The Synthesis of Sterically Demanding Ligands and Examples of Their Copper Complexes

by

Ryan D. Rieth

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Submitted to the Department of Chemistry on August 30, 2004 in Partial Fulfillment of the Requirements for the Degree of Master of Science in Chemistry

Abstract

Conditions for promoting the Pd-catalyzed arylation of (*N*-pyrrolyl)zinc derivatives have been established using aryl bromides, chlorides, and iodides as substrates. In most cases, 0.5 mol% $Pd(OAc)_2$ can achieve the desired transformation in roughly 24 hours, with the more sterically demanding substrates requiring altered conditions. Typical isolated yields are in excess of 70%. Moreover, methyl- and aryl-substituted pyrrolyl anions have been shown to display similar chemistry using 5.0 mol% $Pd(OAc)_2$. Though they require longer reaction times, the isolated yields rival those of the unsubstituted analogs.

Two new copper(I) N-heterocyclic carbene complexes containing the 2,4,6,2",4",6"-hexaisopropyl-1,1':3',1"-terphenyl moiety have been synthesized and isolated. The LCuCl complex (92% isolated yield) was made via a one-pot synthesis from the corresponding imidazolinium tetrafluoroborate salt, NaH, and CuCl (L = [1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]). The LCuOAc complex (71% isolated yield) was made the same way using CuOAc in place of CuCl.

Thesis Supervisor: Joseph Sadighi
Title: Assistant Professor of Chemistry

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List of Abbreviations Used in Text

°	degree(s)
Å	angstrom(s)
Anal. Cald.	Analysis Calculated
ArX	aryl halide (X = Cl, Br, I)
br	broad
cat.	catalyst
cm^{-1}	wavenumbers
CuOAc	copper(I) acetate
Cy	cyclohexyl, *cyclo*-C_6H_{11}
d	doublet
δ	chemical shift downfield from tetramethylsilane in ppm
dd	doublet of doublets
dec	decomposed
e^-	electron
Et	ethyl, C_2H_5
Et_2O	diethyl ether
g	gram(s)
H	proton(s)
hrs	hours
HCl	hydrochloric acid
Hz	hertz
IPr	[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]
IR	infrared
J	C-H coupling constant in Hz
L	[1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]
M	molar
m	multiplet
Me	methyl, CH_3
mg	milligrams
$MgSO_4$	magnesium sulfate, anhydrous
MHz	megahertz
min	minute(s)
mL	milliliters
mmol	millimoles
mol	mole
mp	melting point
NaO^tBu	sodium *tert*-butoxide
NHCs	N-heterocyclic carbenes
NMR	nuclear magnetic resonance
Pd_2dba_3	tris(dibenzylideneacetone) dipalladium (0)
$Pd(OAc)_2$	palladium acetate
ppm	parts per million
quint	quintet

rac-BINAP	racemic 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
rxn	reaction
s	singlet
sept	septet
sext	sextet
t	triplet
t-Bu	*tert*-butyl, $C(CH_3)_3$
td	triplet of doublets
THF	tetrahydrofuran
Trip	2,4,6-triisopropylphenyl

Chapter 1

Palladium-Catalyzed Cross-Coupling of Pyrrole Anions with Aryl Chlorides, Bromides and Iodides

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Introduction

Palladium-catalyzed arylation of heterocycles has been the subject of recent experimental efforts, in part due to the inclusion of functionalized heterocycles in structural motifs of natural products and biologically significant molecules.[1] Expanding upon previous work aimed at arylating pyrroles in the electron-rich 2-position,[2] experimentation focusing on establishing reaction conditions suitable to promote C-C bond formation for a number of aryl halides, with a wide variety of steric and electronic properties, has been performed.

Previously, activation of relatively inert azole C-H bonds has been reported by numerous sources, often with emphasis placed on the choice of base.[3] While metal carbonates and Grignard salts have been shown to effectively foster C-C bond formation in the presence of a phosphine-substituted Pd catalyst, harsh reaction conditions are often necessary to achieve even modest yields of desired product.[4] As a marked improvement, the presented methodology can not only be used for a broad scope of aryl halides, but in most cases achieves reasonable product yields under mild reaction conditions.

A previously known system leads to moderately selective *C*-arylation of pyrrolyl anions through the formation in situ of pyrrol-1-yl-zinc halides followed by transmetallation to the palladium catalyst.[5] However, these reported transformations are achieved under harsh reaction conditions (140°C) and with high catalyst loading (10 mol% Pd). In an attempt to make the reaction conditions less harsh by generating a more active catalyst, a class of bulky phosphine ligands developed by Buchwald and associates – which have been utilized in several coupling reactions of interest, including the *N*-arylation of indoles[6] – was used. Initial experimentation[7] featured the use of 2-(di-*t*-butylphosphino)biphenyl as a supporting ligand to afford 2-mesitylpyrrole from bromomesitylene in THF.

This initial result prompted the exploration of optimized reaction conditions for this initial substrate and introduced the question of whether other aryl halides would also couple effectively. These additional coupling reactions were then optimized with respect to reaction conditions and catalyst precursors

Several alkyl- and aryl-substituted pyrrolyl anions were the subject of similar experimentation, in an attempt to further broaden the scope of the methodology and increase its potential utility. Based on either commercial or synthetic availability, 2,4-dimethylpyrrole, 3-methylpyrrole, and 2-(2'-methoxyphenyl)-1H-pyrrole were chosen as starting materials for coupling with aryl bromides. In many instances, the desired product was successfully isolated and characterized, providing an encouraging route to valuable polysubstituted pyrroles.

References

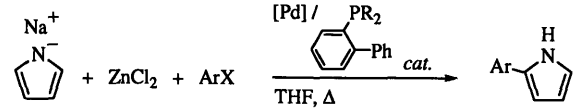
1. (a) Katrizky, A.R.; Li, J.; Gordeev, M.F. *Synthesis* **1994**, 93-96. (b) Pivsa-Art, S.; Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 467-473. (c) Kondo, Y.; Komine, T.; Sakamoto, T. *Org. Lett.* **2000**, *2*, 3111-3113.
2. Boukou-Poba, J.P.; Farnier, M.; Guilard, R. *Tetrahedron Lett.* **1979**, *19*, 1717-1720.
3. A review article: Miura, M.; Nomura, M. *Top. Curr. Chem.* **2002**, *219*, 211-241.
4. Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2003**, *125*, 5274-5275.
5. Filippini, L.; Gusmeroli, M.; Riva, R. *Tetrahedron Lett.* **1992**, *33*, 1755-1758.
6. a) Aranyos, A.; Old, D.W.; Kiyomori, A.; Wolfe, J.P.; Sadighi, J.P.; Buchwald, S.L. *J. Am. Chem. Soc.* **1999**, *121*, 4369-4378. b) Kaye, S.; Fox, J.M.; Hicks, F.A.; Buchwald, S.L. *Adv. Syn. Cat.* **2001**, *343*, 789-794. c) Tomori, H.; Fox, J.M.; Buchwald, S.L. *J. Org. Chem.* **2000**, *65*, 5334-5341. d) Old, D.W.; Wolfe, J.P.; Buchwald, S.L. *J. Am. Chem. Soc.* **1998**, *120*, 9722-9723. e) Old, D.W.; Harris, M.C.; Buchwald, S.L. *Org. Lett.* **2000**, *2*, 1403-1406. f) Fox, J.M.; Huang, X.; Chieffi, A.; Buchwald, S.L. *J. Am. Chem. Soc.* **2000**, *122*, 1360-1370.
7. Initial experiments were performed by Elisa Calimano and Neal P. Mankad.

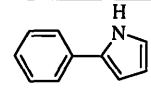
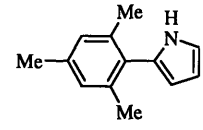
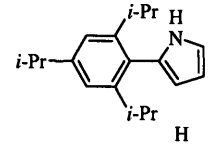
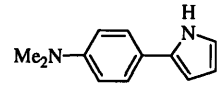
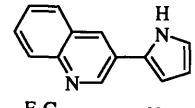
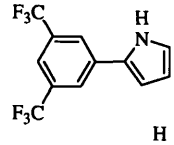
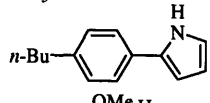
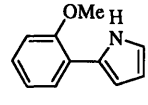
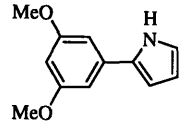
Results and Discussion

The catalytic arylation of the pyrrolyl anion most likely occurs via oxidative addition of the organic substrate at the palladium metal center, followed by transmetallation of the pyrrolyl moiety from pyrrolylzinc chloride (generated in situ)[1] to palladium, and concluding with the reductive elimination of the arylated pyrrole.[2] In general, the pyrrolyl sodium salt and $ZnCl_2$ are combined in THF in order to generate the pyrrolylzinc chloride. The palladium precatalyst and supporting phosphine were then added followed by the organic substrate. The reactions were allowed to proceed to completion as judged by GC-MS analysis. The results and conditions of the reactions involving the unsubstituted pyrrolyl anion are summarized in Table 1.[3]

Several variables were qualitatively explored. For example, the rate at which the

Table 1. Pd-catalyzed Arylation of (Pyrrolyl)zinc Chloride[a]



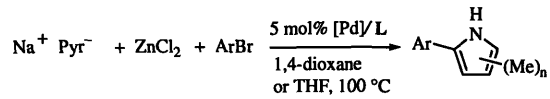
Entry	X =	Rxn time	Product	Yield (%)
1[b]	I	21 hrs.		90
2[b,c]	Br	44 hrs.		90
3[d,e]	Br	41 hrs.		70
4	Br	19 hrs.		48
5[f]	Br	18 hrs.		70
6[b,e,g]	Br	18 hrs.		90
7[h]	Cl	16 hrs.		71
8[h]	Cl	25 hrs.		93
9[h]	Cl	23 hrs.		81

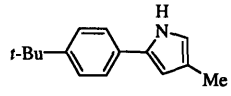
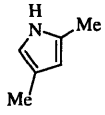
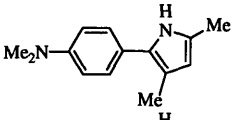
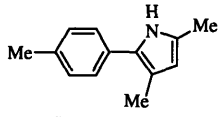
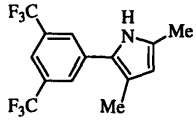
[a] Unless noted otherwise: 1.0 equiv ArX, 1.0M in THF; 1.6 equiv $[Na^+ (C_4H_4N^-)]/ZnCl_2$; 0.5 mol% $Pd(OAc)_2$ and ligand (R = *t*-Bu); 16–25 h. [b] With 3.0 equiv $[Na^+ (C_4H_4N^-)]/ZnCl_2$. [c] With 8.2 mmol ArBr in 20 mL THF, and 0.25 mol% $Pd_2(dba)_3$; 44 h. [d] With 2.0 mol% $Pd_2(dba)_3$, 4.0 mol % phosphine, and 4.0 equiv $[Na^+ (C_4H_4N^-)]/ZnCl_2$; 41 h. [e] Ligand with R = cyclohexyl was used. [f] When R = Cy, reaction at 60 °C for 16 h gave 72% yield of *N*-arylpyrrole.

reaction progresses appears to depend upon reaction temperature and molar ratio of pyrrolyl anion to aryl halide: as either variable is increased, the reaction concludes more rapidly. Another alteration that was briefly studied involved changing the source of palladium. However, the reaction appears to proceed in a similar fashion regardless of whether the source of palladium used is Pd_2dba_3 or $Pd(OAc)_2$. Finally, the dialkylphosphinobiphenyl ligand was altered and in some cases was shown to affect the selectivity of the product distribution. Perhaps the most notable example occurred when the aryl halide used was 3-bromoquinoline. The use of 2-(Di-*tert*-butylphosphino)-biphenyl leads to primarily the *C*-arylated product while 2-(dicyclohexylphosphino)biphenyl affords the *N*-arylated derivative. The factors that control product selectivity are unknown at present.

The same reaction was performed in the same manner with methylated derivatives of the pyrrolyl anion. While aryl bromides, chlorides, and iodides were used for the unsubstituted pyrrolyl anion, only aryl bromides were used for the methylated versions. In the case of 2,4-dimethylpyrrole, several aryl bromides were used to demonstrate the effectiveness of this methodology over a range of electronic properties. Higher reaction temperatures and catalyst loadings were required in order to achieve the desired transformations. The results for the methylated pyrrolyl anions are summarized in Table 2.

Table 2. Pd-catalyzed Arylation of *C*-Methylated Pyrrole Anions.

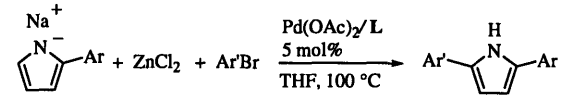


Entry	Pyr–H	Rxn time	Product	Yield (%)
1[a,e]		43 hrs.		64
2[b,d,e]		17 hrs.		78
3[c,d,f]		37 hrs.		64
4[b,d,g]		54 hrs.		75

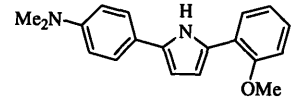
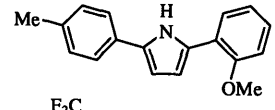
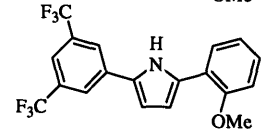
[a] 0.5M ArBr in THF; 1.6 equiv [Na^+ Pyr^-]/$ZnCl_2$; with 2.5 mol% $Pd_2(dba)_3$. [b] 0.4M ArBr in THF. [c] 1.3M ArBr in 1,4-dioxane. [d] With $Pd(OAc)_2$; 2.0 equiv [Na^+ Pyr^-]/ $ZnCl_2$.[e] **L** = 2-(di-*tert*-butyl-phosphino)biphenyl. [f] **L** = 2-(dicyclohexylphosphino)biphenyl. [g] **L** = 2-(dicyclohexylphosphino)-2',6'-dimethoxybiphenyl.

Finally, the coupling reaction was carried out using 2- arylated pyrrolyl anions. Because they resulted in complete reactions, aryl bromides were again used to illustrate the usefulness of the reaction. In addition, higher reaction temperatures and catalyst loadings (relative to the unsubstituted pyrrolyl anion) were employed to facilitate the conversion. Results of the completed reactions are tabulated in Table 3.

Table 3. Synthesis of 5-aryl-2-(2'-methoxyphenyl)pyrroles.[a]



Ar = 2-methoxyphenyl

Entry	Rxn time	Product	Yield (%)
1[b]	17 hrs.		82
2[c]	24 hrs.		83
3[d]	54 hrs.		92

[a] [ArBr] = 0.34M; 1.5 equiv [Na^+ Pyr^-]/$ZnCl_2$. [b] [ArBr] = 0.5M; 2.0 equiv [Na^+ Pyr^-]/ $ZnCl_2$. [c] **L** = 2-(di-*tert*-butylphosphino)biphenyl. [d] **L** = 2-(di-*tert*-butylphosphino)-2'-dimethylaminobiphenyl. [e] **L** = 2-(dicyclohexyl-phosphino)biphenyl.

While the reported examples were observed to proceed without difficulty, several other reactions were less successful in their initial attempts and were not optimized. Some of the more problematic substituted pyrrolyl anion/aryl halide combinations include 2,4-dimethylpyrrolylsodium with 3-bromoquinoline; 2,4-dimethylpyrrolylsodium with 2-chloroanisole and 4-n-butyl-chlorobenzene;

3-methylpyyrolylsodium with 2-chloroanisole; 2-phenylpyrrolylsodium with 4-bromotoluene and 1-bromo-3,5-bis(trifluoromethyl)benzene; 2-mesitylpyrrolylsodium with 1-chloro-3,5-dimethoxybenzene and 2-chloroanisole; 2-anisolylpyrrolylsodium with 4-n-butyl-chlorobenzene and 1-chloro-3,5-dimethoxybenzene.

References

1. See Reference 5, Chapter 1 Introduction.
2. a) Morita, D.K.; Stille, J.K.; Norton, J.R. *J. Am. Chem. Soc.* **1995**, *117*, 8576-8581. b) A recent review: Littke, A.F.; Fu, G.C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176-4211.
3. In most cases, the principle undesired byproducts were determined by GC-MS to be the *N*-substituted product and biaryl.

Conclusion

A versatile and effective method for arylating pyrroles has been explored and shown to be useful for a broad variety of organic substrates that differ in terms of steric and electronic considerations. Unsubstituted pyrrolyl anions can couple with aryl bromides, chlorides, and iodides in the presence of a palladium catalyst (typically 0.5 mol% Pd) at temperatures between 60-100°C in order to generate the respective 2-arylpyrroles in good yield (typically >70%). Methylated and arylated pyrrolyl anions have been shown to behave similarly (typical yields >60%) upon reaction with aryl bromides despite requiring a higher reaction temperature (100°C) and catalyst loading (5.0 mol% Pd). These results represent an important advance in Pd-catalyzed C-C bond formation that could be useful in the assembly of sterically demanding chelate ligands, natural products, or industrial products.

Experimental

General considerations: Unless stated otherwise, all synthetic experimentation was carried out using Schlenk techniques under an argon atmosphere, or in an Innovative Technologies glovebox under a nitrogen atmosphere. Reactions were carried out in flame-dried glassware cooled under vacuum. Anhydrous hexanes and THF, inhibitor-free, were purchased from Aldrich in 18 L Pure-Pac™ solvent kegs, and sparged vigorously with argon for 40 minutes prior to first use. Hexanes were further purified by passage through one column of neutral alumina and one column of copper(II) oxide; THF, by passage through two columns of neutral alumina and one column of activated 4Å molecular sieves. 1,4-Dioxane, anhydrous, was purchased from Aldrich in Sure-Seal™ bottles and used as received.

Iodobenzene, 3-bromoquinoline, 2-chloroanisole, and 1-bromo-4-*tert*-butylbenzene were purchased from Aldrich and were either filtered through alumina (EM Science, 80-325 mesh) or stored over 3Å molecular sieves prior to use. Palladium acetate, 4-bromotoluene, and 2,4-dimethylpyrrole were purchased from Aldrich and used as received. Sodium hydride (60% dispersion in mineral oil) was purchased from Aldrich. For in situ deprotonation of pyrroles (see General Procedure B, below) it was used as received. For all other reactions, it was washed free of mineral oil with anhydrous hexanes under inert atmosphere, and dried in vacuo. Pyrrole was purchased from Aldrich, stored over 3Å molecular sieves, and sparged for 20 min with argon prior to each use. 2-Bromomesitylene was purchased from Acros Chemical company and filtered through alumina (EM Science, 80-325 mesh) prior to use. 3,5-Dimethoxychlorobenzene was purchased from Acros Chemical company and was used as received. 1-Bromo-2,4,6-triisopropylbenzene was purchased from Avocado Chemical company and filtered through

alumina (EM Science, 80-325 mesh) prior to use. 4-Bromo-*N,N*-dimethylaniline was purchased from Avocado Chemical company and used as received. 1-Chloro-4-(*n*-butyl)benzene was purchased from Lancaster Chemical company and filtered through alumina (EM Science, 80-325 mesh) prior to use. 3,5-bis(trifluoromethyl)bromobenzene was purchased from Oakwood Products and was filtered through alumina (EM Science, 80-325 mesh) prior to use. Anhydrous zinc chloride beads were purchased from Alfa Aesar and used as received. 3-Methylpyrrole was purchased from TCI and used as received. 2-(Di-*tert*-butylphosphino)-biphenyl, 2-(dicyclohexylphosphino)biphenyl, 2-(dicyclohexyl-phosphino)-2'-methylbiphenyl, 2-(di-*tert*-butylphosphino)-2'-(*N,N*-dimethylamino)biphenyl, 2-dicyclohexylphosphino-2'-(*N,N*-dimethylamino)biphenyl, 2-(dicyclohexylphosphino)-2',6'-dimethoxybiphenyl, and Pd_2dba_3 were purchased from Strem Chemical company and used as received. Ethyl acetate (HPLC grade) and diethyl ether (Reagent ACS grade) were used as received from Mallinckrodt. Hexanes for chromatography (HPLC grade) were used as received from Burdick & Jackson. Silica gel (230-400 mesh), Celite, and pentane (HPLC grade) were used as received from EMD Chemicals, Inc.. TLC plates (Silica Gel 60, F_{254}), alumina (80-325 mesh), and magnesium sulfate (anhydrous) were purchased from EM Science.

IR spectra were recorded on a Perkin-Elmer 2000 series FT-IR as KBr pellets. $CDCl_3$ and acetone-d_6 (Cambridge Isotope Laboratories) were used as received. ^{1}H NMR spectra were recorded on Varian 300 MHz and Varian 500 MHz instruments, with shifts reported relative to the residual solvent peak. ^{13}C NMR spectra were recorded on a Varian 500 MHz instrument, with shifts reported relative to the residual solvent peak. ^{19}F NMR spectra were recorded on a Varian 300 MHz instrument, with shifts reported relative to external $CFCl_3$. Gas chromatographic analyses were performed on an Agilent Technologies Model 5973N Gas

chromatograph/Mass spectrometer equipped with an Rtx-1 column. Melting points, uncorrected, were measured using Mel-Temp II instruments. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA.

All reported yields represent an average of two independent runs in which product was isolated in $\geq$ 95% purity as judged by a combination of ^{1}H NMR and GC-MS. Characterization data were determined from a single run with isolated yields.

General procedure for the deprotonation of pyrroles: In a nitrogen glovebox, NaH (2 equiv) was placed in a pear-shaped Schlenk flask, which was capped with a septum and removed from the glovebox. The flask was then connected to a Schlenk line, placed under vacuum for 30 min, and back-filled with argon. THF (anhydrous, 10–20 mL) was added via syringe. With a mercury bubbler open to relieve excess H_2 pressure, the pyrrole was added dropwise via syringe. (In the case of 2-(2'-methoxyphenyl)pyrrole, a solution in anhydrous THF was prepared under argon and transferred via cannula to the NaH suspension.) After several hours, excess NaH was removed by Schlenk-filtration under an argon atmosphere. The filtrate was concentrated and dried in vacuo for roughly 12 hours, affording the pyrrolylsodium as a light-colored solid (yield typically >90%), which was stored in the glovebox.

Procedures for palladium-catalyzed cross-coupling:

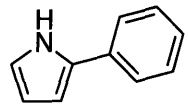
General Procedure A: In a nitrogen glovebox, the pyrrolylsodium and $ZnCl_2$ were weighed and transferred to a resealable 15-mL Schlenk tube containing a magnetic stirbar. The tube was then capped with a Teflon screwcap, removed from the glovebox, and connected to a Schlenk line. The atmosphere of the tube was evacuated, and replaced with argon. The Teflon screwcap was replaced under a flow of argon with a rubber septum. THF was added, via

syringe; the septum was replaced with the Teflon screwcap, and the reaction mixture was stirred magnetically for about 10 minutes. The screwcap was removed under a flow of argon, which was then halted while the solid palladium precatalyst and phosphine supporting ligand, weighed out under air, were added as quickly as possible. The tube was then fitted with a septum and a needle extending below the tube neck, and purged under a flow of argon for about 5 min. The aryl halide, if liquid, was then added via syringe, and the septum and needle were replaced with the Teflon screwcap. Solid aryl halides were added in the same manner as the precatalyst and ligand, and the tube was purged as before for 5 minutes prior to capping. The reaction vessel was then heated in an oil bath as described in the individual entries.

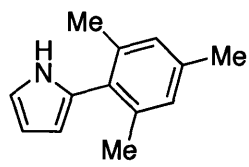
General procedure B: NaH dispersion was weighed out in air and placed in a 15-mL resealable Schlenk tube, equipped with a Teflon screwcap and magnetic stirbar and connected to a Schlenk line. The atmosphere in the tube was evacuated, and replaced with argon; the screwcap was removed under a flow of argon and replaced with a rubber septum. THF (~0.5 mL) was added via syringe, followed by pyrrole. The septum was replaced with the Teflon screwcap, left slightly open to allow relief of H_2 pressure through the Schlenk line and a mercury bubbler. After the effervescence had ceased (several hours), the screwcap was replaced under a flow of argon with a rubber septum, and a solution of $ZnCl_2$ (anhydrous, 0.50 M in THF)[1] was added via syringe. Roughly 10 minutes later, the palladium precatalyst and phosphine ligand were added, and the tube was purged, as described in Procedure A. The aryl halide was then added as described in procedure A. The reaction vessel was then capped with a Teflon screwcap and heated in an oil bath as described in the individual entries.

General procedure for workup: After the reaction was complete, the reaction mixture was cooled to room temperature. The tube was opened, and Et_2O (~10 mL) and water (~10 mL) were

added. The resulting mixture was transferred to a separatory funnel, and the phases were separated. The aqueous layer was extracted with Et_2O (2 x 5 mL); the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel.

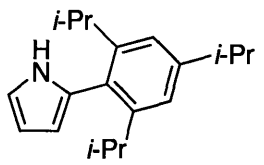


2-Phenyl-1H-pyrrole. General procedure A was followed using iodobenzene (0.112 mL, 1.00 mmol), pyrrolylsodium (0.267 g, 3.00 mmol), $ZnCl_2$ (0.409 g, 3.00 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(di-*tert*-butylphosphino)biphenyl (1.5 mg, 0.005 mmol, 0.50 mol %), and THF (1 mL). The reaction was run for 21 hours at 100 °C. Standard workup and isolation, using 95:5 hexanes:ethyl acetate as eluant, afforded the title compound as a light red solid, 0.129 g (91%): mp 128-130 °C (lit.[2] 129–130 °C); ^{1}H NMR (500 MHz, acetone-d_6) δ 10.67 (br s, 1 H), 7.62 (d, J = 7.6 Hz, 2 H), 7.32 (t, J = 7.6 Hz, 2 H), 7.13 (t, J = 7.3 Hz, 1 H), 6.84 (m, 1 H), 6.51 (m, 1 H), 6.15 (m, 1 H); ^{13}C NMR (500 MHz, acetone-d_6) δ 134.4, 132.6, 129.6, 126.4, 124.4, 120.0, 110.0, 106.5; IR (KBr, cm^{-1}) 3432, 3393, 3038, 1604, 1496, 1466, 757, 718, 691. Anal. Calcd for $C_{10}H_9N$: C, 83.88; H, 6.34. Found: C, 84.07; H, 6.34.

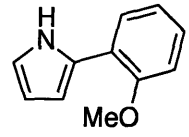


2-(2',4',6'-Trimethylphenyl)-1H-pyrrole.[3] General procedure A was followed, except for the use of a 50-mL resealable Schlenk tube as the reaction vessel, using 2-bromomesitylene (1.25 mL, 8.17 mmol), pyrrolylsodium (2.320 g, 26.0 mmol), $ZnCl_2$ (3.560 g, 26.1 mmol), Pd_2dba_3 (18.7 mg, 0.020 mmol, 0.25 mol %), 2-(di-*tert*-butylphosphino)biphenyl (12.2 mg, 0.041 mmol,

0.50 mol %), and THF (20 mL). The reaction was run for 44 hours at 100 °C. Standard workup and isolation, using 90:10 hexanes:ethyl acetate as eluant, afforded the title compound as a pale pink solid, 1.360 g (90%): mp 99–100 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (br s, 1 H), 6.95 (s, 2 H), 6.86 (m, 1 H), 6.32 (m, 1 H), 6.07 (m, 1 H), 2.33 (s, 3 H), 2.14 (m, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 138.8, 137.8, 130.9, 129.7, 128.3, 117.0, 108.6, 108.4, 21.3, 20.7; IR (KBr, cm^{-1}) 3375, 2968, 2916, 1455, 1099, 1025, 852, 794, 576. Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16. Found: C, 84.31; H, 8.26.



2-(2',4',6'-Triisopropylphenyl)-1H-pyrrole. General procedure A was followed using 1-bromo-2,4,6-triisopropylbenzene (0.180 mL, 1.00 mmol), pyrrolylsodium (0.356 g, 4.00 mmol), $ZnCl_2$ (0.546 g, 4.00 mmol), Pd_2dba_3 (18.0 mg, 0.020 mmol, 2.0 mol %), 2-(dicyclohexylphosphino)biphenyl (14.6 mg, 0.042 mmol, 4.0 mol %), and THF (1 mL). The reaction was run for 41 hours at 100 °C. Standard workup and isolation, using 95:5 hexanes:ethyl acetate as eluant, afforded the title compound as a pale brown solid, 0.189 g (70%): mp 143–144 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (br s, 1 H), 7.08 (s, 2 H), 6.86 (m, 1 H), 6.33 (m, 1 H), 6.11 (m, 1 H), 2.97 (sept, J = 6.8 Hz, 1 H), 2.75 (sept, J = 6.8 Hz, 2 H), 1.33 (d, J = 6.8 Hz, 6 H), 1.16 (d, J = 6.8 Hz, 12 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 149.8, 149.4, 129.2, 128.9, 120.8, 116.8, 109.2, 108.5, 34.6, 30.8, 24.8, 24.3; IR (KBr, cm^{-1}) 3424, 2960, 2925, 2866, 1458, 882, 721. Anal. Calcd for $C_{19}H_{27}N$: C, 84.70; H, 10.10. Found: C, 84.38; H, 10.10.



2-(2'-Methoxyphenyl)-1H-pyrrole. General procedure A was followed using 2-chloroanisole (0.127 mL, 1.000 mmol), pyrrolylsodium (0.267 g, 3.00 mmol), $ZnCl_2$ (0.409 g, 3.00 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(di-*tert*-butylphosphino)biphenyl (1.5 mg, 0.005 mmol, 0.5 mol %), and THF (1 mL). The reaction was run for 25 hours at 60 °C. Standard workup and isolation, using 80:20 hexanes:ethyl acetate as eluant, afforded the title compound as a light yellow solid, 0.157 g (91%): mp 65–66 °C (lit.[4] 66–67 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.90 (br s, 1 H), 7.77 (dd, J = 7.8 Hz and 1.7 Hz, 1 H), 7.24 (distorted td, J = 7.8 Hz and 1.7 Hz, 1 H), 7.08 (distorted td, J = 7.8 Hz and 0.6 Hz, 1 H), 7.03 (d, J = 8.4 Hz, 1 H), 6.94–6.96 (m, 1 H), 6.73–6.75 (m, 1 H), 6.39–6.41 (m, 1 H), 4.00 (s, 3 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 154.8, 129.9, 126.8, 126.7, 121.5, 121.2, 117.9, 111.7, 108.9, 106.2, 55.7; IR (KBr, cm^{-1}) 3443, 1493, 1235, 1112, 1023, 754, 726.

Note: We have been unable to obtain satisfactory elemental analyses for this compound. The ^{1}H and ^{13}C NMR spectra are reproduced below as a measure of purity.

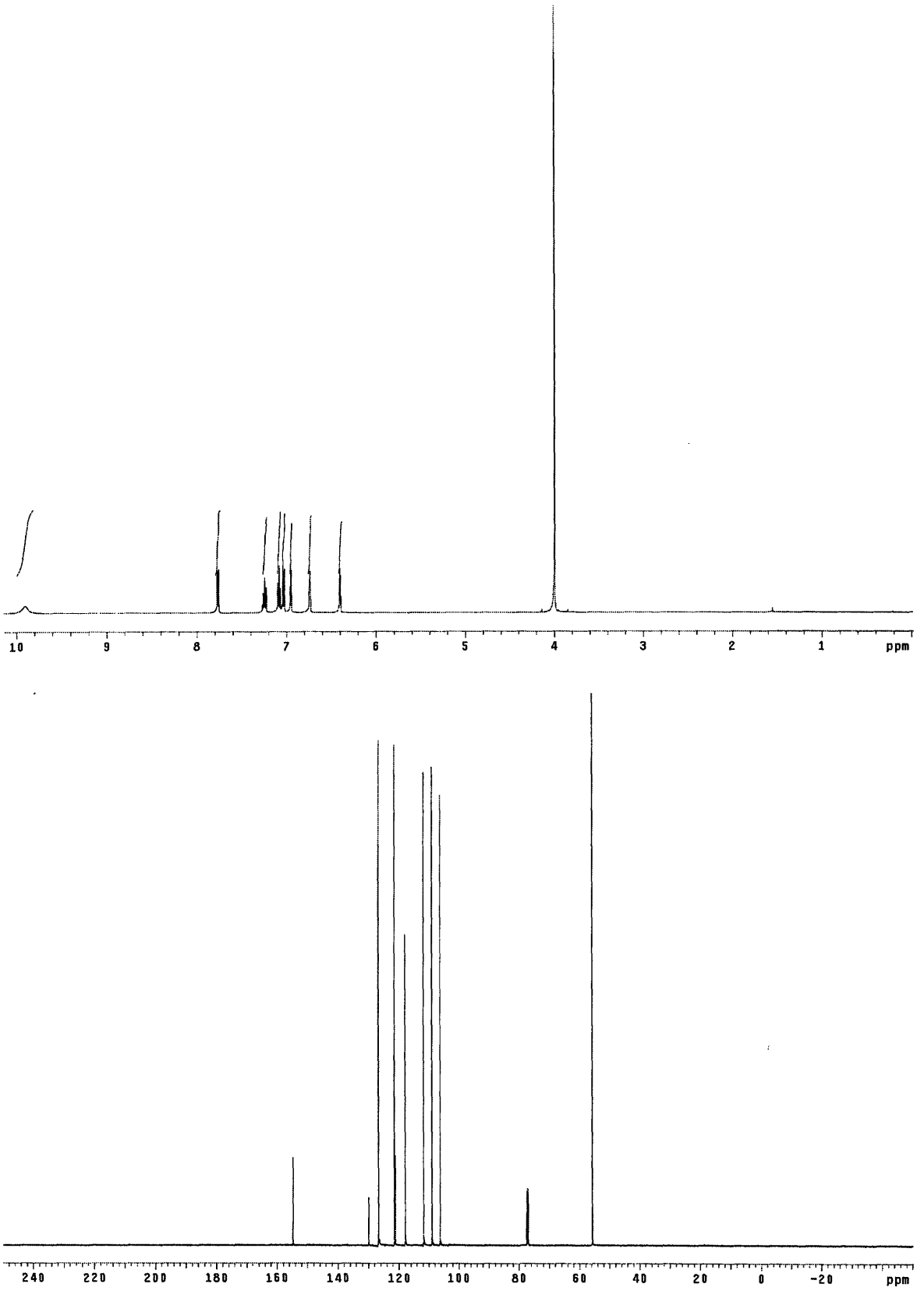
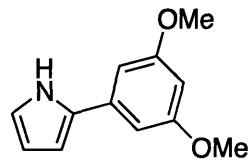
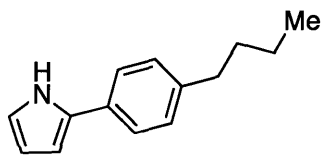


Figure S1. ^{1}H and ^{13}C NMR of 2-(2'-methoxyphenyl)-1H-pyrrole in $CDCl_3$.

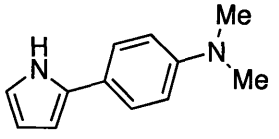


2-(3',5'-Dimethoxyphenyl)-1H-pyrrole. General procedure A was followed using 3,5-dimethoxychlorobenzene (0.173 g, 1.00 mmol), pyrrolylsodium (0.142 g, 1.60 mmol), $ZnCl_2$ (0.218 g, 1.60 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(di-*tert*-butylphosphino)biphenyl (1.5 mg, 0.005 mmol, 0.5 mol %), and THF (1 mL). The reaction was run for 23 hours at 60 °C. Standard workup and isolation, using 80:20 hexanes:ethyl acetate as eluant, afforded the title compound as a pale orange solid, 0.159 g (78%): mp 77–78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (br s, 1 H), 6.86 (s, 1 H), 6.64 (s, 2 H), 6.53 (m, 1 H), 6.36 (m, 1 H), 6.31 (m, 1 H), 3.84 (s, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 161.4, 134.9, 132.2, 119.1, 110.2, 106.5, 102.5, 98.4, 55.6; IR (KBr, cm^{-1}) 3398, 1597, 1475, 1247, 1195, 1156, 1063, 835, 718. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45. Found: C, 70.54; H, 6.44.



2-(4'-*n*-Butylphenyl)-1H-pyrrole. General procedure A was followed using 4-(*n*-butyl)-chlorobenzene (0.169 mL, 1.00 mmol), pyrrolylsodium (0.142 g, 1.60 mmol), $ZnCl_2$ (0.218 g, 1.60 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(di-*tert*-butylphosphino)biphenyl (1.5 mg, 0.005 mmol, 0.5 mol %), and THF (1 mL). The reaction was run for 16 hours at 60 °C. Standard workup and isolation, using 95:5 hexanes:ethyl acetate as eluant, afforded the title compound as an amorphous brown-orange solid, 0.136 g (68%): mp 104–107 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (br s, 1 H), 7.42 (d, J = 8.1 Hz, 2 H), 7.22 (d, J = 8.1 Hz, 2 H), 6.85 (d, J = 1.2 Hz, 1 H), 6.54 (s, 1 H), 6.34 (q, J = 2.8 Hz, 1 H), 2.66 (t, J = 7.6 Hz, 2 H), 1.67

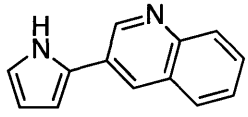
(quint, J = 7.6 Hz, 2 H), 1.43 (sext, J = 7.3 Hz, 2 H), 1.00 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 141.1, 132.4, 130.4, 129.1, 124.0, 118.7, 110.1, 105.5, 35.5, 33.8, 22.6, 14.2; IR (KBr, cm^{-1}) 3432, 2958, 2928, 2857, 1509, 1458, 1034, 794, 713. Anal. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60. Found: C, 84.29; H, 8.69.



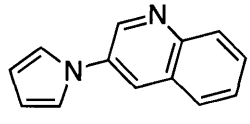
2-(4'-Dimethylaminophenyl)-1H-pyrrole.

General procedure A: followed using 4-bromo-*N,N*-dimethylaniline (0.200 g, 1.00 mmol), pyrrolylsodium (0.142 g, 1.60 mmol), $ZnCl_2$ (0.218 g, 1.60 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(di-*tert*-butylphosphino)biphenyl (1.5 mg, 0.005 mmol, 0.5 mol %), and THF (1 mL). The reaction was run for 19 hours at 60 °C. Standard workup and isolation, using 50:50 hexane:diethyl ether as eluant, afforded the title compound as a light yellow solid (which after several hours' exposure to air forms a dark blue-violet material), 0.096 g (52%).

General procedure B: followed using pyrrole (0.111 mL, 1.6 mmol), NaH (60% dispersion in mineral oil, 0.060 g, 1.5 mmol), $ZnCl_2$ solution (0.50 M in THF, 3.2 mL, 1.6 mmol), and the same quantities of aryl bromide, precatalyst and ligand as in Procedure A. The reaction was allowed to run for 17 hours at 60 °C; isolation and purification as described above afforded 0.110 g (60%) of the title compound: mp 167–169 °C (dec.) (lit.[5] 160 °C, dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (br s, 1 H), 7.38 (d, J = 8.8 Hz, 2 H), 6.76 (d, J = 8.8 Hz, 2 H), 6.81 (m, 1 H), 6.37 (m, 1 H), 6.28 (m, 1 H), 2.98 (s, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 149.4, 133.1, 125.3, 122.0, 117.7, 113.1, 109.9, 104.1, 40.8; IR (KBr, cm^{-1}) 3421, 2879, 2798, 1615, 1517, 818. Anal. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58. Found: C, 77.13; H, 7.36.

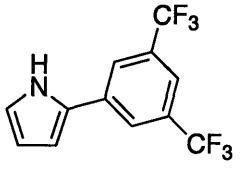


2-(3'-Quinolyl)-1H-pyrrole. General procedure A was followed using 3-bromoquinoline (0.136 mL, 1.00 mmol), pyrrolylsodium (0.142 g, 1.60 mmol), $ZnCl_2$ (0.218 g, 1.60 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(Di-*tert*-butylphosphino)biphenyl (1.5 mg, 0.005 mmol, 0.5 mol %), and THF (1 mL). The reaction was run for 18 hours at 100 °C. Standard workup and isolation, using 50:50 hexanes:ethyl acetate as eluant, afforded the title compound as a yellow solid, 0.142 g (73%): mp 172–173 °C (lit.[6] 174–175 °C); ^{1}H NMR (500 MHz, acetone-d_6) δ 10.90 (br s, 1 H), 9.27 (d, J = 1.8 Hz, 1 H), 8.39 (d, J = 1.8 Hz, 1 H), 8.00 (d, J = 8.2 Hz, 1 H), 7.86 (d, J = 8.2 Hz, 1 H), 7.64 (td, J = 7.7 Hz and 1.5 Hz, 1 H), 7.54 (td, J = 7.6 Hz and 1.2 Hz, 1 H), 7.02 (m, 1 H), 6.83 (m, 1 H), 6.28 (m, 1 H); ^{13}C NMR (500 MHz, acetone-d_6) δ 148.9, 147.5, 130.1, 129.7, 129.3, 129.1, 128.6, 128.0, 127.9, 127.5, 121.5, 110.8, 108.3; IR (KBr, cm^{-1}) 3092 (broad), 1617, 1561, 1497, 1477, 1425, 1125, 1114, 780, 711. Anal. Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19. Found: C, 80.27; H, 5.35.



***N*-(3'-Quinolyl)pyrrole.** General procedure A was followed using 3-bromoquinoline (0.136 mL, 1.00 mmol), pyrrolylsodium (0.142 g, 1.60 mmol), $ZnCl_2$ (0.218 g, 1.60 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(dicyclohexylphosphino)biphenyl (1.8 mg, 0.005 mmol, 0.5 mol %), and THF (1 mL). The reaction was run for 16 hours at 60 °C. Standard workup and

isolation, using 80:20 hexanes:ethyl acetate as eluant, afforded the title compound as a pale yellow solid, 0.133 g (69%): mp 86–87 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (d, J = 2.6 Hz, 1 H), 8.14 (dd, J = 8.5 Hz and 0.4 Hz, 1 H), 8.02 (d, J = 2.6 Hz, 1 H), 7.82 (dd, J = 8.1 Hz and 0.5 Hz, 1 H), 7.69 (dtd, J = 7.7 Hz and 1.5 Hz and 1.5 Hz, 1 H), 7.58 (dtd, J = 7.5 Hz and 1.3 Hz and 1.2 Hz, 1 H), 7.22 (t, J = 2.1 Hz, 2 H), 6.46 (t, J = 2.1 Hz, 2 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 146.4, 144.7, 134.1, 129.5, 129.1, 128.1, 127.8, 127.6, 124.7, 119.6, 111.7; IR (KBr, cm^{-1}) 3128, 3103, 1494, 1356, 1300, 734. Anal. Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19. Found: C, 80.16; H, 5.09.

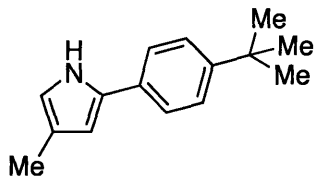


2-[3',5'-bis(trifluoromethyl)phenyl]-1H-pyrrole.

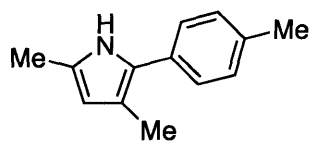
General procedure A: followed using 3,5-bis(trifluoromethyl)bromobenzene (0.172 mL, 1.00 mmol), pyrrolylsodium (0.267 g, 3.00 mmol, 3.0 equivalents), $ZnCl_2$ (0.409 g, 3.00 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), 2-(dicyclohexylphosphino)biphenyl (1.8 mg, 0.005 mmol, 0.5 mol %), and THF (1 mL). The reaction was run for 18 hours at 80 °C. Standard workup and isolation, using 90:10 hexanes:ethyl acetate as eluant, afforded the title compound as a pale yellow solid, 0.263 g (94%).

General procedure B: followed using pyrrole (0.139 mL, 2.0 mmol), NaH (60% dispersion in mineral oil, 0.080 g, 2.0 mmol), $ZnCl_2$ solution (0.50 M in THF, 4.0 mL, 2.0 mmol), and the same quantities of aryl bromide, precatalyst and ligand as in Procedure A. The reaction was allowed to run for 25 hours at 80 °C. Isolation and purification as described above afforded 0.202 g (72%) of the title compound: mp 64–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58

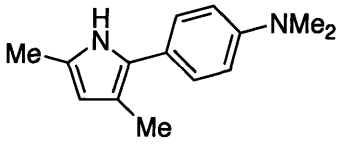
(br s, 1 H), 7.85 (s, 2 H), 7.68 (s, 1 H), 6.97 (m, 1 H), 6.69 (m, 1 H), 6.37 (m, 1 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 134.8, 132.4 (q, J = 33.2 Hz), 129.4, 123.6 (q, J = 272.8 Hz), 123.5, 121.1, 119.4 (m, J = 3.8 Hz), 111.2, 108.8; ^{19}F NMR (300 MHz, $CDCl_3$) δ –63.4; IR (KBr, cm^{-1}) 3489, 3395, 1474, 1375, 1284, 1186, 1123, 1068, 895, 884, 744, 734, 705, 684. Anal. Calcd for $C_{12}H_7F_6N$: C, 51.63; H, 2.53. Found: C, 51.74; H, 2.42.



2-(4'-*tert*-Butylphenyl)-4-methyl-1H-pyrrole.[7] General procedure A was followed using 4-*tert*-butyl-bromobenzene (0.087 mL, 0.50 mmol), 3-methylpyrrolylsodium (0.083 g, 0.80 mmol), $ZnCl_2$ (0.109 g, 0.800 mmol), Pd_2dba_3 (11.5 mg, 0.013 mmol, 2.5 mol %), 2-(di-*tert*-butylphosphino)biphenyl (7.5 mg, 0.025 mmol, 5.0 mol %), and THF (1 mL). The reaction was run for 43 hours at 100°C. Standard workup and isolation, using 90:10 hexanes:ethyl acetate as eluant, afforded the title compound as a green solid, 0.071 g (67%): mp 93–100 °C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (br s, 1 H), 7.40 (s, 4 H), 6.62 (m, 1 H), 6.36 (m, 1 H), 2.19 (s, 3 H), 1.37 (s, 9 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 149.2, 132.3, 130.4, 125.9, 123.7, 120.7, 116.6, 107.2, 34.7, 31.5, 12.2; IR (KBr, cm^{-1}) 3457, 2962, 1523, 1435, 1113, 835, 799, 559. Anal. Calcd for $C_{15}H_{19}N$: C, 84.46; H, 8.98. Found: C, 84.43; H, 8.60.

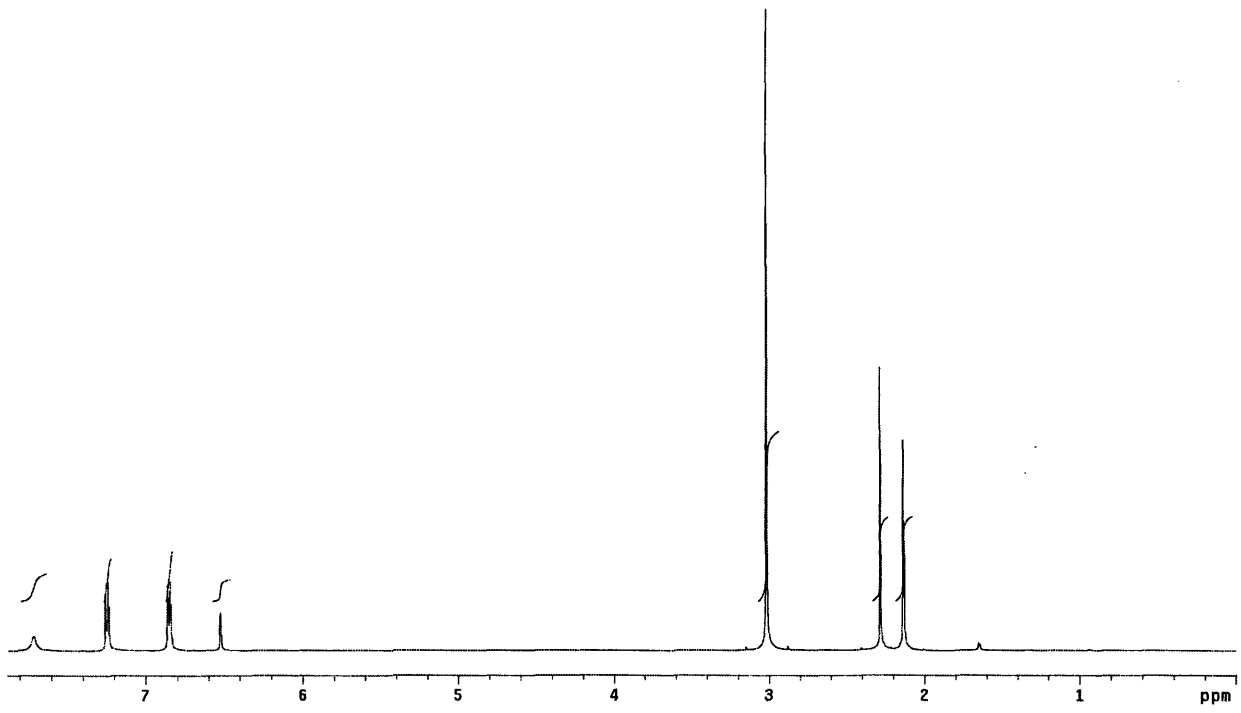


2-(*p*-Tolyl)-3,5-dimethyl-1H-pyrrole. General procedure A was followed using 4-bromotoluene (0.222 g, 1.30 mmol), 2,4-dimethylpyrrolylsodium (0.300 g, 2.56 mmol), $ZnCl_2$ (0.348 g, 2.55 mmol), $Pd(OAc)_2$ (14.4 mg, 0.064 mmol, 5.0 mol %), 2-(Dicyclohexylphosphino)biphenyl (22.2 mg, 0.063 mmol, 5.0 mol %), and 1,4-dioxane (1 mL). The reaction was run for 37 hours at 100 °C. Standard workup and isolation, using 75:25 hexanes:ethyl acetate as eluant, afforded the title compound as a dark red solid, 0.151 g (63%): mp 34–35 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (br s, 1 H), 7.30 (d, J = 8.2 Hz, 2 H), 7.21 (d, J = 8.6 Hz, 2 H), 5.84 (m, 1 H), 2.38 (s, 3 H), 2.30 (s, 3 H), 2.24 (s, 3 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 135.4, 131.2, 129.5, 127.3, 127.0, 126.1, 116.1, 110.3, 21.3, 13.2, 12.6; IR (KBr, cm^{-1}) 3416, 2920, 1528, 1259, 821, 789, 551. Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16. Found: C, 84.28; H, 8.12.



2-(4'-Dimethylaminophenyl)-3,5-dimethylpyrrole. General procedure A was followed using 4-bromo-*N,N*-dimethylaniline (0.086 g, 0.43 mmol), 2,4-dimethylpyrrolylsodium (0.100 g, 0.850 mmol), $ZnCl_2$ (0.116 g, 0.850 mmol), $Pd(OAc)_2$ (4.8 mg, 0.021 mmol, 5.0 mol %), 2-(di-*tert*-butylphosphino)-biphenyl (6.4 mg, 0.021 mmol, 5.0 mol %), and THF (1 mL). The reaction was run for 17 hours at 100 °C. Standard workup and isolation, using 80:20 hexanes:ethyl acetate as eluant, afforded the title compound as a dark red solid, 0.070 g (76%): mp 104–105 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (br s, 1 H), 7.21 (d, J = 8.9 Hz, 2 H), 6.81 (d, J = 8.9 Hz, 2 H), 6.51 (s, 1 H), 2.98 (s, 6 H), 2.26 (s, 3 H), 2.09 (s, 3 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 148.7, 130.6, 124.9, 124.4, 121.4, 118.1, 113.6, 112.7, 41.0, 12.4, 11.4; IR (KBr, cm^{-1}) 3341, 1616, 1535, 1512, 1351, 819.

Note: We have been unable to obtain satisfactory elemental analyses for this compound. The ^{1}H and ^{13}C NMR spectra are reproduced below as a measure of purity.



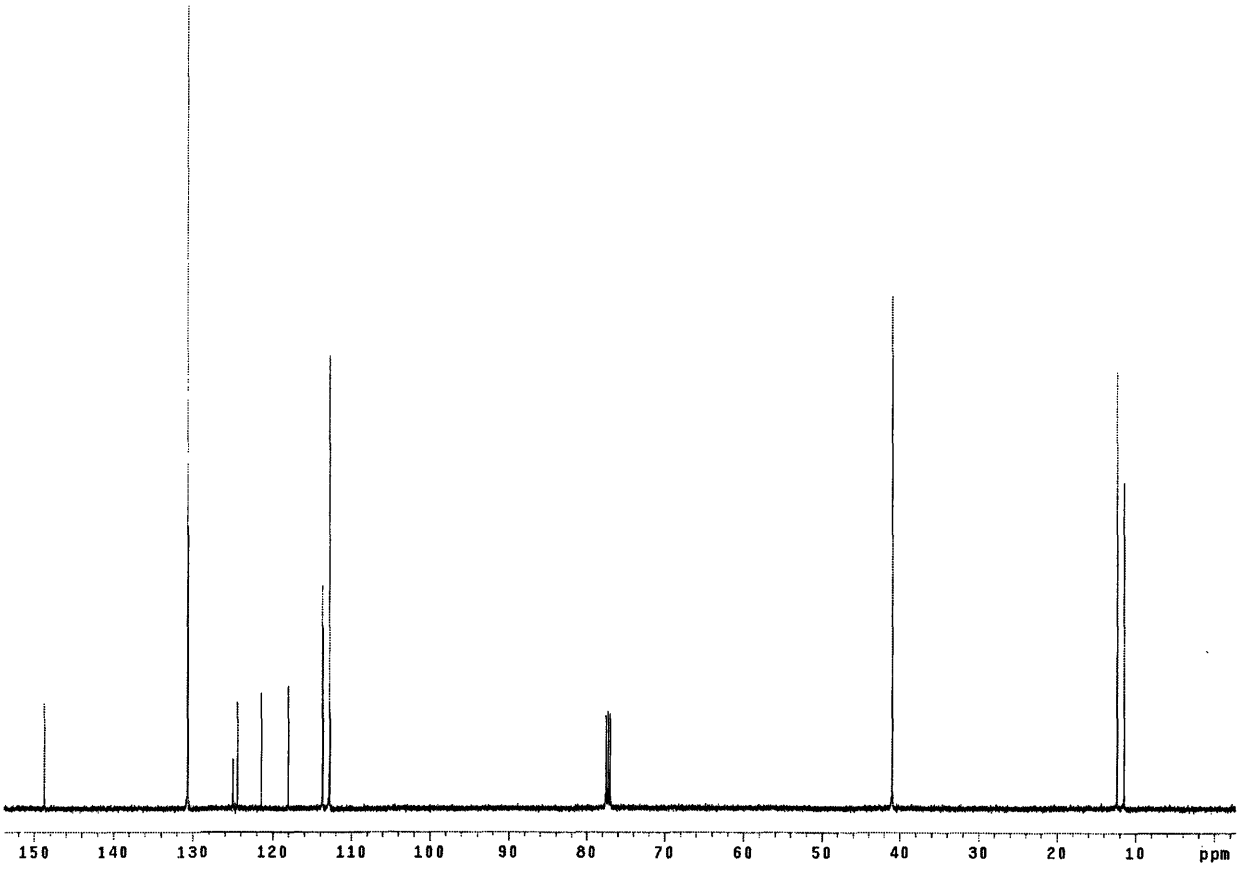
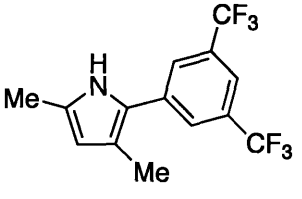
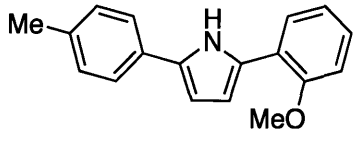


Figure S2. ^{1}H and ^{13}C NMR of 2-(4'-Dimethylaminophenyl)-3,5-dimethylpyrrole in $CDCl_3$.

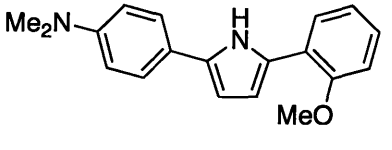


2-[3,5-bis(trifluoromethyl)phenyl]-3,5-dimethyl-1H-pyrrole. General procedure A was followed using 3,5-bis(trifluoromethyl)bromobenzene (0.296 mL, 1.72 mmol), 2,4-dimethylpyrrolylsodium (0.400 g, 3.410 mmol), $ZnCl_2$ (0.464 g, 3.4000 mmol), $Pd(OAc)_2$ (19.2 mg, 0.085 mmol, 5.0 mol %), 2-(dicyclohexylphosphino)-2',6'-dimethoxy-1,1'-biphenyl (35.2 mg, 0.085 mmol, 5.0 mol %), and THF (4 mL). The reaction was run for 54 hours at 100 °C. Standard workup and isolation, using 90:10 hexanes:ethyl acetate as eluant, afforded the title compound as a red solid, 0.370 g (70%): mp 45–46 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (br s,

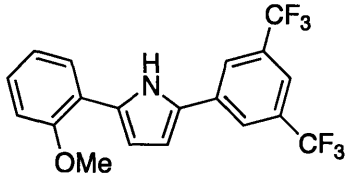
1 H), 7.78 (s, 2 H), 7.66 (s, 1 H), 5.89 (s, 1 H), 2.33 (s, 3 H), 2.27 (s, 3 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 135.9, 132.3 (q, J = 33.0 Hz), 130.0, 125.2, 124.2, 123.7 (q, J = 272.9 Hz), 119.8, 118.5 (m, J = 3.9 Hz), 111.7, 13.2, 12.8; ^{19}F NMR (300 MHz, $CDCl_3$) δ –63.4; IR (KBr, cm^{-1}) 3490, 1367, 1279, 1171, 1130, 1089. Anal. Calcd for $C_{14}H_{11}F_6N$: C, 54.73; H, 3.61. Found: C, 54.82; H, 3.63.



2-(2'-Methoxyphenyl)-5-(*p*-tolyl)-1H-pyrrole. General procedure A was followed using 4-bromotoluene (0.058 g, 0.34 mmol), 2-(2'-methoxyphenyl)pyrrolylsodium (0.100 g, 0.513 mmol), $ZnCl_2$ (0.070 g, 0.51 mmol), $Pd(OAc)_2$ (3.8 mg, 0.017 mmol, 5.0 mol %), 2-(di-*tert*-butylphosphino)-2'-(*N,N*-dimethylamino)biphenyl (5.8 mg, 0.017 mmol, 5.0 mol %), and THF (1 mL). The reaction was run for 24 hours at 100 °C. Standard workup and isolation, using 75:25 hexanes:ethyl acetate as eluant, afforded the title compound as a pale orange solid, 0.070 g (78%): mp 101–103 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 10.38 (br s, 1 H), 7.70 (dd, J = 7.8 Hz and 1.7 Hz, 1 H), 7.55 (d, J = 8.1 Hz, 2 H), 7.18 (m, 2 H), 7.10 (d, J = 8.2 Hz, 1 H), 6.98 (td, J = 7.5 Hz and 1.1 Hz, 2 H), 6.68 (m, 1 H), 6.55 (m, 1 H), 4.01 (s, 3 H), 2.32 (s, 3 H); ^{13}C NMR (500 MHz, acetone-d_6) δ 156.1, 136.2, 132.9, 131.3, 131.1, 130.3, 127.7, 127.2, 124.5, 122.2, 121.9, 112.6, 109.9, 107.1, 56.0, 21.4; IR (KBr, cm^{-1}) 3457, 1487, 1258, 1232, 779, 745. Anal. Calcd for $C_{18}H_{17}NO$: C, 82.10; H, 6.51. Found: C, 82.17; H, 6.53.



2-(2'-Methoxyphenyl)-5-(4'-dimethylaminophenyl)-1H-pyrrole. General procedure A was followed using 4-bromo-*N,N*-dimethylaniline (0.068 g, 0.34 mmol), 2-(2'-methoxyphenyl)pyrrolylsodium (0.100 g, 0.513 mmol), $ZnCl_2$ (0.070 g, 0.513 mmol), $Pd(OAc)_2$ (3.8 mg, 0.017 mmol, 5.0 mol %), 2-(di-*tert*-butylphosphino)biphenyl (5.0 mg, 0.017 mmol, 5.0 mol %), and THF (1 mL). The reaction was run for 17 hours at 100 °C. Standard workup and isolation, using 70:30 hexanes:ethyl acetate as eluant, afforded the title compound as a red solid, 0.079 g (79%): mp 120–126 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.95 (br s, 1 H), 7.69 (d, J = 7.3 Hz, 1 H), 7.44 (d, J = 8.7 Hz, 2 H), 7.16 (t, J = 7.4 Hz, 1 H), 6.96–7.03 (m, 2 H), 6.80 (d, J = 8.7 Hz, 2 H), 6.67 (m, 1 H), 6.44 (m, 1 H), 4.02 (s, 3 H), 3.00 (br s, 6 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 154.7, 149.4, 132.9, 129.7, 126.5, 126.4, 125.1, 122.1, 121.7, 121.4, 113.2, 111.9, 108.0, 105.0, 56.0, 40.9; IR (KBr, cm^{-1}) 3450, 1491, 1020, 768, 741. Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89. Found: C, 77.78; H, 6.89.



2-[3',5'-bis(trifluoromethyl)phenyl]-5-(2"-methoxyphenyl)-1H-pyrrole. General procedure A was followed using 3,5-bis(trifluoromethyl)bromobenzene (0.086 mL, 0.50 mmol), 2-(2'-methoxyphenyl)-pyrrolylsodium (0.196 g, 1.00 mmol), $ZnCl_2$ (0.138 g, 1.00 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5.0 mol %), 2-(dicyclohexylphosphino)biphenyl (8.8 mg, 0.025 mmol, 5.0 mol %), and THF (1 mL). The reaction was run for 54 hours at 100 °C. Standard workup and isolation, using 90:10 hexanes:ethyl acetate as eluant, afforded the title compound as a pale yellow solid, 0.180 g (93%): mp 127–128 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 10.90 (br s, 1 H), 8.29 (s, 2 H), 7.75 (s, 1 H), 7.71 (dd, J = 7.8 Hz and 1.8 Hz, 1 H), 7.26 (distorted td, J = 7.8

Hz and 1.7 Hz, 1 H), 7.11 (dd, J = 8.3 Hz and 1.1 Hz, 1 H), 6.97–7.03 (m, 2 H), 6.76 (distorted dd, J = 3.9 Hz and 2.5 Hz, 1 H), 3.97 (s, 3 H); ^{13}C NMR (500 MHz, acetone-d_6) δ 206.3, 156.7, 136.3, 133.7, 132.6 (q, J = 32.8 Hz), 129.9, 128.8, 128.0, 124.7 (q, J = 272.4 Hz), 124.4, 121.8, 118.9 (m, J = 4.0 Hz), 112.5, 111.3, 110.8, 56.0; ^{19}F NMR (300 MHz, acetone-d_6) δ –68.1; IR (KBr, cm^{-1}) 3435, 1370, 1279, 1169, 1125, 1092, 756. Anal. Calcd for $C_{19}H_{13}F_6NO$: C, 59.23; H, 3.40. Found: C, 59.34; H, 3.37.

References

1. Prepared from anhydrous $ZnCl_2$, weighed in the glovebox, and anhydrous THF; the resulting solution was stored in a resealable Schlenk tube under argon. Solutions of $ZnCl_2$ in THF may also be purchased commercially (*e.g.* from Aldrich).
2. Rapoport, H.; Look, M. *J. Am. Chem. Soc.* **1953**, *75*, 4605.
3. Reported experimental data collected by Neal P. Mankad. Initial experimentation instrumental in proof of principle was conducted by Elisa Calimano.
4. Xu, Z.; Lu, X. *J. Org. Chem.* **1998,** *63*, 5031.
5. Guizzardi, B.; Mella, M.; Fagnoni, M.; Albini, A. *Tetrahedron* **2000,** *56*, 9383.
6. Ohkura, K.; Seki, K.; Terashima, M.; Kanaoka, Y. *Heterocycles* **1990,** *30*, 957.
7. Reported experimental data collected by Neal P. Mankad.

Chapter 2

The Synthesis of N-Heterocyclic Carbene Copper(I) Complexes Using the 2,4,6, 2”, 4”, 6”-hexaisopropyl-1,1’:3’,1”-Terphenyl Moiety

Introduction

In recent years, N-heterocyclic carbenes (NHCs) have emerged as an important class of ligands in coordination and organometallic chemistry. Their ubiquitous nature has been evidenced by their involvement in a number of reactions – including C-H activation and the formation of C-C, C-H, and C-N bonds – that serve as key steps in targeted catalytic cycles.[1-4] Moreover, these ligands have shown to be versatile, binding not only to metals exhibiting a wide range of oxidation states, but also to main group elements such as sulfur and iodine.[5-7]

The properties of NHCs have compared to those of electron-rich phosphine ligands. While it has previously been asserted that NHCs resemble electron-rich phosphine ligands in terms of their coordination chemistry – the similarity arising from the suggestion that both are σ-donor ligands that do not participate heavily in π-backbonding interactions – recent work involving Group 11 NHCs challenges this belief and indicates that π-backbonding interactions may be responsible for as much as 30% of the overall orbital interaction in the analyzed complexes.[8-9] Although there is an apparent disagreement regarding the nature of the metal-carbene bond, NHCs are growing increasingly popular in organometallic synthesis in part because they have shown the ability to substitute other 2 e^- ligands (like amines) and generally seem to resist spontaneous dissociation that often occurs with phosphines.[7]

Another important feature of the NHC ligand framework that makes this an attractive synthetic target is its reliable preparation from a number of different synthetic schemes. While NHCs containing an unsaturated C-C backbone can be easily made through a one-pot synthesis including glyoxal, amine, and formaldehyde,[7] the route more relevant to the present work relies on Pd-catalyzed C-N bond formation[10] to yield 1,2-diamines, which are subsequently converted

to the desired product upon reaction with triethyl orthoformate in the presence of NH_4BF_4.[11]

In the current work, Cu(I) complexes supported by the saturated NHC ligand framework have been targeted, with the ultimate goal being the formation and isolation of a monomeric (NHC)CuH species. Such a complex would be interesting for several reasons. One reason is that it would be structurally interesting since it would serve as a rare example of a mononuclear Cu(I) hydride complex,[12] which are typically found as polynuclear clusters.[13] This goal seems to be reasonable in light of the sterically demanding nature of the ligand, which has been designed to flank the metal center, projecting beyond it and thereby protecting it from further coordination. Another reason why the monomeric copper hydride complexes would be of interest is due to their expected reactivity in terms of insertion chemistry, which would ultimately lend itself to catalytic cycles of interest.[14] Previous work in the Sadighi group has focused on the *IPr* [1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene] supporting ligand, which has successfully been incorporated into a copper complex of the form (*IPr*)CuCl.[15] In an effort to isolate the corresponding Cu(I) hydride complex, (*IPr*)CuCl was treated with NaO^tBu (to generate the (*IPr*)CuO^tBu intermediate) followed by $(EtO)_3SiH$ in order to arrive at the desired Cu(I) hydride complex. Despite the steric hinderance provided by the large ligand framework, the final product was determined to be an $[(IPr)CuH]_2$ dimer. This dimer reacts with alkynes to yield vinylcopper complexes, suggesting that the targeted Cu(I) hydride complexes could indeed be instrumental in reductive catalysis.[16]

While the work done with $[(IPr)CuH]_2$ has been encouraging, experimental effort geared toward the formation and isolation of a monomeric Cu(I) hydride complex has been ongoing. This chapter details attempts at generating important precursors to the monomeric Cu(I) hydride. Two routes were planned: one involving conversion of LCuCl to $LCuO^tBu$ followed by reaction

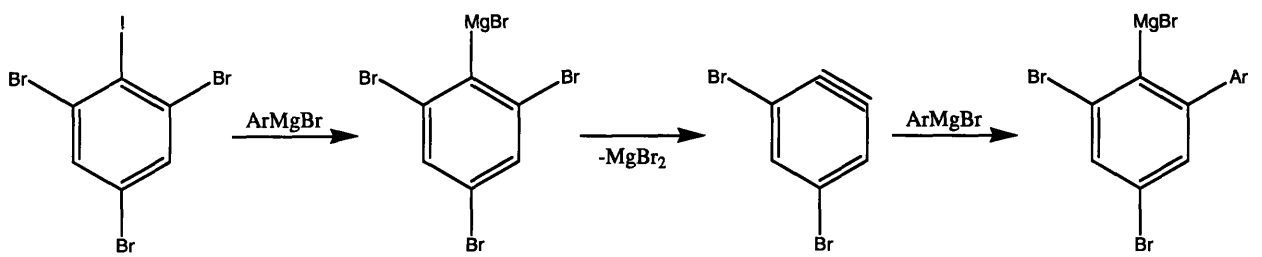
with R_3SiH, and one involving the direct synthesis of LCuOAc, which might subsequently react with silane to generate the same product (L = [1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]). Synthesis of both precursors, LCuCl and LCuOAc, has been successful and will be detailed below.

References

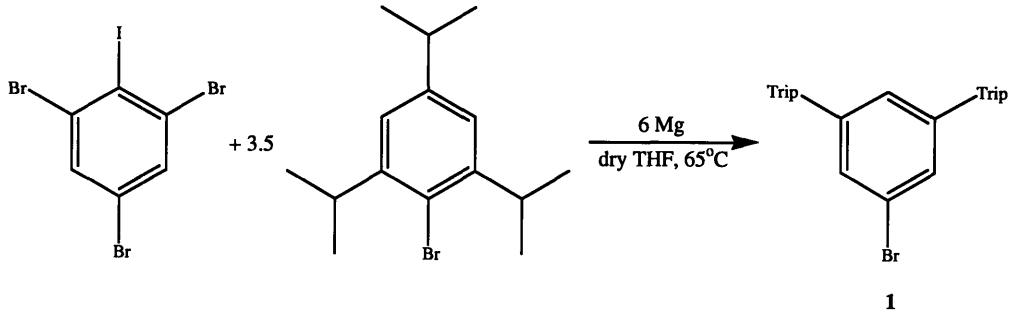
1. Selected examples of C-H activation: a) Prinz, M.; Grosche, M.; Herdtweck, E.; Herrmann, W.A. *Organometallics* **2000**, *19*, 1692. b) Mülhofer, M.; Strassner, T.; Herrmann, W.A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1745.
2. Selected examples of C-C bond formation: a) Fürstner, A.; Leitner, A. *Synlett* **2001**, *2*, 290. b) Herrmann, W.A.; Reisinger, C.-P.; Spiegler, M. *J. Organomet. Chem.* **1998**, *557*, 93. c) Zhang C.; Huang, J.; Trudell, M.L.; Nolan, S.P. *J. Org. Chem.* **1999**, *64*, 3804. d) Yang, C.; Lee, H.M.; Nolan, S.P. *Org. Lett.* **2001**, *3*, 1511. e) Lee, S.; Hartwig, J.F. *J. Org. Chem.* **2001**, *66*, 3402. f) Lee, H.M.; Nolan, S.P. *Org. Lett.* **2000**, *2*, 2053. g) Weskamp, T.; Böhm, V.P.W.; Herrmann, W.A. *J.Organomet. Chem.* **1999**, *585*, 348. h) Caddick, S.; Cloke, F.G.N.; Clentsmith, G.K.B.; Hitchcock, P.B.; McKeirecher, D.; Titcomb, L.R.; Williams, M.R.V. *J. Organomet. Chem.* **2001**, *617-618*, 635. i) Huang, J.; Nolan, S.P. *J. Am. Chem. Soc.* **1999**, *121*, 9889.
3. Selected examples of C-H bond formation: a) Lee, H.M.; Jiang, T.; Stevens, E.D.; Nolan, S.P. *Organometallics* **2001**, *20*, 1255. b) Herrmann, W.A.; Kulpe, J.A.; Konkol, W.; Bahrmann, H. *J. Organomet. Chem.* **1990**, *389*, 85. c) Chen, A.C.; Ren, L.; Decken, A.; Crudden, C.M. *Organometallics* **2000**, *19*, 3459. d) Herrmann, W.A.; Kellner, J.; Riepl, H. *J. Organomet. Chem.* **1990**, *389*, 103. e) Hillier, A.C.; Lee, H.M.; Stevens, E.D.; Nolan, S.P. *Organometallics* **2001**, *20*, 4246.
4. Selected examples of C-N bond formation: a) Herrmann, W.A.; Gooβen, L.J.; Spiegler, M. *Organometallics* **1998**, *17*, 2162. b) Cheng, J.; Trudell, M.L. *Org. Lett.* **2001**, *3*, 1371. c) Huang, J.; Grasa, G.; Nolan, S.P. *Org. Lett.* **1999**, *1*, 1307. d) Stauffer, S.R.; Lee, S.; Stambuli, J.P.; Hauck, S.I.; Hartwig, J.F. *Org. Lett.* **2000**, *2*, 1423.
5. Karkhanis, D. W.; Field, L. *Phosphorous Sulfur* **1985**, *22*, 49.
6. Kuhn, N.; Kratz, T.; Henkel, G. *J. Chem. Soc., Chem. Comm.* **1993**, *23*, 1778.
7. Herrmann, W.A. *Angew Chem., Int. Ed.* **2002**, *41*, 1290-1309.
8. Öfele, K.; Herrmann, W.A.; Mihalios, D.; Elison, M.; Herdtweck, E.; Priermeier, T.; Kiprof, P. *J. Organomet. Chem.* **1995**, *498*, 1.
9. Hu, X.; Castro-Rodriguez, I.; Olsen, K.; Meyer, K. *Organometallics* **2004**, *23*, 755.
10. Early examples of Pd-catalyzed C-N bond formation: a) Wolfe, J.P.; Wagaw, S.; Buchwald, S.L. *J. Am. Chem. Soc.* **1996**, *118*, 7215. b) Wolfe, J.P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S.L. *Acc. Chem. Res.* **1998**, *31*, 805. c) Hartwig, J.F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046.
11. Jensen, D.R.; Sigman, M.S. *Org. Lett.* **2003**, *5*, 63.
12. Example: Dilts, J. A.; Shriver, D. F. *J. Am. Chem. Soc.* **1969**, *91*, 4088-4091.
13. a) Albert, C. F.; Healy, P. C.; Kildea, J. D.; Raston, C. L.; Skelton, B. W.; White, A. H. *Inorg. Chem.* **1989**, *28*, 1300. b) Lemmen, T. H.; Folting, K.; Huffman, J. C.; Caulton, K. G. *J.Am. Chem. Soc.* **1985**, *107*, 7774. c) Stevens, R. C.; McLean, M. R.; Bau, R.; Koetzle, T. F. *J. Am. Chem. Soc.* **1989**, *111*, 3472.
14. Examples of copper(I) hydride complex catalytic activity: a) Lipshutz, B. H.; Shimizu, H. *Angew.Chem., Int. Ed.* **2004**, *43*, 2228. b) Hughes, G.; Kimura, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 11253.
15. Jurkauskas, V.; Sadighi, J. P.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2417.
16. Mankad, N.P.; Laitar, D.S.; Sadighi, J.P. *Organometallics* **2004**, *23*, 3369.

Results and Discussion

Preparation of [1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]copper (I) chloride (4) and [1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]copper (I) acetate (5). Using the Hart reaction (Scheme 1)[1], 1,3,5-tribromo-2-iodobenzene and 3.5 equivalents of 1-bromo-2,4,6-triisopropylbenzene were converted to 5'-Bromo-2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl (**1**) in the presence of excess magnesium (Scheme 2).[2] Isolation of the final product in modest (44%) yield following hydrolysis could be achieved by crystallization from diethyl ether/methanol at subzero temperatures. However, washing the crude product with methanol prior to crystallization is suggested to partially remove the undesired triisopropylbenzene byproduct.

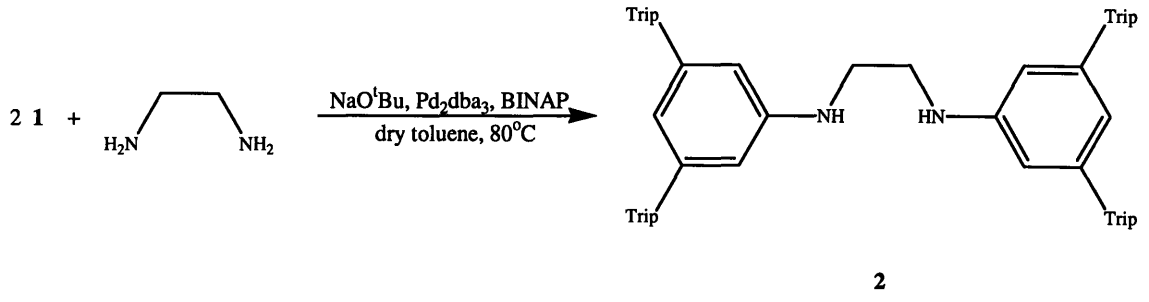


Scheme 1.[1] In this case, the Hart reaction proceeds initially due to the iodine-magnesium exchange involving 1,3,5-tribromo-2-iodobenzene, which results in formation of a Grignard. Loss of $MgBr_2$ forms the intermediate benzyne, which subsequently adds an equivalent of ArMgBr across the triple bond. The loss of magnesium halide and ArMgBr addition are repeated followed by hydrolysis to yield the final product (**1**).



Scheme 2. The formation of **1** from 1,3,5-tribromo-2-iodobenzene and 3.5 equivalents of 1-bromo-2,4,6-triisopropylbenzene.

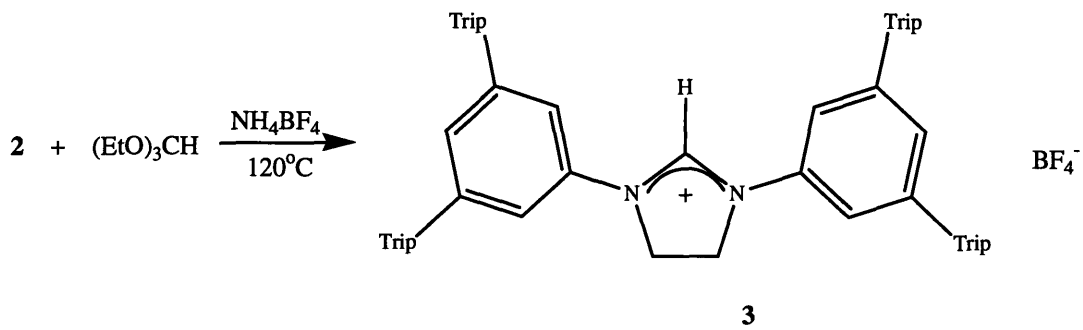
Palladium-catalyzed coupling[3] using ethylenediamine and two equivalents of **1** in the presence of NaO^{t}Bu was performed in toluene at 80°C, producing the yellow final product N,N'-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-ethane-1,2-diamine (**2**) in 51% isolated yield (Scheme 3). A large amount of nearly colorless byproduct, believed to be 2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl based on GC-MS and ^{1}H NMR considerations, was also isolated.



Scheme 3. Formation of **2** by the palladium-catalyzed cross-coupling[3] of **1** and ethylenediamine.

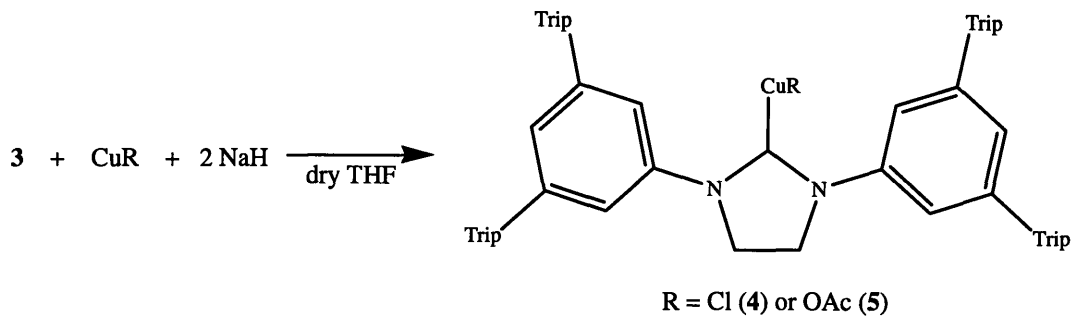
A ring-closing reaction between **2** and triethyl orthoformate in the presence of ammonium chloride[4] was attempted and, although successful, was modified in large part due to the length of time required for the product to separate from solution.[5] As an alternative, the reaction was carried out using ammonium tetrafluoroborate[6] in place of ammonium chloride and

run at 120°C for 6 hours (Scheme 4). Product isolation was altered by removing triethyl orthoformate under vacuum and passing a solution of the residue in dichloromethane through activated alumina.[7] The filtrate was allowed to evaporate and the yellow product (63%) could then be isolated by allowing a solution of **3** in 1,1,1,3,3,3-hexamethyl-1,3-disiloxane to stand at -15°C.



Scheme 4. The reaction of **2** with triethyl orthoformate in the presence of ammonium tetrafluoroborate to yield **3**.

The formation of copper(I) complexes **4** and **5** were both accomplished through reactions analogous to the synthesis of (*IPr*)CuCl.[8] The copper(I) salt (chloride or acetate), **3**, and roughly two equivalents of sodium hydride were allowed to react in dry THF for several hours (Scheme 5). Isolation of the yellow copper chloride complex and white copper acetate complex was achieved by removing solvent under vacuum, taking up the residue in benzene and filtering, and drying the filtrate.



Scheme 5. General reaction of **3**, copper(I) salt (chloride or acetate), and sodium hydride to arrive at the final products **4** and **5**.

As a practical consideration, wet THF seems to inhibit desired product formation, especially in the case of the copper acetate complex. An unidentified product is repeatedly observed by NMR analysis in cases where the reaction fails, with a possible explanation being undesired modification of the saturated C-C backbone. Attempts to crystallize the undesired product have been unsuccessful and not rigorously pursued at this time.

References

1. Du, C.-J.F.; Hart, H.; Ng, K.-K. D. *J. Org. Chem.* **1986**, *51*, 3162.
2. a) Yandulov, D.V.; Schrock, R.R. *J. Am. Chem. Soc.* **2002**, *124*, 6252. b) Yandulov, D.V.; Schrock, R.R.; Rheingold, A.L.; Ceccarelli, C; Davis, W.M. *Inorg. Chem.* **2003**, *42*, 796.
3. See Reference 10, Chapter 2 Introduction for specific examples.
4. Arduengo, A.J., III; Krafczyk, R.; Schmutzler, R.; Craig, H.A.; Goerlich, J.R.; Marshall, W.J.; Unverzagt, M. *Tetrahedron* **1999**, *55*, 14523.
5. Observable powder was discovered after roughly 2 weeks of allowing a solution of the targeted chloride salt (derivative of **3**) to stand in 1,1,1,3,3,3-hexamethyl-1,3-disiloxane at -15°C.
6. See Reference 11, Chapter 2 Introduction.
7. Ku, R.-Z.; Huang, J.-C.; Cho, J.-Y.; Kiang, F.-M.; Reddy, K.R.; Chen, Y.-C.; Lee, K.-J.; Lee, J.-H.; Lee, G.-H.; Peng, S.-M.; Liu, S.-T. *Organometallics* **1999**, *18*, 2145.
8. See Reference 15, Chapter 2 Introduction for synthesis of similar (*IPr*)CuCl.

Conclusion

The copper(I) complexes [1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]copper (I) chloride (**4**) and [1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]copper (I) acetate (**5**) were successfully prepared from their spectroscopically characterized precursors. Complex **4** was isolated in 92% yield while the yield for **5** was 71%. Both complexes are potentially important in the eventual synthesis of an (NHC)CuH monomeric species.

Experimental

General considerations: Unless stated otherwise, all synthetic experimentation was carried out using Schlenk techniques under an argon atmosphere, or in an Innovative Technologies glovebox under a nitrogen atmosphere. Reactions were carried out in flame-dried glassware cooled under vacuum. Anhydrous hexanes, toluene, and THF, inhibitor-free, were purchased from Aldrich in 18 L Pure-Pac™ solvent kegs, and sparged vigorously with argon for 40 minutes prior to first use. Hexanes and toluene were further purified by passage through one column of neutral alumina and one column of copper(II) oxide; THF, by passage through two columns of neutral alumina and one column of activated 4Å molecular sieves. Benzene and pentane, anhydrous, were purchased from Aldrich in Sure-Seal™ bottles and were stored over 3Å molecular sieves.

Pd_2dba_3, *rac*-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, copper (I) chloride, and copper (I) acetate were purchased from Strem Chemical company and used as received. Magnesium turnings were purchased from Strem Chemical company and were acid-washed (according to the procedure of Armarego and Perrin)[1] and stored in a glovebox under nitrogen prior to use. Sodium *tert*-butoxide, ammonium tetrafluoroborate, triethyl orthoformate, and 1,1,1,3,3,3-hexamethyl-1,3-disiloxane (anhydrous) were purchased from Aldrich and used as received. Sodium hydride (60% dispersion in mineral oil) was purchased from Aldrich and was washed free of mineral oil with anhydrous hexanes under inert atmosphere, and dried in vacuo prior to use. 1-Bromo-2,4,6-triisopropylbenzene and ethylenediamine were purchased from Avocado Chemical company and used as received. Ethyl acetate (HPLC grade), dichloromethane (HPLC grade), diethyl ether (Reagent ACS grade), concentrated HCl (Reagent ACS grade), methanol, iodine, sodium sulfite, and sodium chloride were used as received from Mallinckrodt. Hexanes for chromatography (HPLC grade) were used as received from Burdick

& Jackson. Silica gel (230-400 mesh), Celite, and pentane (HPLC grade) were used as received from EMD Chemicals, Inc.. TLC plates (Silica Gel 60, F_{254}), alumina (80-325 mesh), and magnesium sulfate (anhydrous) were purchased from EM Science. Alumina was activated in a 100°C oven for at least 48 hours prior to use. 1,3,5-tribromo-2-iodobenzene[2] was made by methods previously reported in the literature.[3]

IR spectra were recorded on a Perkin-Elmer 2000 series FT-IR as KBr pellets. C_6D_6 (Cambridge Isotope Laboratories) was dried over purple sodium/benzophenone ketyl, degassed by three freeze-pump-thaw cycles and vacuum-transferred prior to use. $CDCl_3$ (Cambridge Isotope Laboratories) was used as received. ^1H NMR spectra were recorded on Varian 300 MHz and Varian 500 MHz instruments, with shifts reported relative to the residual solvent peak. ^{13}C NMR spectra were recorded on a Varian 500 MHz instrument, with shifts reported relative to the residual solvent peak. ^{19}F NMR spectra were recorded on a Varian 300 MHz instrument, with shifts reported relative to external $CFCl_3$. Gas chromatographic analyses were performed on an Agilent Technologies Model 5973N Gas chromatograph/Mass spectrometer equipped with an Rtx-1 column. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA.

[1,3-bis-(2,4,6,2'',4'',6''-hexaisopropyl-[1,1':3',1'']terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]copper (I) chloride (4). In a nitrogen glovebox, (previously acid-washed) magnesium turnings (4.13 g, 0.170 mol) were deposited in a resealable 300-mL Schlenk tube containing a magnetic stirbar. The tube was then capped with a Teflon screwcap, removed from the glovebox, and connected to a Schlenk line. The atmosphere of the tube was evacuated, and replaced with argon. The Teflon screwcap was replaced under a flow of argon with a rubber septum. THF was added (50 mL), via syringe; the septum was removed under a flow of argon,

which was then halted while 3 flakes of iodine were added as quickly as possible. The tube was then fitted with a septum and a needle extending below the tube neck, and purged under a flow of argon for about 5 min. The needle was removed from the septum and the argon bubbler of the Schlenk line was opened to relieve any excess pressure anticipated from the subsequent vigorous reaction. The 1-bromo-2,4,6-triisopropylbenzene (25.0 g, 0.088 mol) was then added via syringe over a period of roughly 15 minutes, and the septum and needle were replaced with the Teflon screwcap. The reaction vessel was then heated in a 65°C oil bath for 3 hrs. The argon bubbler for the Schlenk line was then closed and the Teflon screwcap was replaced under a flow of argon with a rubber septum. A THF solution (10 mL) of 1,3,5-tribromo-2-iodobenzene (10.57 g, 0.024 mol) was added via syringe and the septum was replaced with the Teflon screwcap. The resulting mixture was allowed to continue stirring at 65°C for an additional 9 hrs. The reaction mixture was then cooled to room temperature and transferred by cannula to a stirring 3.6 M solution of HCl chilled in an ice bath. Excess THF was used as necessary to complete the transfer. Roughly 100 mL of diethyl ether was added to the stirring mixture and said mixture was stopped from stirring and allowed to warm to room temperature. A majority of the organic phase was isolated by decantation and the remaining material was transferred to a 500-mL separatory funnel, where the aqueous phase was extracted with diethyl ether (3 x 100 mL). All organic fractions were combined and concentrated to a final volume of ~100 mL in vacuo. The organic phase was then washed with saturated Na_2SO_3 solution (3 x 50 mL), washed with water (2 x 50 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. 5'-Bromo-2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl (**1**) was obtained by washing the obtained solid with methanol (3 x 100 mL) followed by crystallization from methanol/diethyl ether at -15°C. Additional crops could be obtained by concentrating the mother liquor from earlier crops in

vacuo, purifying the product by column chromatography on silica gel using pentane as eluant, concentrating the resulting solution in vacuo, and allowing the solution to stand at -15°C. The product was isolated as white needle-like crystals, 5.97 g (44%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (m, 4 H), 7.04 (s, 8 H), 6.97 (m, 2 H), 2.93 (sept, J = 6.9 Hz, 4 H), 2.69 (sept, J = 6.9 Hz, 8 H), 1.29 (d, J = 6.9 Hz, 24 H), 1.17 (d, J = 6.6 Hz, 24 H), 1.05 (d, J = 6.9 Hz, 24 H).

In air, **1** (4.54 g, 8.09 mmol), NaO^{t}Bu (1.09 g, 11.3 mmol), Pd_2dba_3 (0.150 g, 0.163 mmol), and *rac*-BINAP (0.200 g, 0.326 mmol) were weighed and transferred to a resealable 100-mL Schlenk tube containing a magnetic stirbar. The tube was then capped with a Teflon screwcap and connected to a Schlenk line. The atmosphere of the tube was evacuated, and replaced with argon. The Teflon screwcap was replaced under a flow of argon with a rubber septum. Toluene was added (50 mL), via syringe; the septum pierced by a needle extending below the tube neck, and purged under a flow of argon for about 5 min. Distilled ethylenediamine (0.267 mL, 4.05 mmol) was then added via syringe, and the septum and needle were replaced with the Teflon screwcap. The reaction vessel was then heated in an 80°C oil bath for 36 hrs. The reaction mixture was then cooled to room temperature and transferred in air to a 250-mL separatory funnel along with ~50 mL of saturated NaCl and ~30 mL of diethyl ether. The phases were separated and the aqueous layer was extracted with Et_2O (2 x 50 mL); the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using 97:3 hexanes:ethyl acetate as eluant. N,N'-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-ethane-1,2-diamine (**2**) was isolated as a yellow amorphous solid, 2.11 g (51%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (s, 8 H), 6.48 (s, 4 H), 6.42 (s, 2 H), 3.42 (s, 4 H), 2.92 (sept, J = 7.0 Hz, 4 H), 2.81 (sept, J = 6.7 Hz, 8 H), 1.30 (d, J = 7.0 Hz, 24 H), 1.15 (d, J = 6.7 Hz, 24 H), 1.05 (d, J = 7.0 Hz, 24 H).

In air, **2** (0.335 g, 0.328 mmol) and NH_4BF_4 (0.043 g, 0.410 mmol) were weighed and transferred to a 25-mL pear-shaped Schlenk flask containing a magnetic stirbar and sealed with a rubber septum. The flask was connected to a Schlenk line and the atmosphere of the flask was evacuated and replaced with argon. Triethyl orthoformate was added (3.0 mL, 18 mmol) via syringe. The argon bubbler of the Schlenk line was opened to relieve any excess pressure resulting from the generation of ammonia and ethanol. The reaction vessel was then heated in a 120°C oil bath for 6 hrs. The reaction mixture was then cooled to room temperature before being concentrated to a brownish-orange oil in vacuo. The oil was dissolved in dichloromethane and was passed through activated alumina. The collected solution was allowed to evaporate, resulting in an orange oil. The oil was treated with ~5 mL of 1,1,1,3,3,3-hexamethyl-1,3-disiloxane and the resulting mixture was sonicated for ~30 seconds and allowed to stand at -15°C for ~12 hours. After filtering the cold mixture and washing the collected solid with cold 1,1,1,3,3,3-hexamethyl-1,3-disiloxane, 1,3-bis-(2,4,6,2",4",6"-hexaisopropyl-[1,1':3',1"]terphenyl-5'-yl)-4,5-dihydro-3H-imidazol-1-ium tetrafluoroborate (**3**) was isolated as a pale yellow solid, 0.232 g (63%): ^{1}H NMR (500 MHz, C_6D_6) δ 8.53 (br s, 1 H), 7.25 (s, 8 H), 7.14 (m, 4 H), 7.10 (m, 2 H), 3.69 (s, 4 H), 3.08 (sept, J = 6.7 Hz, 8 H), 2.87 (sept, J = 7.0 Hz, 4 H), 1.41 (d, J = 6.7 Hz, 24 H), 1.28 (d, J = 7.0 Hz, 24 H), 1.21 (d, J = 6.7 Hz, 24 H); ^{13}C NMR (500 MHz, C_6D_6) δ 151.2, 149.7, 147.4, 143.8, 136.2, 132.3, 121.5, 118.8, 48.5, 35.3, 31.4, 25.2, 24.9, 24.7 (C2 not observed); ^{19}F NMR (300 MHz, C_6D_6) δ –153.5.

In a nitrogen glovebox, **3** (0.110 g, 0.098 mmol), NaH (0.005 g, 0.2 mmol), and CuCl (0.010 g, 0.098 mmol) were weighed and transferred to a 20-mL scintillation vial containing a magnetic stirbar. The contents of the vial were treated with about 4 mL of THF and the vial was capped. The contents of the vial were allowed to stir for 5 hrs before being dried in vacuo,

resulting in a dark-colored residue. The residue was treated with benzene and the resulting mixture was filtered through Celite. The filtrate was concentrated in vacuo, affording the title compound as a yellow powder, 0.103 g (92%): ^{1}H NMR (500 MHz, C_6D_6) δ 7.47 (s, 4 H), 7.27 (s, 8 H), 7.05 (s, 2 H), 3.12 (sept, J = 6.9 Hz, 8 H), 2.88 (sept, J = 6.9 Hz, 4 H), 2.81 (s, 4 H), 1.43 (d, J = 6.9 Hz, 24 H), 1.29 (d, J = 6.9 Hz, 24 H), 1.23 (d, J = 6.9 Hz, 24 H); ^{13}C NMR (500 MHz, C_6D_6) δ 196.7, 149.4, 147.3, 143.1, 141.6, 136.9, 130.9, 121.3, 120.8, 49.6, 35.3, 31.4, 25.3, 25.0, 24.8; IR (KBr, cm^{-1}) 2960, 2868, 1608, 1583, 1478, 1459, 1426, 1383, 1362, 1270, 876.

Note: We have been unable to obtain satisfactory elemental analyses for this compound. The ^{1}H NMR spectrum is reproduced below to show that the desired product was isolated.

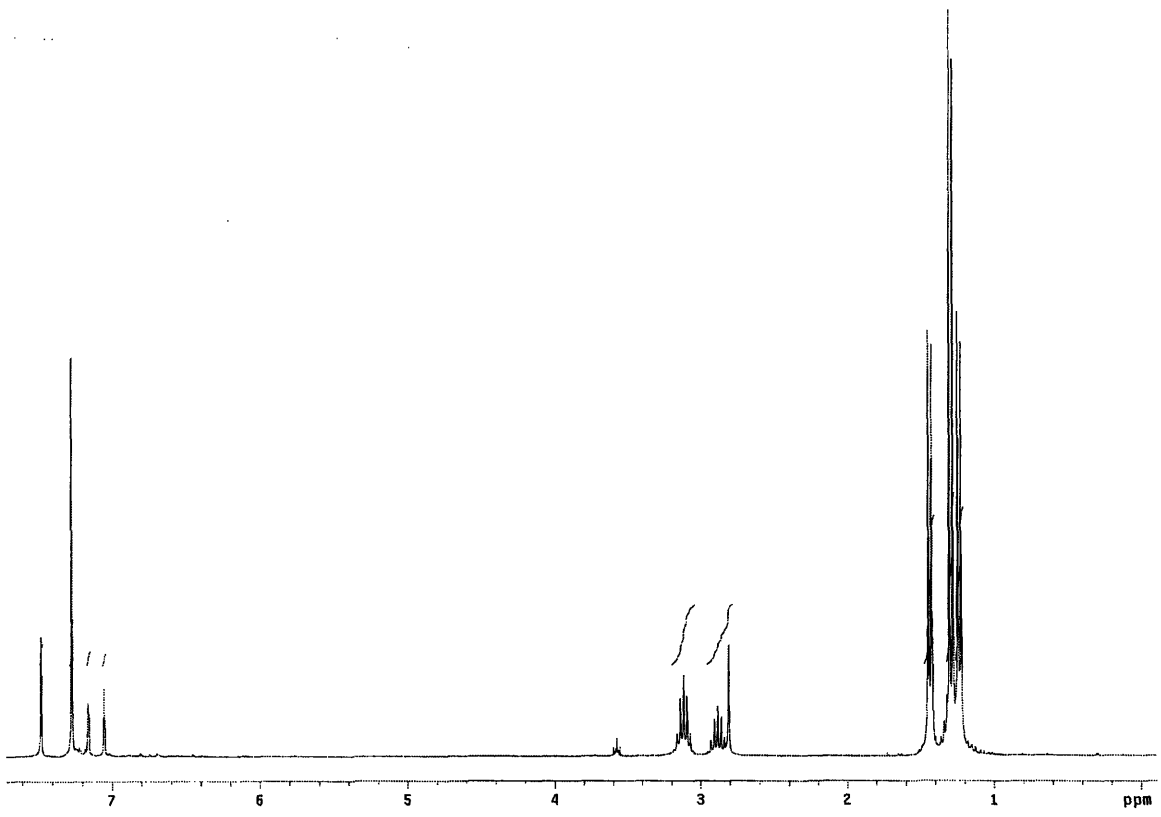


Figure 1. ^{1}H NMR of **4** (estimated to be 98% pure) in C_6D_6.

[1,3-bis-(2,4,6,2'',4'',6''-hexaisopropyl-[1,1':3',1'']terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]copper (I) acetate (5). In a nitrogen glovebox, **3** (0.130 g, 0.116 mmol), NaH (0.006 g, 0.25 mmol), and CuOAc (0.014 g, 0.114 mmol) were weighed and transferred to a 20-mL scintillation vial containing a magnetic stirbar. The contents of the vial were treated with about 4 mL of THF and the vial was capped. The contents of the vial were allowed to stir for 8.5 hrs before being dried in vacuo, resulting in a dark-colored residue. The residue was treated with benzene and the resulting mixture was filtered through Celite. The filtrate was concentrated in vacuo, affording the title compound as an off-white powder, 0.094 g (71%): ^{1}H NMR (500 MHz, C_6D_6) δ 7.73 (m, 4 H), 7.27 (s, 8 H), 7.02 (m, 2 H), 3.12 (sept, J = 6.9 Hz, 8 H), 2.90 (sept, J = 6.9 Hz, 4 H), 2.72 (s, 4 H), 1.89 (s, 3 H), 1.43 (d, J = 6.9 Hz, 24 H), 1.31 (d, J = 6.9 Hz, 24 H), 1.25 (d, J = 6.9 Hz, 24 H); ^{13}C NMR (500 MHz, C_6D_6) δ 196.9, 178.8, 149.2, 147.2, 142.9, 142.0, 137.0, 130.1, 121.2, 119.6, 48.9, 35.2, 31.5, 26.2, 25.3, 24.8, 23.2; IR (KBr, cm^{-1}) 2961, 2868, 1647, 1608, 1585, 1477, 1461, 1439, 1362, 1301, 1253, 1054, 878, 844.

Note: We have been unable to obtain satisfactory elemental analyses for this compound. The ^{1}H NMR spectrum is reproduced below to show that the desired product was isolated.

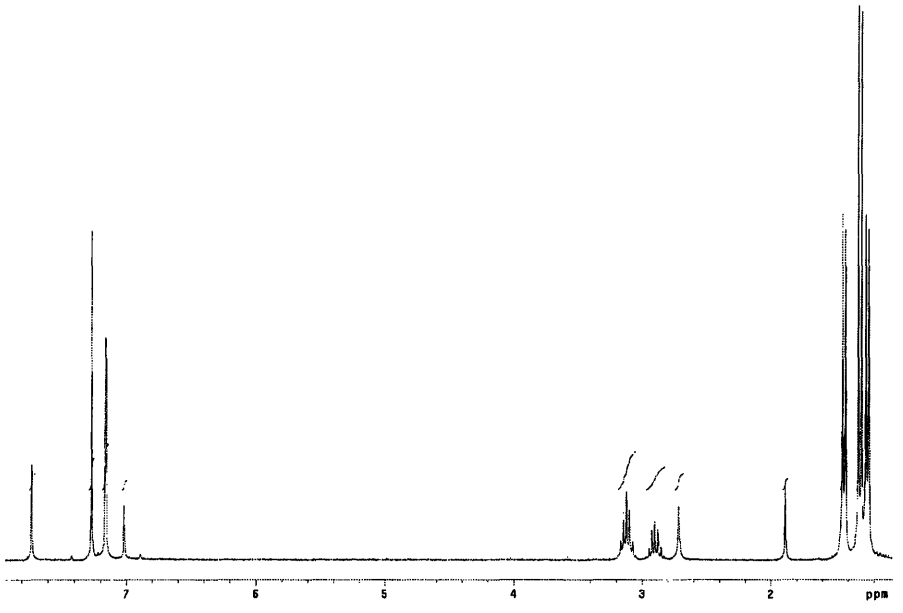


Figure 2. ^{1}H NMR of **5** (estimated to be 93% pure) in C_6D_6.

X-ray Crystallography

General considerations. Crystals of **4** were transferred onto a microscope slide from a scintillation vial and coated with STP. A crystal was selected, mounted on a glass fiber, and optically centered. The data were collected on a Siemens platform goniometer with a Bruker SMART APEX CCD detector. The structures were solved by direct methods in conjunction with standard difference Fourier techniques (SHELXTL v5.1, Sheldrick, G. M. and Siemens Industrial Automation, 1997). Nonhydrogen atoms were treated anisotropically, and hydrogen atoms, unless otherwise noted, were placed in calculated positions ($d_{C\text{-}H} = 0.96$ Å).

[1,3-bis-(2,4,6,2'',4'',6''-hexaisopropyl-[1,1':3',1'']terphenyl-5'-yl)-4,5-dihydroimidazol-2-ylidene]copper (I) chloride (4):

X-ray quality crystals were grown by diffusion of hexane vapor into a benzene solution of **4** (Figure 3).

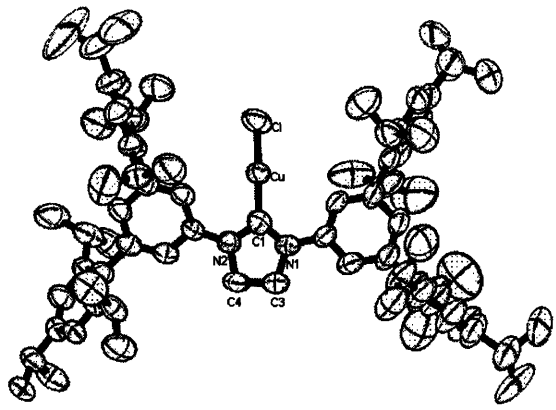


Figure 3. Connectivity diagram of **4**. Although the data did not refine sufficiently to be suitable for publication, this illustration serves to show that the desired product was isolated, and to indicate the steric encumbrance of the ligand. (Data may be retrieved upon request from pmueller@MIT.EDU.)

References

1. Armarego, W.L.F.; Perrin, D.D. *Purification of Laboratory Chemicalsm Fourth Edition,* Pergamon, Oxford, **1997**.
2. Barbero, M.; Degani, I.; Diulgheroff, N.; Dughera, S.; Fochi, R. *Synthesis* **2001**, *14*, 2180.
3. The material used was supplied by Han Sen Soo, then in the Cummins research group, and recrystallized prior to use.

Curriculum Vitae

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Education

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Fall 2002 and Fall 2003 – Introductory Chemical Experimentation (chemistry majors)

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Industrial Experience

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Organic Synthesis Monitored by GC-MS

May 2000 – August 2000; Supervisor: Dr. Raymond Fernando
Rheological Studies on Latex-Based Coating Formulations

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Publications

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"Novel Process for Generating Useful Electrophiles from Common Anions Using Selectfluor® Fluorination Agent." Syvret, R. G.; Butt, K. M.; Nguyen, T. P.; Bulleck, V. L.; Rieth, R. D. *J. Org. Chem.* **2002**, *67(13)*, 4487-4493.

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