22.97, 24.00, 30.22, 31.69, 116.38, 117.93, 120.05, 126.99, 128.00, 128.38, 129.12, 129.87, 142.23, 144.28, 146.46, 150.95, 152.74; IR (KBr) 2961, 2934, 2872, 1615, 1591, 1564, 1520, 1489, 756, 698 cm$^{-1}$. Anal. Calcd for $C_{27}H_{34}N_2$: C, 83.89; H, 8.87; N, 7.25. Found: C, 83.86; H, 8.96; N, 7.25.

**3,4-Diethyl-1-phenyl-2-phenylimino-5,6-dipropyl-1,2-dihydropyridine (9c):** isolated yield 69%; yellow solid, mp 85−86 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.60 (t, $J$ = 7.3 Hz, 3H), 1.00 (t, $J$ = 7.4 Hz, 3H),

1.18 (t, $J$ = 7.5 Hz, 3H), 1.30−1.36 (m, 5H), 1.54−1.60 (m, 2H), 2.14−2.18 (m, 2H), 2.34−2.38 (m, 2H), 2.50 (q, $J$ = 7.5 Hz, 2H), 2.86 (q, $J$ = 7.2 Hz, 2H), 6.66−6.67 (m, 2H), 6.74−6.78 (m, 1H), 6.90−7.07 (m, 7H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 13.49, 14.20, 14.60, 14.88, 21.19, 22.47, 22.86, 24.93, 30.51, 32.17, 115.57, 118.00, 120.21, 127.05, 128.05, 128.32, 129.99, 130.75, 142.22, 143.48, 147.27, 150.79, 152.81; IR (KBr) 2971, 2870, 1616, 1590, 1557, 1520, 1489, 692 cm$^{-1}$. Anal. Calcd for $C_{27}H_{34}N_2$: C, 83.89; H, 8.87; N, 7.25. Found: C, 83.86; H, 8.80; N, 7.13.

**1,5,6-Triphenyl-2-phenylimino-3,4-dipropyl-1,2-dihydropyridine (9d):** isolated yield 35%; yellow solid, mp 153−154 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.70 (t, $J$ = 6.9 Hz, 3H), 0.89 (t, $J$ = 6.9 Hz, 3H), 1.39 (m, 2H), 1.66 (m, 2H), 2.25 (t, $J$ = 7.5 Hz, 2H), 2.60 (t, $J$ = 7.3 Hz, 2H), 6.42−6.44 (m, 2H), 6.52−6.55 (m, 1H), 6.70−7.06 (m, 17H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.45, 14.54, 22.15, 23.29, 30.48, 32.89, 118.70, 120.41, 120.82, 126.15, 126.24, 126.66, 127.30, 127.68, 127.99, 130.49, 130.66, 130.80, 131.38, 135.38, 138.12, 142.10, 144.10, 145.55, 149.83, 151.81; IR (KBr) 2961, 2870, 1618, 1603, 1591, 1520, 1485, 694 cm$^{-1}$; HRMS calcd for $C_{35}H_{34}N_2$ 482.2722, found 482.2700.

**1,3,4-Triphenyl-2-phenylimino-5,6-dipropyl-1,2-dihydropyridine (9e):** isolated yield 78%; orange solid, mp 199−200 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.68 (t, $J$ = 7.3 Hz, 3H), 0.73 (t, $J$ = 7.2 Hz, 3H), 1.30−1.36 (m, 2H), 1.48−1.54 (m, 2H), 2.18−2.22 (m, 2H), 2.35−2.39 (m, 2H), 6.29−6.40 (m, 3H), 6.62−6.77 (m, 7H), 6.95−6.97 (m, 2H), 7.08−7.14 (m, 3H), 7.38−7.49 (m,5H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.00, 22.36, 23.71, 31.13, 32.70, 119.01, 120.11, 120.50, 125.29, 126.25, 126.38, 126.90, 127.12, 128.01, 128.16, 128.37, 128.91, 128.99, 130.76, 135.41, 137.26, 140.30, 147.95, 150.53, 154.11; IR (KBr) 2963, 2930, 2870, 1613, 1590, 1557, 1512, 1493, 1477, 1452, 752, 694 cm$^{-1}$; HRMS calcd for $C_{35}H_{34}N_2$ 482.2722, found 482.2719.

**General Procedure for Synthesis of α,β-Unsaturated Ketones (12).** To a solution of zirconacyclopentadiene, prepared from $Cp_2ZrCl_2$ (292 mg, 1.0 mmol), was added a nitrile (1.0 mmol) at room temperature, and the mixture was stirred for 3 h at 50 °C. Then 3 N HCl was added and the reaction mixture was stirred for 12 h at room temperature. Column chromatography on silica gel afforded the products.

**(1*E*)-2-Butyl-1-(trimethylsilyl)pent-1-en-3-one (12a):** isolated yield 91%; pale yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.16 (s, 9H), 0.87 (t, $J$ = 6.9 Hz, 3H), 1.06 (t, $J$ = 7.3 Hz, 3H), 1.24−1.33 (m, 4H), 2.32 (t, $J$ = 7.8 Hz, 2H), 2.68 (q, $J$ = 7.3 Hz, 2H), 6.49 (s, 1H,); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ −0.26, 8.65, 13.92, 23.10, 30.75, 31.14, 32.32, 138.41, 156.79, 203.41; IR (neat) 2959, 2938, 1678, 1460, 1379, 1250, 1175, 862, 839, 691 cm$^{-1}$; HRMS calcd for $C_{12}H_{24}OSi$ 212.1596, found 212.1596.

**(1*E*)-2-Butyl-1-(trimethylsilyl)hex-1-en-3-one (12b):** isolated yield 90%; pale yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.16 (s, 9H), 0.87 (t, $J$ = 7.1 Hz, 3H), 0.91 (t, $J$ = 7.4 Hz, 3H), 1.22−1.33 (m, 4H), 1.59 (tq, $J$ = 7.4, 7.3 Hz, 2H), 2.32 (t, $J$ = 7.3 Hz, 2H), 2.62 (t, $J$ = 7.4 Hz, 2H), 6.48 (s, 1H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ −0.25, 13.85, 13.93, 18.14, 23.10, 31.10, 32.29, 39.54, 138.52, 157.09, 203.00; IR (neat) 2959, 2936, 2874, 1676, 1593, 1461, 1379, 1250, 1172, 845, 754, 694 cm$^{-1}$; HRMS calcd for $C_{13}H_{26}OSi$ 226.1753, found 226.1746.

**(2*E*)-2-Butyl-1-(2-pyridyl)-3-(trimethylsilyl)prop-2-en-1-one (12c):** isolated yield 85%; brown liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.15 (s, 9H), 0.85 (t, $J$ = 7.1 Hz, 3H), 1.29−1.46 (m, 4H), 2.55 (t, $J$ = 7.0 Hz, 2H), 6.33 (s, 1H), 7.34 (ddd, $J$ = 7.3, 4.8, 1.5 Hz, 1H), 7.68 (ddd, $J$ = 7.9, 1.1, 1.1, Hz, 1H), 7.75 (ddd, $J$ = 7.8, 7.6, 1.6 Hz, 1H), 8.62 (ddd, $J$ = 4.9, 1.7, 1.1 Hz, 1H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.28, 13.87, 18.34, 22.92, 31.73, 123.92, 125.31, 136.52, 144.25, 148.67, 155.29, 156.01, 196.55; IR (neat) 2959, 2932, 2874, 1665, 1584, 1468, 1433, 1250, 995, 860, 841, 752, 693 cm$^{-1}$; HRMS calcd for $C_{15}H_{24}OSi$ 262.1627, found 262.1633.

**(3*E*)-3-Hexyl-4-(trimethylsilyl)but-3-en-2-one (12d):** isolated yield 87%; pale yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.16 (s, 9H), 0.84 (t, $J$ = 7.1 Hz, 3H), 1.23−1.38 (m, 8H), 2.28−2.31 (m, 5H), 6.53 (s, 1H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ −0.32, 14.01, 22.55, 25.94, 29.69, 30.15, 31.07, 31.64, 140.43, 157.03, 200.52; IR (neat) 2957, 2930, 2859, 1676, 1593, 1366, 1250, 1211, 1051, 853, 750, 693 cm$^{-1}$; HRMS calcd for $C_{13}H_{26}OSi$ 226.1753, found 226.1757.

**(2*E*)-2-Hexyl-1-(4-methylphenyl)-3-(trimethylsilyl)prop-2-en-1-one (12e):** isolated yield 76%; pale yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.17 (s, 9H), 0.83 (t, $J$ = 7.0 Hz, 3H), 1.22−1.38 (m, 8H), 2.39 (s, 3H), 2.53 (t, $J$ = 7.3 Hz, 2H), 5.98 (s, 1H), 7.21 (d, $J$ = 8.0 Hz, 2H), 7.65 (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ −0.11, 13.99, 21.59, 22.51, 29.23, 29.50, 31.61, 32.63, 128.83, 129.92, 134.99, 138.58, 142.90, 156.42, 198.99; IR (neat) 2957, 2928, 2859, 1657, 1607, 1408, 1337, 1248, 1177, 928, 860, 841, 760, 693 cm$^{-1}$; HRMS calcd for $C_{19}H_{31}OSi$ 303.2144, found 303.2139.

**General Procedure for Synthesis of Pyridines (11).** To a solution of zirconacyclopentadiene, prepared from $Cp_2ZrCl_2$ (292 mg, 1.0 mmol), was added a nitrile (1.0 mmol) at room temperature, and the mixture was stirred for 3 h at 50 °C. Then the reaction mixture was dried under reduced pressure, and dissolved in THF (5 mL) again. To the solution were added the second alkyne (2.5 mmol) and $NiCl_2(PPh_3)_2$ (654 mg, 1.0 mmol) at room temperature, and the mixture was stirred for 12 h at 50 °C. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ and extracted with EtOAc. Column chromatography on silica gel afforded the title compounds.

**3-Butyl-2-ethyl-5-methyl-6-phenyl-4-(trimethylsilyl)pyridine (11a):** GC yield 77%; isolated yield 52%; yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.45 (s, 9H), 0.98 (t, $J$ = 7.0 Hz, 3H), 1.29 (t, $J$ = 7.5 Hz, 3H), 1.43−1.52 (m, 4H), 2.30 (s, 3H), 2.74−2.78 (m, 2H), 2.83 (q, $J$ = 7.5 Hz, 2H), 7.33 (tt, $J$ = 7.0, 1.6 Hz, 1H), 7.38−7.45 (m, 4H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 3.74, 14.01, 14.55, 21.80, 23.11, 28.24, 31.68, 35.27, 127.25, 128.04, 129.24, 133.04, 139.46, 142.21, 147.76, 155.97, 157.74; IR (neat) 2961, 2932, 2872, 1719, 1535, 1460, 1385, 1254, 860, 843, 764, 700 cm$^{-1}$; HRMS calcd for $C_{21}H_{31}NSi$ 325.2226, found 325.2223.

**3-Butyl-5-ethyl-6-phenyl-2-propyl-4-(trimethylsilyl)pyridine (11b):** GC yield 75%; isolated yield 53%; yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.44 (s, 9H), 0.81 (t, $J$ = 7.4 Hz, 3H), 0.98 (t, $J$ = 7.3 Hz, 3H), 0.99 (t, $J$ = 6.9 Hz, 3H), 1.42−1.49 (m, 4H), 1.72 (qt, $J$ = 7.4, 6.8 Hz, 2H), 2.71−2.79 (m, 6H), 7.32 (tt, $J$ = 7.4, 1.6 Hz, 1H), 7.37−7.41 (m, 4H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 4.13, 13.94, 14.38, 16.98, 23.14, 23.66, 25.18, 32.09, 35.03, 37.19, 127.08, 128.01, 129.00, 139.85, 140.08, 142.52, 146.71, 155.93, 156.50; IR (neat) 2961, 2932, 2872, 1534, 1466, 1383, 1254, 860, 843,762, 700 cm$^{-1}$; HRMS calcd for $C_{23}H_{35}NSi$ 353.2539, found 353.2542.

**2,2′-[3-Butyl-5-ethyl-6-phenyl-4-(trimethylsilyl)]bipyridine (11c):** GC yield 62%; isolated yield 49%; brown liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.49 (s, 9H), 0.66 (t, $J$ = 7.3 Hz, 3H), 0.86 (t, $J$ = 7.4 Hz, 3H), 1.09−1.21 (m, 4H), 2.85 (q, $J$ = 7.4 Hz, 2H), 3.00 (t, $J$ = 8.2 Hz, 2H), 7.24 (ddd, $J$ = 7.7, 7.3, 1.8 Hz, 1H), 7.33 (d, $J$ = 7.2 Hz, 1H), 7.38 (dd, $J$ = 8.0, 7.7 Hz, 2H), 7.44 (d, $J$ = 7.7 Hz, 2H), 7.61 (d, $J$ = 8.0 Hz, 1H), 7.74 (ddd, $J$ = 7.7, 7.6, 1.8 Hz, 1H), 8.60 (d, $J$ = 7.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 4.00, 13.58, 16.84, 22.61, 25.46, 31.32, 34.42, 122.20, 124.79, 127.24, 128.01, 129.08, 136.54, 141.18, 142.02, 142.60, 148.15, 148.39, 153.86, 155.90, 160.41; IR (neat) 3058, 2961, 2930, 2872, 1588, 1568, 1470, 1379, 1254, 1071, 1049, 1026, 852, 762, 747, 702 cm$^{-1}$; HRMS calcd for $C_{25}H_{32}N_2Si$ 388.2335, found 388.2346.

**3-Ethyl-5-hexyl-6-methyl-2-phenyl-4-(trimethylsilyl)pyridine (11d):** GC yield 69%; isolated yield 59%; yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.44 (s, 9H), 0.81 (t, $J$ = 7.4 Hz, 3H), 0.90 (t, $J$ = 6.7 Hz, 3H), 1.31−1.34 (m, 4H), 1.42−1.46 (m, 4H), 2.54 (s, 3H), 2.73 (t, $J$ = 7.4 Hz, 2H), 2.76 (q, $J$ = 6.6 Hz, 2H), 7.32 (tt, $J$ = 8.3, 1.5 Hz, 1H), 7.37−7.40 (m, 4H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 4.06, 14.05, 17.08, 22.65, 22.76, 25.14, 29.74, 31.47, 31.69, 33.01, 127.15, 128.07, 128.93, 140.17, 140.77, 142.33, 146.60, 152.79, 155.88; IR (neat) 2957, 2928, 2827, 1468, 1445, 1383, 1254, 860, 843, 762, 700 cm$^{-1}$; HRMS calcd for $C_{25}H_{35}NSi$ 353.2539, found 353.2531.

**3-Hexyl-5-methyl-2-(4-methylphenyl)-6-phenyl-4-(trimethylsilyl)-pyridine (11e):** GC yield 58%; isolated yield 45%; yellow liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.49 (s, 9H), 0.79 (t, $J$ = 7.1 Hz, 3H), 1.04−1.16 (m, 6H), 1.23−1.33 (m, 2H), 2.36 (s, 3H,), 2.39 (s, 3H,), 2.78 (t, $J$ = 8.0 Hz, 2H), 7.18 (d, $J$ = 7.9 Hz, 2H), 7.30−7.36 (m, 3H), 7.39 (d, $J$ = 7.8 Hz, 2H,), 7.47 (dd, $J$ = 7.9, 1.8 Hz, 2H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 3.62, 13.95, 21.21, 21.94, 22.28, 29.02, 31.22, 32.11, 32.67, 127.28, 127.94, 128.59, 128.98, 129.36, 134.51, 136.73, 139.24, 140.20, 141.88, 148.52, 155.74, 156.41; IR (neat) 3027, 2957, 2926, 2857, 1726, 1599, 1510, 1493, 1445, 1377, 1254, 1020, 856, 839, 766, 700 cm$^{-1}$; HRMS calcd for $C_{28}H_{37}NSi$ 415.2695, found 415. 2693.

**A Typical Procedure for the Preparation of Alkyl−Aryl-Substituted Pyridines (15a−e).** To a solution of $Cp_2ZrCl_2$ (365 mg, 1.25 mmol) in THF (5 mL) was added EtMgBr (2.5 mmol) at −78 °C. After the mixture was stirred for 1 h at the same temperature an alkyne (1.0 mmol) was added and the reaction mixture was allowed to warm to 0 °C for 3 h. Then a nitrile (1.0 mmol) was added to the reaction mixture which was then stirred at 50 °C for 1 h. After cooling to 0 °C propargyl bromide (1.5 mmol) and CuCl (1.0 mmol) were added to the reaction mixture which was then stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated $NaHCO_3$ and extracted with ether. The extract was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by column chromatography on silica gel.

**2-(4-*tert*-Butylphenyl)-6-methyl-3,4-dipropylpyridine (15a):** GC yield 93%; isolated yield 81%; orange liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.78 (t, $J$ = 7.5 Hz, 3H), 1.00 (t, $J$ = 7.5 Hz, 3H), 1.34−1.46 (m, 11H), 1.63 (*q*, $J$ = 7.5 Hz, 2H), 2.50−2.62 (m, 7H), 6.93 (s, 1H), 7.30 (d, $J$ = 8.1 Hz, 2H), 7.40 (d, $J$ = 8.4 Hz, 2H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.31, 14.39, 23.81, 24.18, 24.31, 30.63, 31.38, 34.33, 34.53, 122.39, 124.95, 128.32, 130.87, 139.06, 150.03, 150.33, 154.45, 159.15; IR (neat) 2961, 2934, 2872, 1591, 1553, 1466, 1433, 1399, 1379, 1364, 1267, 1109, 1020, 839 cm$^{-1}$; HRMS calcd for $C_{22}H_{30}N$ 308.2378, found 308.2354.

**3,4-Diethyl-6-methyl-2-phenylpyridine (15b):** GC yield 98%; isolated yield 77%; orange liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.96 (t, $J$ = 7.5 Hz, 3H), 1.25 (t, $J$ = 7.5 Hz, 3H), 2.52−2.61 (m, 5H), 2.65 (*q*, $J$ = 7.5 Hz, 2H), 6.98 (s, 1H), 7.32−7.40 (m, 5H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.65, 15.20, 21.45, 24.21, 25.02, 121.98, 127.37, 128.08, 128.68, 132.01, 141.92, 151.69, 154.75, 158.90; IR (neat) 2969, 2934, 2876, 1591, 1555, 1497, 1464, 1449, 1429, 1387, 1339, 1055, 1028, 872, 764, 700 cm$^{-1}$; HRMS calcd for $C_{16}H_{18}N$ 224.1439, found 224.1443.

**2-Ethyl-6-methyl-3,4-dipropylpyridine (15c):** GC yield 57%; isolated yield 43%; orange liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.97 (t, $J$ = 7.5 Hz, 3H), 1.00 (t, $J$ = 7.5 Hz, 3H), 1.24 (t, $J$ = 7.5 Hz, 3H), 1.43−1.67 (m, 4H), 2.45 (s, 3H), 2.49−2.59 (m, 4H), 2.75 (q, $J$ = 7.5 Hz, 2H), 6.77 (s, 1H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.26, 14.64, 14.70, 23.78, 24.07, 24.34, 28.50, 30.00, 34.44, 121.42, 130.14, 149.79, 154.42, 160.89; IR (neat) 2961, 2934, 2874, 1593, 1559, 1456, 1379, 1256, 1233, 1090, 1051, 949, 845 cm$^{-1}$; HRMS calcd for $C_{14}H_{23}N$ 205.1830, found 205.1820.

**2-(4-*tert*-Butylphenyl)-6-methyl-3,4-diphenylpyridine (15d):** GC yield 73%; isolated yield 50%; orange solid, mp 159 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 1.24 (s, 9H), 2.67 (s, 3H), 6.85−6.88 (m, 2H), 7.01−7.07 (m, 5H), 7.18−7.19 (m, 8H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 24.45, 31.25, 34.42, 122.97, 124.56, 126.29, 127.13, 127.54, 127.78, 129.29, 129.48, 131.38, 131.52, 138.00, 138.05, 139.80, 149.92, 149.99, 156.81, 157.78; IR (KBr) 2963, 2867, 1584, 1537, 1474, 1429, 1364, 1271, 1113, 841, 770, 700 cm$^{-1}$; HRMS calcd for $C_{28}H_{26}N$ 376.2065, found 376.2057.

**6-Methyl-3,4-diphenyl-2-propylpyridine (15e):** GC yield 66%; isolated yield 57%; orange solid, mp 67 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.79 (t, $J$ = 7.2 Hz, 3H), 1.55−1.68 (m, 2H), 2.60−2.65 (m, 5H), 7.01−7.04 (m, 5H), 7.12−7.25 (m, 6H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.20, 23.57, 24.36, 38.14, 121.66, 126.70, 127.05, 127.69, 127.81, 129.20, 130.59, 132.11, 138.32, 139.78, 149.35, 156.48, 159.93; IR (KBr) 2957, 2901, 2870, 1586, 1541, 1499, 1462, 1439, 1381, 1358, 1201, 1074, 868, 771, 700 cm$^{-1}$; HRMS calcd for $C_{21}H_{21}N$ 287.1674, found 287.1667.

**A Typical Procedure for the Preparation of Trimethylsilyl-Substituted Pyridines (15f,g).** To a solution of $Cp_2ZrCl_2$ (365 mg, 1.25 mmol) in THF (5 mL) was added *n*-BuLi (2.5 mmol) at −78 °C. After the mixture was stirred for 1 h at the same temperature 1-trimethylsilyl-1-hexyne (2.0 mmol) was added and the reaction mixture was allowed to warm to room temperature for 1 h. Then a nitrile (1.0 mmol) was added to the reaction mixture which was then stirred at 50 °C for 1 h. After cooling to 0 °C propargyl bromide (1.5 mmol) and CuCl (1.0 mmol) were added to the reaction mixture which was then stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated $NaHCO_3$ and extracted with ether. The extract was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by column chromatography on silica gel.

**3-Butyl-6-methyl-2-phenyl-4-(trimethylsilyl)pyridine (15f):** GC yield 54%; isolated yield 46%; orange liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.36 (s, 9H), 0.63 (t, $J$ = 7.2 Hz, 3H), 1.06−1.20 (m, 4H), 2.54 (s, 3H), 2.65 (t, $J$ = 7.2 Hz, 2H), 7.18 (s, 3H), 7.33−7.41 (m, 5H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.35, 13.48, 22.78, 24.17, 32.39, 33.51, 127.38, 127.77, 128.10, 128.82, 137.69, 141.85, 149.20, 153.72, 158.44; IR (neat) 2957, 2930, 2874, 1570, 1524, 1495, 1460, 1447, 1416, 1368, 1298, 1252, 1092, 918, 855, 839, 754, 700 cm$^{-1}$; HRMS calcd for $C_{19}H_{27}N$ 297.1913, found 297.1894.

**3-Butyl-6-methyl-2-propyl-4-(trimethylsilyl)pyridine (15g):** GC yield 34%; isolated yield 27%; orange liquid; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.32 (s, 9H), 0.95−1.04 (m, 6H), 1.43−1.49 (m, 4H), 1.68−1.76 (m, 2H), 2.47 (s, 3H), 2.63−2.75 (m, 4H), 7.01 (s, 1H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.31, 13.90, 14.46, 23.33, 23.87, 24.13, 32.60, 34.29, 37.01, 126.41, 137.29, 148.33, 153.75, 159.05; IR (neat) 2959, 2934, 2874, 1574, 1530, 1433, 1373, 1252, 1148, 1084, 860, 839, 756, 689 cm$^{-1}$; HRMS calcd for $C_{16}H_{29}NSi$ 263.2069, found 263.2076.

**2-Ethyl-6-methyl-3-phenyl-4-(triethylsilyl)pyridine (15h).** To a solution of $Cp_2ZrCl_2$ (365 mg, 1.25 mmol) in THF (5 mL) was added *n*-BuLi (2.5 mmol) at −78 °C. After the mixture was stirred for 1 h at the same temperature triethylsilylphenylethyne (1.0 mmol) was added and the reaction mixture was allowed to warm to room temperature for 3 h. Then propionitrile (1.0 mmol) was added to the reaction mixture which was then stirred at room temperature for 3 h. After cooling to 0 °C propargyl bromide (1.5 mmol) and CuCl (1.0 mmol) were added to the reaction mixture which was then stirred at 50 °C for 3 h. The reaction mixture was quenched with saturated $NaHCO_3$ and extracted with ether. The extract was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuo and column chromatography on silica gel afforded 253 mg (81%) of the product as an orange solid (GC yield 94%): mp 60 °C; $^1$H NMR ($CDCl_3$, $Me_4Si$) $\delta$ 0.43 (q, $J$ = 7.8 Hz, 6H), 0.76 (t, $J$ = 7.8 Hz, 9H), 1.32 (t, $J$ = 7.5 Hz, 3H), 2.51(s, 3H), 2.92 (q, $J$ = 7.5 Hz, 2H), 6.77 (s, 1H), 7.20−7.23 (m, 2H), 7.32−7.36 (m, 3H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) $\delta$ 5.39, 8.04, 15.26, 24.13, 32.37, 122.09, 124.10, 127.64, 127.70, 128.90, 143.81, 156.76, 159.10, 168.96; IR (neat) 2957, 2874, 1574, 1520, 1493, 1466, 1441, 1375, 1350, 1073, 1001, 880, 768, 733, 700 cm$^{-1}$; HRMS calcd for $C_{20}H_{29}NSi$ 311.2069, found 311.2059.

**Supporting Information Available:** Crystallographic data, positional and thermal parameters, and lists of bond lengths and angles for **9a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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