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Nickel(0)-Catalyzed Couplings of Vinyl- Alanes & - Zirconocenes with Chloromethylated Heteroaromatics: A Route to *E*-Allylated Heterocycles#

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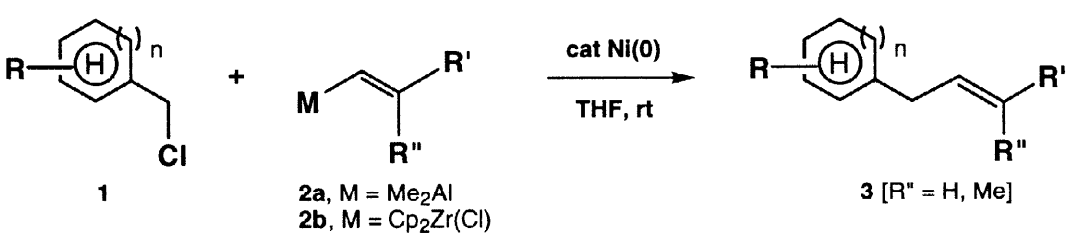
Abstract. *Treatment of selected chloromethylated heteroaromatics, including pyridines, thiophenes, and furans, with vinyl alanes or vinyl zirconocenes in the presence of Ni(0) results in E-allylated products in good yields.* © 1998 Elsevier Science Ltd. All rights reserved.

Allylated heteroaromatics are commonplace structural motifs associated not only with natural products (*e.g.*, the well-known antibiotic piericidin A_1),[1] but also compounds of interest that serve as intermediates for various purposes. Many approaches for installing a substituted allyl fragment are available, some of which include Pd(0)-catalyzed couplings of heteroarylstannanes with allylic carbonates,[2a] Sn(IV) chloride-promoted attack of allylic stannanes onto a heteroaromatic nucleus,[2b] Lewis acid-catalyzed prenylations *via* prenylphosphates,[2c] and silver ion-induced allylations by way of cyclopropyl halide rearrangements.[2d] Controlling both regiochemistry of attachment and resulting olefin geometry are oftentimes problematic, and when mixtuires prevail, separations can be tedious and yields may suffer. An alternative disconnection, which relies on a stereodefined vinylic organometallic, as demonstrated previously *en route* to the ubiquinones,[3] obviates both issues of stereo- and regiocontrol. We now report that stereodefined *E*-vinyl organometallics, in particular of



1 **2a**, M = Me_2Al; **2b**, M = $Cp_2Zr(Cl)$ **3** [R" = H, Me]

Scheme 1. A Ni(0)-catalyzed approach to allylated heteroaromatics.

#Dedicated to a colleague and personal friend, Professor Madeleine M. Joullie, in celebration of 40 years of distinguished teaching and research at the University of Pennsylvania.

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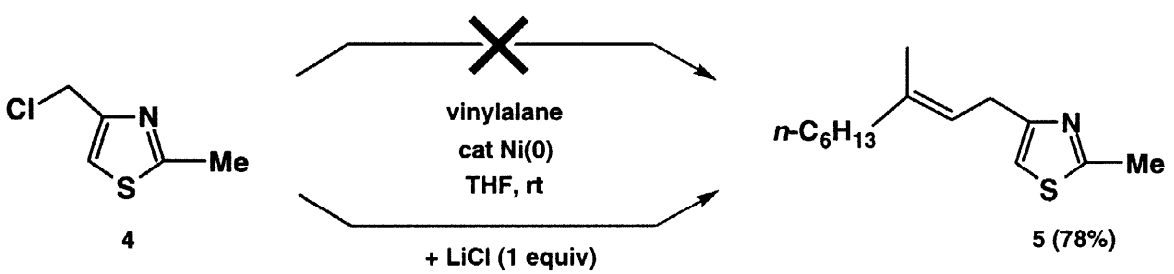
aluminum (**2a**) and zirconium (**2b**), can be used in the presence of catalytic amounts of Ni(0) to allylate chloromethylated heteroaromatics **1** giving *E*-allylated products **3** (Scheme 1).

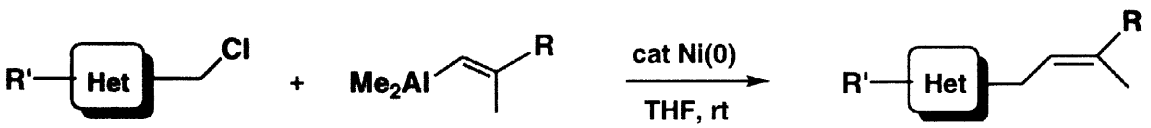
Carboalumination of alkynes, following the standard Negishi recipe[4] but using the more polar 1,2-dichloroethane in place of CH_2Cl_2, provides *E*-vinyl alanes **2a**. The Ni(0) catalyst is prepared by simply suspending $NiCl_2$ and triphenylphosphine (2 equiv) in dry THF (0.06 M) to which is *slowly* added *n*-BuLi in hexanes (2 equiv) at room temperature.[5] A blood-red solution results which is immediately ready for use. Addition of the heterocycle (in THF) to the catalyst *via* cannula leads to a deep brown coloration, after which cannulation of the vinylalane into this solution produces the coupled product within a few hours.[6] Several examples are illustrated in Table 1 based on which the following comments are offered: (1) substituted pyridines, furans, and thiophenes all readily and efficiently participate, giving very good isolated yields of allylated materials; (2) derived vinylalanes subsequently couple well independent of the functionality present in the chain; (3) Ni(0)-mediated reactions appear to tolerate an electrophilic group present within the educt (*e.g.*, an ester; entry 2); (4) the percentage of Ni(0) used, herein between 1 and 10%, is of no consequence in terms of yield; (5) all products **3** possessed the *E*-stereochemistry at the olefinic site.

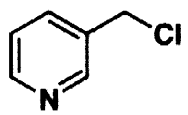
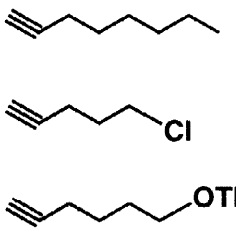
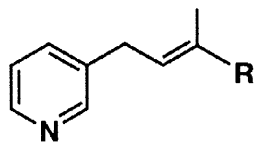
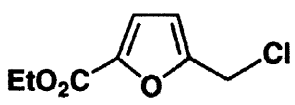
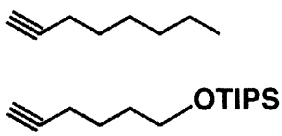
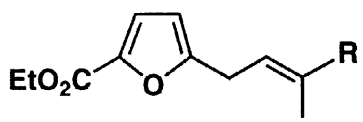
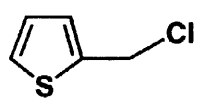
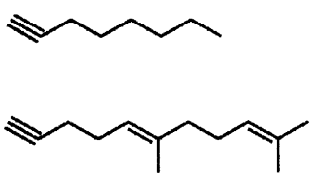
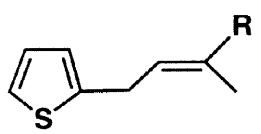
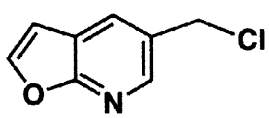
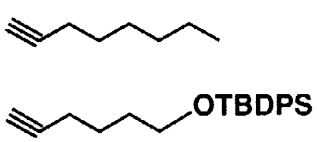
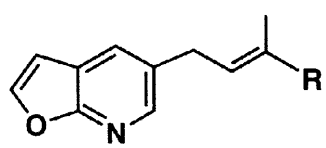
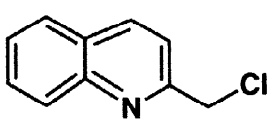
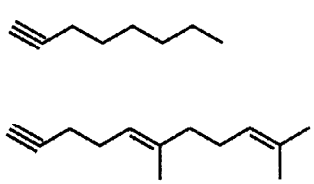
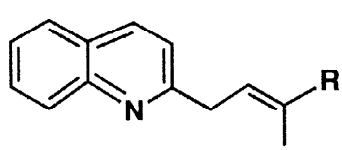
In the case of chloromethylated thiazole **4**, unfortunately, mainly homocoupled vinylalane along with several other materials of unknown composition were obtained. *None* of the desired cross-coupled product **5** was observed (Scheme 2). However, during the course of these studies, we took note of the beneficial impact which controlled amounts of LiCl can have,[7] and therefore tested this additive on thiazole **4**. Remarkably, under otherwise identical conditions, the presence of one equivalent of LiCl (per equivalent of thiazole) essentially negated the homocoupling pathway to afford the desired cross-coupling product **5** in good isolated yield (78%).



Scheme 2. Remarkable impact of LiCl on the coupling of a chloromethylated thiazole (**4**).

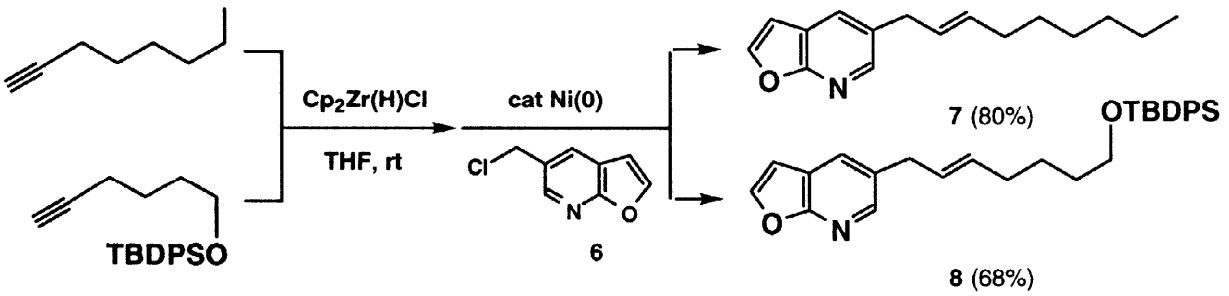
Table 1. Ni(0)-Mediated couplings of vinylalanes with chloromethylated heteroaromatics.



Heteroaromatic	1-Alkyne	Allylated Product[a]	Yield (%)
			92 87 88
			86 87
			84 80
			93 87
			89 69

[a]Fully characterized by spectral means and high resolution mass spectrometry; see the Experimental Section.

Rather than arriving at trisubstituted allylic residues, an outgrowth of carboalumination,[4] *E-disubstituted* allylated systems can be prepared by initial hydrozirconation of a terminal alkyne.[8] Hydroalumination is also an option,[9] although this process takes far longer than the corresponding hydrozirconation. Once the alkyne has been treated with $Cp_2Zr(H)Cl$ in THF at ambient temperatures, addition of the intermediate vinyl zirconocene to the substrate (*e.g.*, **6**)/Ni(0) combination affords allylated products (Scheme 3) typified by **7** and **8** (TBDPS = *t*-BuPh_2Si).



Scheme 3. Ni(0)-catalyzed couplings of vinylzirconocenes to give *E*-disubstituted allylated products.

In summary, a method for arriving at selected *E*-allylated heteroaromatics has been developed which involves readily available vinyl organometallics and chloromethylated educts. These cross-coupling reactions are driven by small percentages of a very inexpensive yet highly reactive Ni(0) catalyst. Further applications of Ni-catalyzed couplings,[10,11] as well as development of a source of Ni(0) on a solid support for mediating C-C bonds, will be reported in due course.

Acknowledgment. We warmly thank the NIH (GM 40287) for continued support of our programs. Precursor alcohol to educt **6** was generously provided by Dr. Ioannis Houpis (Merck Process R & D).

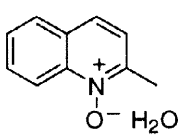
Experimental Section

THF and hexanes were distilled from Na/benzophenone ketyl prior to use. Ethyl-5-(chloromethyl)-2-furancarboxylate was commercially avalable (Aldrich), 2-(chloromethyl)-quinoline was prepared by a literature procedure, and 3-chloromethylpyridine hydrochloride and 4-chloromethyl-2-methylthiazole were purchased from Lancaster, the former being free-based with saturated aqueous sodium carbonate solution. Column chromatography was performed on ICN Biomedicals Silica, 32-63, 60A. TLC was carried out on pre-coated silica gel 60Å F_{254} plates (EMx Science), 0.25 mm layer thickness. ^1H and ^{13}C NMR spectra were run at either 400 or 200 MHz on a Varian Unity-400 or Gemini-200 spectrometer; chemical shifts listed are relative to tetramethylsilane

as an internal standard. All NMR samples were run in $CDCl_3$ as solvent unless noted otherwise. IR spectra were run neat on a ATI Mattson Infinity Series FT-IR spectrometer and the data is presented in cm^{-1}. High resolution mass spectra were run on either a VG-Autospec or an analytical VG-70-250 HF instrument. Low resolution mass spectra were obtained on an HP GCMS (5972A MSD) and the data are presented as a tabulation of m/z values followed by relative intensities. All reactions were carried out under an inert atmosphere of Ar using oven-dried glassware and standard syringe /septa techniques.

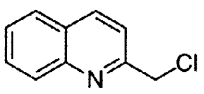
A **general procedure** for the preparation of cross-coupled products is as follows: *Carboalumination:* To a 10 mL round-botton Schlenk-flask (equipped with a medium ground glass filter frit) was added zirconocene dichloride (73 mg, 0.25 mmol) under an argon atmosphere. A solution of trimethylaluminum (0.75 mL, 2.0 M in hexanes, 1.5 mmol) was added at 0°C and stirred under reduced pressure until the hexanes were removed. 1,2-Dichloroethane was added (1.0 mL) and the solution was allowed to stir and warm to rt over 10 min. To this solution was added an alkyne (1.0 mmol, neat if a liquid, otherwise dissolved in a minimum of 1,2-dichloroethane) and the mixture stirred at 0°C for 30 min, after which time carboalumination was usually complete (determined by GC). The dichloroethane was pumped off *in vacuo* and freshly distilled hexanes (2 mL) was added and then also removed *in vacuo*. Additional hexanes (5 mL) were then added to the flask so as to precipitate the zirconium salts. The hexanes layer was removed by careful decanting and filtering through the frit with great care taken to avoid contamination by the zirconium salts. The leftover salts were not washed. The orange hexanes solution was concentrated under reduced pressure and dissolved in THF (2.0 mL).

Nickel-catalyzed Coupling: To a 5 mL round-bottom flask was added *bis*(triphenylphosphine)-nickel(II) dichloride (26 mg, 0.04 mmol) and triphenylphosphine (21 mg, 0.08 mmol)[12] under an argon atmosphere at rt. THF (1.0 mL) was added followed by *n*-butyllithium (56 μL, 1.42 M in hexanes, 0.08 mmol). The deep red solution was allowed to stir at rt for 5 min, at which time a chloromethylated heterocycle (0.80 mmol) was added (neat if a liquid, dissolved in a minium of THF if a solid) and the subsequent clear, colored solution was stirred for an additional 5 min.[6] The solution containing the nickel catalyst was then transferred *via* cannula to the vinylalane at rt, and the cross-coupling reaction followed by GC analysis. When the reaction was complete (usually <4 h), the solution was diluted with diethyl ether (10 mL) and quenched at 0°C by carefully adding 1.0 M HCl dropwise (3 mL). The mixture was allowed to stir for an additional 5 min and then extracted with diethyl ether. The combined organic layers were dried (anhydrous Na_2SO_4 / $MgSO_4$) and concentrated *in vacuo*. Silica gel column chromatograpy was used for purification; the products were normally clear, viscous oils. Unless stated, all reactions were carried out with $NiCl_2(PPh_3)_2$ as the nickel source.

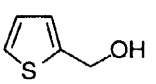


Quinaldine N-oxide monohydrate.[13] To distilled quinaldine (25 g, 170 mmol) was added 30% H_2O_2 (27.7 g, 240 mmol) and glacial acetic acid (76 mL, 1.33 mol). The mixture was warmed to 55°C for 20 h, cooled to 0°C (ice bath), and then treated with a solution of KOH (98 g, 1.75 mol) in water (122 mL) for 2 h. The resulting solid was filtered and the filtrate concentrated and washed with $CHCl_3$ (35 mL). The solid and the concentrated $CHCl_3$ extracts were added to benzene (~220 mL), and the mixture

was dried by azeotropic removal of water in a Dean-Stark trap. The hot, yellow benzene solution was decanted from dark brown, insoluble material and cooled to 0°C (ice bath). The chilled solution was treated dropwise with water (6 mL) resulting in precipitation of a nearly colorless solid which was collected by filtration and air-dried to give 13.2 g (43%) of quinaldine N-oxide monohydrate; mp 74-76°C (lit[13] 75-76°C); R_f = 0.29 (diethyl ether / hexane, 9/1); IR 3069, 2923, 1568, 1516, 1339, 1242, 1090, 907 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.77-7.27 (m, 6H, Ar), 2.69 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 145.70, 141.70, 130. 47, 129.35, 128.16, 127.87, 125.36, 123.15, 119.66, 18.98; LREIMS 159(79), 143(78), 142(100), 128(17), 116(24), 115(53), 89(10), 63(10), 51(9); HREIMS calcd for $C_{10}H_9NO$ M^+ 159.0684; found 159.0682.

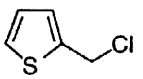


2-Chloromethylquinoline.[14] A solution of quinaldine N-oxide monohydrate (3.6 g, 20.4 mmol) in dry toluene (50 mL) was warmed to 80°C under Ar while a solution of benzenesulfonyl chloride (5.2 mL, 40.74 mmol) in dry toluene (10 mL) was introduced over 0.25 h. After 2 h at 80°C, a red oil separated from the solution. The mixture was cooled to 0°C (ice bath) and treated with 5% aqueous HCl (50 mL). The red, aqueous layer was washed with toluene (50 mL), and the toluene solutions were discarded. The mixture was diluted with $CHCl_3$ (250 mL) and ice-cold 10% aqueous NaOH (50 mL). The layers were separated, and the aqueous solution was extracted with $CHCl_3$ (2 x 50 mL). The combined organic extracts were washed with water (2 x 50 mL) and dried over anhydrous Na_2SO_4. Filtration and concentrated *in vacuo* afforded (after vacuum drying) 2.8 g (77%) of a white solid which slowly changed to yellow; mp 53-54°C (lit[14] 54-55.5°C). Chromatography of the residue (hexanes / diethyl ether, 9.5/0.5) afforded the title compound (72%) as a clear oil; R_f = 0.18 (hexanes / diethyl ether, 1/1); IR 3064, 3048, 2958, 1620, 1599, 1564, 1505, 1427, 1310, 1251, 1140, 1115, 1014 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) δ 8.24-7.54 (m, 7H, Ar), 4.85 (s, 2H, $-CH_2$-Cl); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.75, 147.08, 138.00, 130.47, 129.01, 127.80, 127.65, 127.38, 120.74, 47.14; LREIMS 177(100), 142(67), 128(12), 116(13), 115(25), 100(5), 88(6), 75(6), 63(6), 51(6) ; HREIMS calcd for $C_{10}H_8NCl$, M^+ 177.0345; found 177.0343.

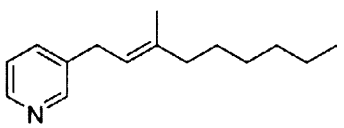


2-Hydroxymethylthiophene. Thiophene (3.3 g, 39.3 mmol) was added to a solution of 39.3 mmol of *n*-butyllithium (1.58 M in hexane) in 30 mL of hexane and 30 mL of THF, cooled to 0°C. After 30 min at 0°C, the solution was warmed to room temperature and $(CH_2O)_n$ (2.1 g, 70.7 mmol), dispersed in 3 mL THF, was transfered by cannula. The reaction mixture was stirred at room temperature for 2 h. The solvent was removed by rotary evaporation and the resulting precipitate was extracted with diethyl ether (2 x 50 mL). The organic layer was separated and the combined organics were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (hexanes / diethyl ether, 1/1) to yield 4.2 g (94%) of the desired product as a viscous clear oil; R_f = 0.40 (hexanes / diethyl ether, 1/1)); IR 3354, 3106, 2930, 2871, 1435, 1378, 1256, 1212, 1161, 853 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) δ 7.30-6.96 (m, 3H, Ar), 4.82 (s, 2H, $-CH_2O$), 2.10 (bs, 1H, -OH); ^{13}C

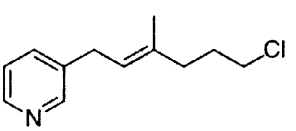
NMR (50 MHz, $CDCl_3$) δ 145.69, 129.42, 128.58, 124.58, 60.06.; LREIMS 114(100), 113(38), 97(62), 85(78), 81(29), 53(13) ; HREIMS calcd for C_5H_6OS, M^+ 114.0139; found 114.0134.



2-Chloromethylthiophene.[15] To a solution of 2-hydroxymethylthiophene (0.34 g, 2.98 mmol) was added $SOCl_2$ (1.8 g, 14.9 mmol) in $CHCl_3$ or CH_2Cl_2 (10 mL). The mixture was stirred for 7 h at 65°C. After cooling, the solvent was removed by rotary evaporation and the resulting precipitate was extracted with diethyl ether (2 x 50 mL). The organic layer was separated, and the combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (hexanes) to yield 0.36 g (91%) of the desired product as a viscous clear oil; R_f = 0.53 (hexanes); IR 3106, 3073, 2958, 2852, 2895, 1535, 1262, 1103, 1038, 852 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) δ 7.39-6.91 (m, 3H, Ar), 4.83 (s, 2H, $-CH_2Cl$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 140.21, 127.84, 127.52, 127.41, 40.53; LREIMS 132(9), 97(6), 96(100), 70(2), 57(3), 53(8), 51(3).

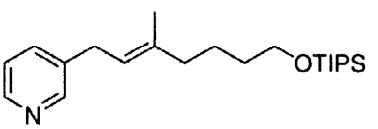


3-(3-Methylnon-2-enyl)-pyridine. Octyne (147 μL, 110 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (1 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF (1 mL), and 3-(chloromethyl)-pyridine (102 mg, 0.8 mmol) were used in the cross-coupling reaction following the procedure above, with the exception that the quench was performed with aqueous Na, K-tartrate instead of 1.0 M HCl. Chromatography of the residue (hexanes / diethyl ether, 1/1) afforded 160 mg of the title compound (92%) as a clear oil; R_f = 0.26 (hexanes / diethyl ether, 1/1); IR 2955, 2927, 2855, 1575, 1472, 1423, 1379, 1156, 1105, 1027, 792 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.440 (s, 2H, Ar), 7.49-7.16 (m, 2H, Ar), 5.28 (tt, J = 8.0 Hz, 1H, vinyl), 3.34 (d, J = 7.3 Hz, 2H, benzyl), 2.02 (t, J = 6.9 Hz, 2H, 4'-CH_2), 1.69 (s, 3H, CH_3), 1.43-1.20 (m, 6H, aliphatic), 0.87 (t, J = 6.4 Hz, 3H, 9'-CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.07, 147.39, 138.04, 137.31, 135.91, 123.47, 121.53, 39.82, 31.93, 31.57, 29.16, 28.05, 22.83, 16.32, 14.29; LREIMS 217(22), 188(5), 146(25), 132(100), 117(35), 105(36), 92(30), 77(8), 65(12), 51(5); HREIMS calcd for $C_{15}H_{23}N$, M^+ 217.1831 ; found 217.1821.

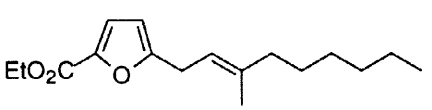


3-(6-Chloro-3-methylhex-2-enyl)-pyridine. 5-Chloro-1-pentyne (211 μL, 204 mg, 2.0 mmol), $AlMe_3$ (1.5 mL, 3.0 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (146 mg, 0.50 mmol), and $ClCH_2CH_2Cl$ (1 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (52 mg 0.08 mmol), PPh_3 (42 mg, 0.16 mmol), *n*-BuLi (113 μL , 0.16 mmol, 1.42 M), THF (2 mL), and 3-(chloromethyl)-pyridine (347 mg, 1.6 mmol) were used in the cross-coupling reaction following the procedure above, with the

exception that the quench was performed with aqueous Na, K-tartrate instead of 1.0 M HCl. Chromatography of the residue (hexanes / diethyl ether, 1/1) afforded 492 mg of the title compound (86%) as a clear oil; R_f = 0.18 (hexanes / diethyl ether, 1/1); IR 3028, 2956, 2935, 2855, 1575, 1476, 1424, 1383, 1293, 1152, 1102, 1026, 877 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.44 (d, J = 2.4 Hz, 2H, Ar), 7.50-7.18 (m, 2H, Ar), 5.37 (t, J = 7.3 Hz, 1H, vinyl), 3.51 (t, J = 6.7 Hz, 2H, 6' -CH_2), 3.36 (d, J = 7.3 Hz, 2H, benzyl), 2.19 (t, J = 7.2 Hz, 2H, 4'-CH_2), 1.97-1.83 (m, 2H, 5'-CH_2, aliphatic), 1.72 (s, 3H, 3'-CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.00, 147.52, 136.97, 135.93, 123.57, 123.08, 44.70, 36.78, 31.59, 30.87, 16.32; LREIMS 209(14), 144(5), 133(11), 132(100), 117(38), 105(11), 92(12), 77(7), 65(11), 51(7); HREIMS calcd for $C_{12}H_{16}NCl$, M^+ 209.0971; found 209.0962.

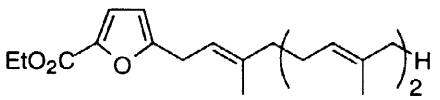


3-(3-Methyl-7-triisopropylsilyloxyhept-2-enyl)-pyridine. Hex-5-ynyloxytriisopropylsilane (254 μL, 265 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (1 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF (1 mL), and 3-(chloromethyl)-pyridine (102 mg, 0.80 mmol) were used in the cross-coupling reaction following the procedure above, with the exception that the quench was performed with aqueous Na, K-tartrate instead of 1.0 M HCl. Chromatography of the residue (hexanes / diethyl ether, 1/1) afforded 254 mg of the title compound (88%) as a clear oil; R_f = 0.24 (hexanes / diethyl ether, 1/1); IR 3028, 2936, 2854, 1575, 1476, 1423, 1383, 1293, 1186, 1102, 1026, 877 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.43 (d, J = 4.5 Hz, 2H, Ar), 7.49-7.15 (m, 2H, Ar), 5.30 (t, J = 7.3 Hz, 1H, vinyl), 3.68 (t, J = 6.1 Hz, 2H, 7'-CH_2OSi), 3.34 (d, J = 7.3 Hz, 2H, benzyl), 2.05 (t, J = 6.7 Hz, 2H, 4'-CH_2), 1.70 (s, 3H, 3'-CH_3), 1.54 -1.49 (m, 4H, aliphatic), 1.08-1.01 (m, 21H, TIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.06, 147.38, 137.76, 137.23, 135.86, 123.44, 121.76, 63.40, 39.53, 32.73, 31.53, 24.24, 18.20, 16.23, 12.16; LREIMS 361(2), 320(7), 319(27), 318(100), 232(2), 188(5), 115(6), 101(5), 93(7), 75(18), 65(2), 59(7), 55(2); HREIMS calcd for $C_{22}H_{39}NOSi$, M^+ 361.2801; found 361.2789.

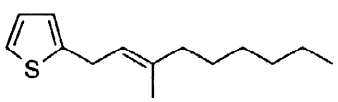


5-(3-Methylnon-2-enyl)-furan-2-carboxylic acid ethyl ester. Octyne (147 μL, 110 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (1 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF (1 mL), and ethyl-5-(chloromethyl)-2-furancarboxylate (149 mg, 0.80 mmol) were used in the cross-coupling reaction following the procedure above. Chromatography of the residue (hexanes / diethyl ether, 9.5/0.5) afforded 194 mg of the title compound (86%) as a clear oil; R_f = 0.37 (hexanes / diethyl ether, 9.5/0.5); IR 2956, 2928, 2857, 1725, 1594, 1525, 1461, 1480, 1301, 1206, 1130, 1016, 965, 862 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.08 (d, J = 3.4 Hz, 1H, Ar), 6.08 (d, J=3.4, 1H, Ar), 5.31 (t, J = 7.0 Hz, 1H, vinyl), 4.34 (q, J = 7.0 Hz, 2H, -CO_2CH_2-), 3.41 (d, J = 6.9 Hz, 2H, benzyl), 2.02 (t, J = 6.7 Hz, 2H, 4' -CH_2-), 1.64 (s, 3H, 3'-CH_3), 1.36 (t,

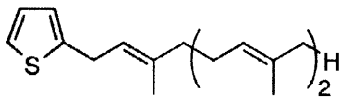
J = 7.2 Hz, 3H, -CH_3), 1.30-1.26 (m, 8H, aliphatic), 0.87 (t, J = 6.7 Hz, 3H, 9'-CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 160.56, 159.13, 143.47, 139.43, 119.26, 117.74, 107.63, 60.85, 39.73, 31.93, 29.12, 27.98, 27.48, 22.83, 16.26, 14.58, 14.26; LREIMS 278(42), 249(7), 233(9), 208(12), 193(81), 180(12), 166(100), 153(38), 124(19), 91(20), 79(11), 69(12), 55(16); HREIMS calcd for $C_{17}H_{26}O_3$, M^+ 278.1882; found 278.1879.



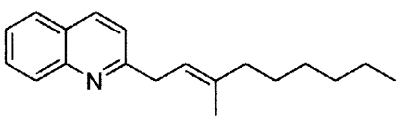
5-(3,7,11-Trimethyldodeca-2,6,10-trienyl)-furan-2-carboxylic acid ethyl ester. 6,10-Dimethyl-undeca-5,9-diene-1-yne (123 μL, 150 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (2 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF (1 mL), and ethyl-5-(chloromethyl)-2-furancarboxylate (149 mg, 0.80 mmol) were used in the cross-coupling reaction following the procedure above. Chromatography of the residue (hexanes / diethyl ether, 9/1) afforded 220 mg of the title compound (80%) as a clear oil; R_f = 0.27 (hexanes / diethyl ether, 9/1) IR 2975, 2921, 2855, 1725, 1594, 1525, 1445, 1380, 1301, 1206, 1130, 1016, 968, 801 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.05 (d, J = 3.4 Hz, 1H, Ar), 6.06 (d, J = 3.4 Hz, 1H, Ar), 5.30 (t, J = 7.3 Hz, 1H, vinyl), 5.08-5.01 (m, 3H, vinyl), 4.31 (q, J = 7.2 Hz, 2H, -CO_2CH_2-), 3.38 (d, J = 7.2 Hz, 2H), 2.08-1.93 (m, 8H, aliphatic), 1.56 (s, 6H, 3',7' 2 x -CH_3), 1.63 (s, 6H, 11'-CH_3 x 2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 160.48, 159.13, 143.42, 139.02, 135.47, 131.50, 124.48, 124.01, 119.27, 118.01, 107.69, 60.87, 39.89, 39.71, 27.46, 26.88, 26.55, 25.89, 17.87, 16.35, 16.21, 14.58; LREIMS 344(2), 301(2), 233(3), 220(4), 208(7), 191(9), 178(15), 153(16), 152(53), 136(36), 121(17), 109(12), 105(15), 91(17), 69(100), 55(13), 53(10); HREIMS calcd for $C_{22}H_{32}O_3$, M^+ 344.2352; found 344.2365.



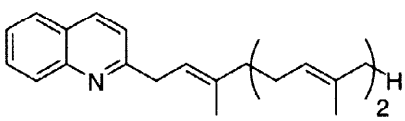
2-(3-Methylnon-2-enyl)-thiophene. Octyne (147 μL, 110 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (1 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF (1 mL), and 2-chloromethylthiophene (106 mg, 0.80 mmol) were used in the cross-coupling reaction following the procedure above. Chromatography of the residue (*n*-hexanes) afforded 150 mg of the title compound (84%) as a clear oil; R_f = 0.62 (*n*-hexanes); IR 2956, 2926, 2855, 1640, 1461, 1440, 1379, 1285, 1118, 1075, 849 cm^{-1}, ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.13-6.77 (m, 3H, Ar), 5.39 (t, J = 7.3 Hz, vinyl), 3.55 (d, J = 7.3 Hz, 2H, benzyl), 2.04 (t, J = 6.9 Hz, 2H, 4' -CH_2-), 1.70 (s, 3H, 3'-CH_3), 1.47-1.29 (m, 8H, aliphatic), 0.90 (t, J = 6.2 Hz, 3H, 9'-CH_3) ^{13}C NMR (50 MHz, $CDCl_3$) δ 145.33, 137.55, 126.88, 123.92, 123.22, 122.19, 39.83, 32.05, 29.22, 28.71, 28.09, 22.94, 16.29, 14.40; LREIMS 222(19), 151(7), 138(11), 137(100), 123(7), 110(28), 97(33), 77(4), 55(5), 53(5), 51(2); HREIMS calcd for $C_{14}H_{22}S$, M^+ 222.1442; found 222.1448.



2-(3,7,11-Trimethyldodeca-2,6,10-trienyl)thiophene. 6,10-Dimethylundeca-5,9-diene-1-yne (220 μL, 176 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (2 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF (1 mL), and 2-chloromethylthiophene (106 mg, 0.80 mmol) were used in the cross-coupling reaction following the procedure above. Chromatography of the residue (*n*-hexane) afforded 185 mg of the title compound (80%) as a yellow oil; R_f = 0.50 (*n*-hexane); IR 2968, 2920, 2854, 1442, 1379, 1285, 1222, 1152, 1082, 1036, 847 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.27-6.79 (m, 3H, Ar), 5.43 (t, J = 6.9 Hz, vinyl), 5.15-5.09 (m, 2H, vinyl), 3.56 (d, J = 7.2 Hz, 2H), 2.18-2.00 (m, 8H, aliphatic), 1.73 (s, 3H, 3'-CH_3), 1.71 (s, 3H, 7'-CH_3), 1.63 (s, 6H, 11'-CH_3 x 2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 145.16, 137.14, 135.30, 131.41, 126.87, 124.56, 124.16, 123.94, 123.23, 122.49, 39.99, 39.83, 28.72, 27.01, 26.72, 25.98, 17.98, 16.39, 16.33; LREIMS 288(2), 245(2), 207(3), 191(7), 151(23), 136(26), 121(11), 97(57), 81(30), 69(100), 67(12), 52(9), 50(2); HREIMS calcd for $C_{19}H_{28}S$, M^+ 288.1912; found 288.1913.

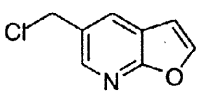


2-(3-Methylnon-2-enyl)-quinoline. Octyne (147 μL, 110 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (1 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF (1 mL), and 2-chloromethylquinoline (142 mg, 0.80 mmol) were used in the cross-coupling reaction following the procedure above. Chromatography of the residue (hexanes / ethyl acetate, 9.5/0.5) afforded 198 mg of the title compound (89%) as a clear oil; R_f = 0.16 (hexanes / ethyl acetate, 9.5/0.5); IR 3134, 3058, 2953, 2928, 2856, 1599, 1561, 1504, 1461, 1427, 1375, 1313, 1143, 1120, 973 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.08-7.24 (m, 7H, Ar), 5.50 (t, J = 7.3 Hz, 1H, vinyl), 3.73 (d, J = 7.2 Hz, 2H, benzyl), 2.04 (t, J = 6.9 Hz, 2H, 4' -CH_2-), 1.75 (s, 3H, 3'-CH_3), 1.44-1.25 (m, 8H, aliphatic), 0.86 (t, J = 6.7 Hz, 3H, 9'-CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.15, 147.94, 138.21, 136.40, 129.41, 128.92, 127.54, 126.84, 125.76, 121.22, 120.78, 39.82, 38.16, 31.86, 29.07, 27.96, 22.76, 16.47, 14.20; LREIMS 267(17), 252(12), 238(11), 224(9), 210(27), 197(27), 196(100), 182(88), 168(19), 156(26), 143(52), 129(10), 128(19), 115(8), 101(8), 77(8); HREIMS calcd for $C_{19}H_{25}N$, M^+ 267.1987; found 267.1979.

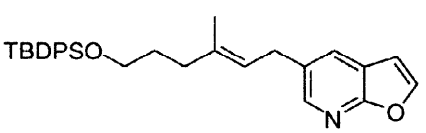


2-(3,7,11-Trimethyldodeca-2,6,10-trienyl)-quinoline. 6,10-Dimethylundca-5,9-diene-1-ene (220 μL, 176 mg, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (2mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$,

(26 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), *n*-BuLi (56 μL, 0.08 mmol, 1.42 M), THF(1 mL), and 2-chloromethylquinoline (142 mg, 0.80 mmol) were used in the cross-coupling reaction following the procedure above. Chromatography of the residue (hexanes) afforded 187 mg of the title compound (69%) as a clear oil; R_f = 0.24 (hexanes / ethyl acetate, 9.5/0.5); IR 3056, 2966, 2920, 2854, 1638, 1600, 1504, 1426, 1379, 1311, 1222, 1113, 822 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.01-7.21 (m, 7H, Ar), 5.45 (t, J = 7.3 Hz, 1H, vinyl), 5.06-4.98 (m, 3H, vinyl), 3.68 (d, J = 7.3 Hz, 2H), 2.05-1.92 (m, 8H, aliphatic), 1.72 (s, 3H, 3'-CH_3), 1.60 (s, 3H, 7'-CH_3), 1.52 (s, 3H, 11'-CH_3), 1.51 (s, 3H, 11'-CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.16, 147.89, 137.97, 136.57, 135.32, 131.44, 129.54, 128.90, 127.62, 126.92, 125.89, 124.50, 124.12, 121.30, 121.10, 39.88, 38.18, 26.88, 26.61, 25.88, 17.85, 16.62, 16.22; LREIMS 333(3), 264(100), 236(2), 222(6), 197(18), 196(51), 182(20), 167(13), 143(35), 121(11), 101(4), 69(30), 55(4), 53(5); HREIMS calcd for $C_{24}H_{31}N$, M^+ 333.2457; found 333.2472.

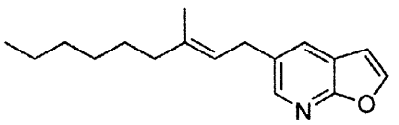


5-Chloromethylfuro[2,3-*b*]pyridine. The precursor alcohol[16] (2.00 g) in 38 mL dichloromethane was cooled to 0°C and 1.05 mL of $SOCl_2$ was added slowly and the reaction allowed to warm to rt for 2 h at which time GC analysis showed no starting material remained. The solvent was removed *in vacuo* and the brown solid dissolved in toluene (30 mL), hot filtered through SiO_2 and concentrated *in vacuo* yielding 2.09 g of a very pale brown solid (93%) which was used without further handling in the following cross-coupling reactions; R_f 0.31 (15% ethyl acetate/petroleum ether); mp 57-58°C; IR (KBr) 3146, 3119, 3006, 2966, 2917, 1592, 1534, 1385, 1331, 1290, 1244, 1196, 1128, 1029, 976, 924, 879 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 1.0 Hz, 1H), 7.96 (d, J = 2.4 Hz, 1H), 7.71 (d, J = 2.4 Hz, 1H), 6.75 (d, J = 2.4 Hz, 1H), 4.68 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 145.8, 144.5, 130.6, 129.1, 119.4, 105.9, 43.5; LREIMS 169(10), 167(30), 133(10), 132(100), 104(3), 77(14), 76(5), 75(5), 63(2), 51(12); HREIMS calcd for C_8H_6NOCl, M^+ 167.0138; found 167.0132.

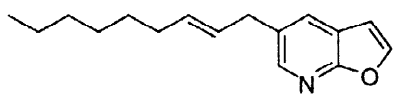


5-[7-(*t*-Butyldiphenylsilyloxy)-3-methylhept-2-enyl]-furo[2,3-*b*]pyridine. TBDPS-protected 5-hexynol (222 mg, 0.66 mmol), $AlMe_3$ (0.58 mL, 1.15 mmol, 2 M in hexanes), Cp_2ZrCl_2 (96 mg, 0.33 mmol) and $ClCH_2CH_2Cl$ (1.5 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (26.0 mg, 0.04 mmol), 160 μL *n*-BuLi (0.79 mmol, 0.49 M in hexanes), THF (2.5 mL) and 5-chloromethylfuro[2,3-*b*]pyridine (66.5 mg, 0.40 mmol) were used in the cross-coupling reaction following the procedure above, with the exception of the quench and extraction, which were performed with an aqueous solution of 2.5 g citric acid monohydrate and chloroform, respectively. Chromatography of the residue on acidic SiO_2 (gradient elution, 1-5% ethyl acetate/petroleum ether) afforded the title compound as a clear brown oil, 168.9 mg (87%); R_f 0.52 (15% ethyl acetate/petroleum ether; IR (neat) 3146, 3119, 3070, 3048, 2931, 2858, 1589, 1532, 1471, 1427, 1389, 1247, 1133, 1111, 1032, 823, 738, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.70 (d, J = 2.0 Hz, 1H), 7.66 (m, 5H), 7.37 (m, 6H), 6.68 (d, J = 2.4 Hz, 1H), 5.30 (t, J = 7.2, 1H), 3.67 (t, J = 6.0 Hz, 2H), 3.43 (d, J = 7.2 Hz, 2 H), 2.03 (t, J = 7.2 Hz, 2 H), 1.71 (s, 3H), 1.53 (m, 4H), 1.04 (s, 9H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 160.7, 144.9, 144.2, 137.5, 135.5, 134.8, 134.0, 132.8, 129.7, 127.6, 127.5, 127.1, 122.3, 119.1, 105.7, 94.3, 63.7, 39.2, 32.1, 31.1, 29.7, 26.8, 26.5, 24.0, 19.2, 16.0; LREIMS 483(1), 427(34), 426(100), 199(21), 183(6), 132(6), 77(4); HREIMS calcd for $C_{31}H_{37}NO_2Si$, M^+ 483.2594; found 483.2592.

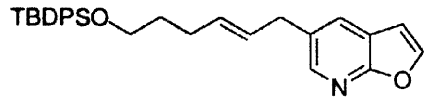


5-(3-Methylnon-2-enyl)-furo[2,3-*b*]pyridine. Octyne (110.2 mg, 147 μL, 1.0 mmol), $AlMe_3$ (0.75 mL, 1.5 mmol, 2 M in hexanes), Cp_2ZrCl_2 (73 mg, 0.25 mmol), and $ClCH_2CH_2Cl$ (3.4 mL) were used in the carboalumination following the procedure above. $NiCl_2(PPh_3)_2$ (24.5 mg, 0.037 mmol), *n*-BuLi (140 μL, 0.53 M in hexanes), THF (3 mL) and 5-chloromethylfuro[2,3-*b*]pyridine (125.2 mg, 0.75 mmol) were used in the cross-coupling reaction following the procedure above with the exception of the quench and extraction, which were done with 3 g citric acid monohydrate in 10 mL water and chloroform, respectively. Chromatography of the residue on acidic SiO_2 (gradient elution using 2.5-5% ethyl acetate/petroleum ether) afforded 180.5 mg of a clear pale brown oil (93%); R_f 0.55 (15% ethyl acetate/petroleum ether); IR (neat) 3117, 3146, 2996, 2927, 2855, 1588, 1532, 1444, 1467, 1389, 1339, 1246, 1190, 1134, 880, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.74 (s, 1H), 7.66 (d, J = 2.4 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 5.30 (m, 1 H), 3.43 (d, J = 7.2 Hz, 2H), 2.01 (t, J = 8.0 Hz, 2H), 1.70 (s, 3H), 1.40 (m, 6H), 0.851 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 144.7, 144.2, 137.3, 132.6, 129.5, 122.0, 118.6, 105.6, 39.5, 31.6, 31.1, 28.8, 27.7, 22.5, 16.0, 14.0; LREIMS 257(17), 187(5), 173(13), 172(100), 157(13), 145(15), 132(25), 77(5); HREIMS calcd for $C_{17}H_{23}NO$, M^+ 257.1780; found 257.1781.

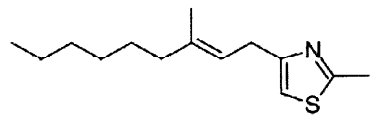


5-Non-2-enylfuro[2,3-*b*]pyridine $Cp_2Zr(H)Cl$ (252 mg, 0.95 mmol) suspended in 2 mL of dichloromethane, protected from light, was treated with 1-octyne (147 μL, 1.0 mmol). After 1 h, the clear yellow solution was concentrated *in vacuo* and the residue dissolved in 2 mL THF. 5-Chloromethylfuro[2,3-*b*]pyridine (83.4 mg, 0.5 mmol) dissolved in 200 μL THF was cannulated into the vinyl zirconocene. In a separate flask, $NiCl_2(PPh_3)_2$ (16.4 mg, 0.025 mmol) in 400 μL THF was treated slowly, dropwise with *n*-BuLi (90 μL, 0.05 mmol, 0.53 M in hexanes) giving a blood red/black solution of the Ni(0) catalyst. The catalyst was then cannulated into the vinyl zirconocene/5-chloromethylfuro[2,3-*b*]pyridine solution and the reaction vessel protected from light. After 12 h the reaction was quenched by addition of 10 mL Et_2O and 4 mL of aqueous Na, K-tartrate. The layers were separated and the aqueous layer extracted (3 x 5 mL). The combined organics were washed once with 10 mL saturated brine solution, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Chromatography of the residue on acidic SiO_2 (gradient elution, 2.5-5% ethyl acetate/ petroleum ether) afforded 97 mg of a pale brown oil; R_f 0.61 (15% ethyl acetate/petroleum ether); IR (neat) 3147, 3117, 3018, 3956, 2925, 2854, 1588, 1522, 1467, 1389, 1339, 1246, 1191, 1134, 1032, 969, 880, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.68 (d, J = 2.0 Hz, 1H), 6.67 (d, J = 2.4 Hz, 1H), 5.50 (m, 2H), 3.37 (d, J = 5.2 Hz, 2H), 1.98 (q, J = 6.8 Hz, J = 6.0 Hz, 2H), 1.31 (m, 8H), 0.82 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 144.8, 144.4, 132.8, 131.9, 129.8, 128.1, 118.9, 105.6, 35.9, 32.4, 31.6,

29.3, 28.8, 22.5, 13.9; LREIMS 243(43), 242(7), 214(4),186(6), 173(5), 172(19), 170(8), 159(16), 158(100), 157(11), 146(20), 145(70), 133(29), 132(47), 115(5), 103(4), 77(12), 69(4), 55(6), 51(6); HREIMS calcd for $C_{16}H_{21}NO$, M^+ 243.1623; found 243.1624.



5-[7-(*t*-Butyldiphenylsilyloxy)-hept-2-enyl]-furo[2,3-*b*]pyridine. $Cp_2Zr(H)Cl$ (188 mg, 0.73 mmol) suspended in 2 mL of dichloromethane, protected from light, was treated with TBDPS protected 5-hexynol (252 mg, 0.75 mmol). After 1.25 h, the clear yellow solution was concentrated *in vacuo* and the residue dissolved in 2 mL THF. 5-Chloromethylfuro[2,3-*b*]pyridine (63 mg, 0.38 mmol) dissolved in 200 μL THF was cannulated into the vinyl zirconocene with 2 x 200 μL THF washes to ensure complete transfer. In a separate flask, $NiCl_2(PPh_3)_2$ (12.4 mg, 0.019 mmol) in 300 μL THF was treated slowly, dropwise with *n*-BuLi (70 μL, 0.04 mmol, 0.53 M in hexanes) giving a blood red/black solution of the Ni(0) catalyst. The catalyst was then cannulated into the vinyl zirconocene/5-chloromethylfuro[2,3-*b*]pyridine solution and the flask protected from light. After 14 h the reaction was quenched by addition of 10 mL Et_2O and 4 mL of aqueous Na, K-tartrate. The layers were separated and the aqueous layer extracted (3 x 5 mL). The combined organics were washed once with 10 mL saturated brine solution, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Chromatography of the residue on acidic SiO_2 (gradient elution, 2.5-10% ethyl acetate/petroleum ether) afforded 120.6 mg of a pale yellow oil (68%); R_f 0.50 (15% ethyl acetate/petroleum ether); IR (neat) 3071, 3049, 2957, 2931, 2858, 1589, 1533, 1472, 1428, 1389, 1134, 1111, 736, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.72 (s, 1H), 7.68 (m, 4 H), 7.65 (d, J = 2.4 Hz, 2 H), 7.39 (m, 6 H), 6.70 (d, J = 2.4 Hz, 1 H), 5.54 (m, J = 5.2 Hz, 2H), 3.67 (t, J = 6.4 Hz, 2H), 3.41 (d, J = 5.2 Hz, 2H), 2.03 (m, J = 7.2 Hz, 2H), 1.59 (m, 2H), 1.47 (m, 2H), 1.09 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 144.9, 135.5, 134.8, 134.0, 132.5, 129.9, 129.4, 128.3, 127.5, 105.7, 63.7, 35.9, 32.1, 32.0, 26.8, 26.5, 25.5, 19.1; LREIMS 469(1), 414(9), 413(36), 412(100), 199(8), 183(2), 132(2), 57(1); HREIMS calcd for $C_{30}H_{35}NO_2Si$, M^+ 469.2437; found 469.2438.



2-Methyl-4-(3-methylnon-2-enyl)-thiazole (5). Octyne (73 μL, 0.49 mmol), $AlMe_3$ (0.32 mL, 0.63 mmol, 2.0 M in hexanes), Cp_2ZrCl_2 (36 mg, 0.12 mmol), and $ClCH_2CH_2Cl$ (1 mL) were used in the carboalumination following the procedure above. THF (1 mL) was added to a mixture of $NiCl_2(PPh_3)_2$ (11 mg, 0.017 mmol) along with LiCl (17 mg, 0.36 mmol) which had been previously weighed under argon in a dry box. Upon cooling to -23°C, methylmagnesium chloride (11 μL, 0.033 mmol, 3 M in THF) and 4-chloromethyl-2-methylthiazole (52 mg, 0.35 mmol) were added sequentially to the blue homogeneous solution. This mixture was then slowly cannulated into a flask containing the vinylalane, also at -23°C, and the combined reaction mixture let stir for 4 h. After this period of time, diethyl ether (5 mL) was added and the reaction was quenched by the addition of 1 N HCl (5 mL). The mixture was extracted with diethyl ether (3 x 20 mL), the solvents were removed *in vacuo* on a rotary evaporator, and the yellow oily residue chromatographed on silica gel (hexanes /

ethyl acetate, 20 / 1) yielding 65 mg (78%) of the title compound as a clear oil; R_f = 0.31 (hexanes / ethyl acetate, 20/1); IR (neat) 2955, 2926, 2855, 1522, 1457, 1377, 1180, 1123 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.68 (t, J = 1.2 Hz, 1H, Ar), 5.42 (tq, J = 7.4; 1.2 Hz, 1H, vinyl), 3.48 (d, J = 7.2 Hz, 2H), 2.70 (s, 3H, CH_3) 2.04 (t, J = 8 Hz, 2H), 1.67 (s, 3H, CH_3), 1.39-1.46 (m, 2H), 1.26-1.31 (m, 6H), 0.89 (t, J = 6.8 Hz, CH_3); ^{13}C NMR (400 MHz, $CDCl_3$) δ 156.56, 138.13, 125.74, 120,48, 112.36, 39.89, 32.00, 30.52, 29.25, 28.13, 22.88, 19.43, 16.31, 14.33; LREIMS 237(10), 222(50), 208(10), 194(7), 180(28), 166(100), 153(71), 152(62), 138(4), 126(27), 113(86), 112(47), 91(23), 77(14), 71(24), 59(14), 55(16); HREIMS calcd for $C_{14}H_{23}NS$, M^+ 237.1551; found 237.1556.

References and Notes

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5. The commercially available $NiCl_2 \bullet 2PPh_3$ complex could be used interchangeably with identical results.
6. Alternatively and experimentally simpler, the vinylalane could be first combined with the heterocyclic substrate to which was then added the Ni(0) catalyst; no difference was noted in yields.
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16. This alcohol was obtained from Dr. Ioannis Houpis at Merck & Co, Process Research, Rahway, N.J. It was used as received *en route* to the chlormethyl derivative described in the Experimental Section.