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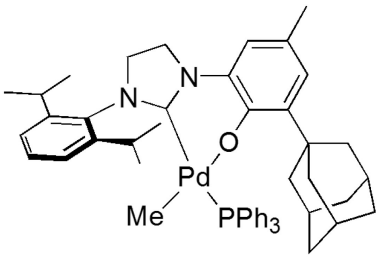

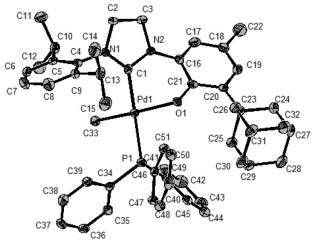

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A New Class of Chelating N-Heterocyclic Carbene Ligands and Their Complexes with Palladium

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Summary: A new series of chelating N-heterocyclic carbene (NHC) ligands and their complexes with palladium are described. The ligands feature a chelating phenolic unit, thereby expanding the class of available NHC ligands for organometallic catalysis.

N-Heterocyclic carbenes (NHCs) are being used increasingly in organometallic chemistry as neutral two-electron-donor ligands, commonly replacing phosphines in that role. The strong σ-donating capability and low level of π-acidity of these ligands provide their metal complexes with electronic properties that are often quite different from those with phosphines or other traditional neutral ligands.[1] This change can sometimes enhance the reactivity of metal-based catalysts that feature NHCs. Examples of this improved reactivity include ruthenium-based olefin metathesis catalysts[2] and palladium-based catalysts for C−C and C−N coupling reactions.[3] Another attractive feature of NHCs is the possible variability in the substituents on the nitrogen atoms, which allows for a wide range of steric,[4] asymmetric,[5,6] and electronic features. Additionally, it is possible to functionalize these nitrogen substituents in such a way as to make ligands capable of chelation.[6,7] Such variability has led to the synthesis of NHC analogues of many traditional ligands.

Seeking to further expand the current repertoire of available carbene ligands, we are interested in the synthesis of *o*-hydroxyaryl-substituted NHCs that are capable of binding through the phenoxide oxygen and the carbene carbon to provide an [L,X]-type chelate (Figure 1). These ligands would be analogous to the salicylaldimine (sal) framework, a common motif in organometallic chemistry.[7] Typically, functionalized NHCs are synthesized via nucleophilic attack of a 1-alkylimidazole on an alkyl halide to give an N-functionalized carbene precursor. This method has been used with success to synthesize a wide range of chelating carbene ligands with functionalized alkyl substitution, including some featuring a [C,O] chelate.[8] However, because nucleophilic attack on an aryl ring by an imidazole is difficult or impossible, the development of ligands with functionalized aryl groups is limited. Thus, a new approach was required to synthesize our targeted ligands. The only previously reported example of an N,N′-diaryl carbene capable of chelation through a phenoxide has been Hoveyda's example that features a binaphthol moiety, used in the synthesis of a ruthenium complex for asymmetric olefin metathesis.[6] However, the synthesis of this ligand is somewhat lengthy. Herein is described a facile, high-yielding, highly modular synthesis of differentially aryl substituted NHCs to give [C,O] chelate ligands, as well as their complexes with palladium.[9] This versatile synthetic method provides a route to NHC ligands with nearly any substitution pattern imaginable.

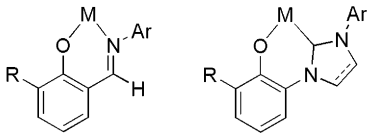

Figure 1. Analogy between salicylaldimine ligands and chelating carbenes.

The general protocol for synthesizing phenoxide chelating carbenes proceeds as shown in Scheme 1: ethyl chlorooxoacetate is treated with an arylamine in the presence of triethylamine to give oxanilic acid ester **1**.

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(9) During preparation of this paper, a synthesis very similar to this one was reported: Dinger, M. B.; Nieczypor, P.; Mol, J. C. *Organometallics* **2003**, *22*, 5291−5296. See also: Lambert, J. B.; Huseland, D. E.; Wang, G.-T. *Synthesis* **1986**, 657−658.

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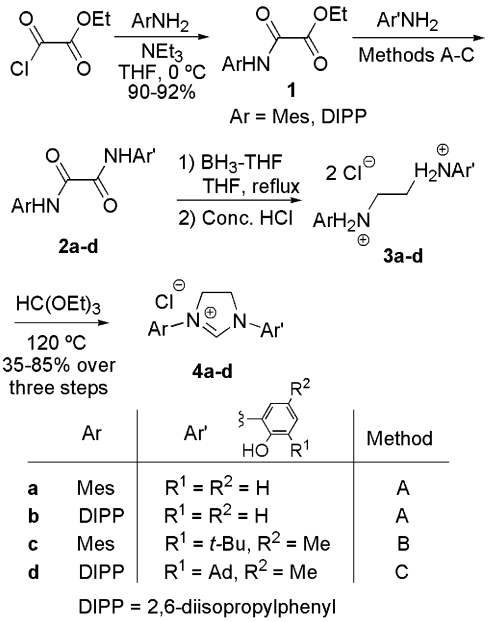
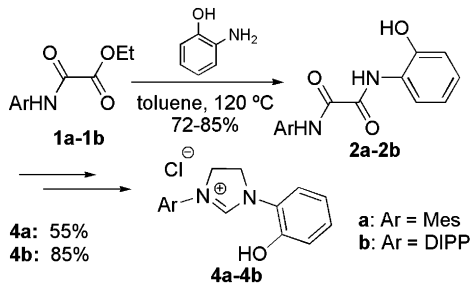
Scheme 1. General Synthesis of Chelating Carbenes



	Ar	Ar'	Method
a	Mes	$R^1 = R^2 = H$	A
b	DIPP	$R^1 = R^2 = H$	A
c	Mes	$R^1 = t$-Bu, R^2 = Me	B
d	DIPP	R^1 = Ad, R^2 = Me	C

DIPP = 2,6-diisopropylphenyl

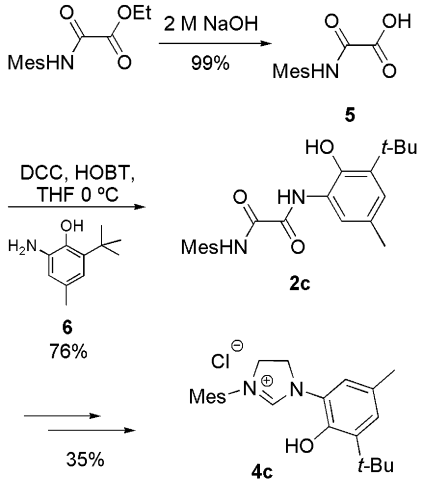
Scheme 2. Method A



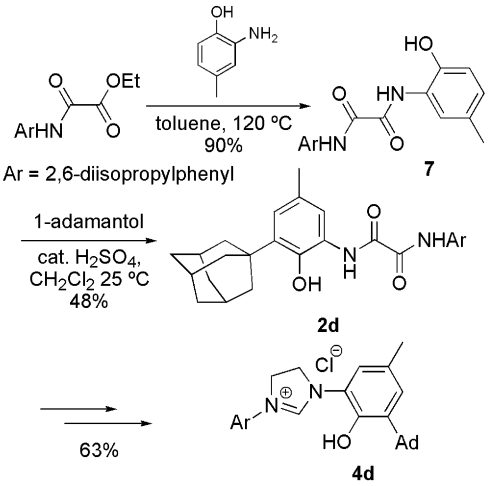
Reaction with the desired aminophenol under a variety of conditions (methods A−C) provides oxalamide **2**. Reduction of **2** with borane−THF complex results in ethylenediamine **3**, which then cyclizes upon treatment with triethyl orthoformate to carbene precursor **4**. This route allows for the formation of N-heterocyclic carbenes limited only by the availability of the starting amines.

For each specific ligand (**4a**−**d**), a different approach was required to append the aminophenol moiety in the second step (methods A−C in Scheme 1). For the syntheses of ligands **4a** and **4b**, treatment of **1** (Ar = mesityl, 2,6-diisopropylphenyl) with 2-aminophenol in refluxing toluene provided bis-amides **2a** and **2b** in good yield (method A, Scheme 2). However, 2-amino-4-methyl-6-*tert*-butylphenol (**6**) proved too bulky to react in this fashion in the synthesis of **4c**. Therefore, peptide coupling of **6** with oxanilic acid **5** was employed to form bis-amide **2c** (method B, Scheme 3). An NHC ligand even bulkier than **4c** was prepared by the introduction of an adamantyl group in the position ortho to the phenol (**4d**; method C, Scheme 4). This was accomplished by treatment of **1b** with 2-amino-4-methylphenol, in a manner similar to that used for **2a** and **2b**, to provide bis-amide **7**. Reaction of **7** with 1-adamantol and catalytic sulfuric acid afforded bis-amide **2d**. It should be noted that the placement of a methyl group para to the hydroxyl functionality prevents reaction with adamantol at that position. The variety of substituents on ligands **4a**−**d** highlights the utility and adaptability of this modular route to differentially substituted carbene ligands.

Scheme 3. Method B



Scheme 4. Method C



To test the viability of this new class of N-heterocyclic carbenes as ligands for transition metals, we decided to study their complexes of palladium. Although silver carbene reagents have previously been used to effect this type of ligation,[6,10] simple deprotonation of the carbene precursor with 2 equiv of potassium hexamethyldisilazide (KHMDS) at room temperature in toluene or THF proved to be an adequate method for generation of active carbene.[11] Reaction with the appropriate metal precursor led to formation of the desired palladium complexes. The monophosphine methylpalladium chloro-bridged dimers $((PR_3)PdMeCl)_2$ (R = Et, Ph) proved to be excellent metal precursors, providing metal complexes of the type $(NHC)PdMe(PR_3)$ (R = Et, Ph; Scheme 5).[12] Complexes **8a**,**d** have been structurally characterized by X-ray crystallography (Figures 2 and 3). They possess square-planar geometry with the anionic donors (methyl and phenoxide) trans to each other.

There have been, hitherto, relatively few examples of stable alkylpalladium complexes of N-heterocyclic carbenes.[13] This can often be attributed to decomposition

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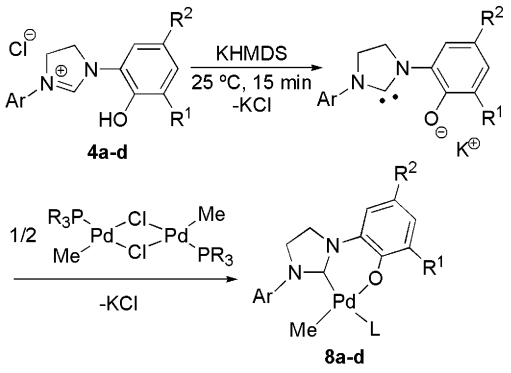
Scheme 5. General Procedure for Synthesis of Metal Complexes



	Ar	R^1,R^2	L
a	Mes	$R^1 = R^2 = H$	PEt_3
b	DIPP	$R^1 = R^2 = H$	PPh_3
c	Mes	$R^1 = t$-Bu, R^2 = Me	PPh_3
d	DIPP	R^1 = Ad, R^2 = Me	PPh_3

of such complexes through a reductive elimination pathway to give imidazolium salts and reduced metal.[14] It should be noted that the palladium complexes presented in this work are quite stable.[15] It has been demonstrated previously that NHC palladium alkyl complexes are much more stable when the ligand is capable of chelation, which presumably prevents the carbene from attaining the orientation necessary for attack by the alkyl group bound to the metal.[16]

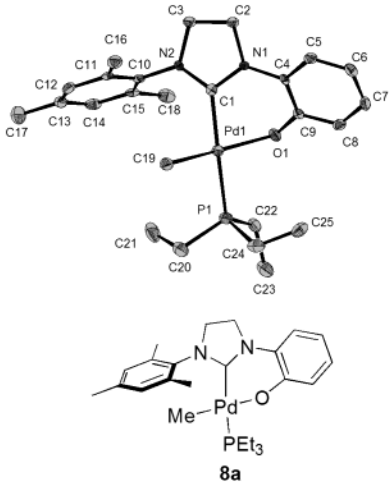


Figure 2. Structure of compound **8a** represented by thermal ellipsoids at 50% probability. Hydrogen atoms have been omitted for clarity.

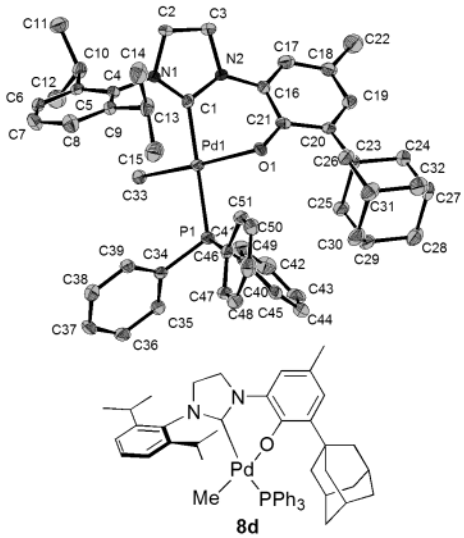


Figure 3. Structure of **8d** represented by thermal ellipsoids at 50% probability. Hydrogen atoms have been omitted for clarity.

A simple, high-yielding, and modular protocol for the synthesis of bidentate diaryl N-heterocyclic carbenes (and differentially substituted carbenes in general) is presented. Their effectiveness as stable ligands for palladium having been established, it is hoped that these ligands may prove useful in organometallic catalysis.

Acknowledgment. We thank the Rohm and Haas Corporation for funding, Dr. Steven Goldberg for important advice, and Mr. Larry Henling and Dr. Mike Day for X-ray crystallographic analysis.

Supporting Information Available: Text, tables, and figures giving detailed synthetic procedures for ligands and metal compounds, as well as crystallographic data; crystallographic data are also available as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K., and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition numbers 235932 (**8a**) and 235931 (**8d**).

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(11) It has been shown that alkali-metal ions will complex with NHCs in solution: (a) Arduengo, A. J.; Tamm, M.; Calabrese, J. C.; Davidson, F.; Marshall, W. J. *Chem. Lett.* **1999**, *10*, 1021−1022. (b) Fränkel, R.; Birg, C.; Kernbach, U.; Habereder, T.; Nöth, H.; Fehlhammer, W. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1907−1910. The ^{13}C NMR (C_6D_6) of carbene precursor **4d** treated with 2 equiv of KHMDS features a resonance at 238.8 ppm (compare to **8d**, where the carbene carbon appears at 197.4 ppm), which is in accordance with the reported chemical shift of the carbene carbon of a potassium carbene complex; see: Alder, R. W.; Blake, M. E.; Bortolotti, C.; Bufali, S.; Butts, C. P.; Linehan, E.; Oliva, J. M.; Orpen, A. G.; Quayle, M. J. *Chem. Commun.* **1999**, 241−242. However, a very high downfield shift may also be indicative of an uncoordinated NHC in solution; see: Arduengo, A. J.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361−363. Because there is likely a potassium ion associated with the anionic phenoxide moiety, it seems probable that the product of two successive deprotonations of **4d** is a potassium carbene complex, although the exact nature of this species is unknown. Investigations into the precise structure are currently underway.

(12) Representative synthesis of Pd complexes (complex **8a**): 1-(mesityl)-3-(2-hydroxyphenyl)-4,5-dihydroimidazolium chloride (**4a**; 75.3 mg, 0.24 mmol, 1 equiv) and potassium hexamethyldisilazide (99.4 mg, 0.50 mmol, 2.1 equiv) were weighed into a vial in the glovebox. THF (5 mL) was added, providing a light yellow solution with a fine precipitate. This was added to a round-bottomed flask and stirred for 10 min. At this point, a suspension of $((PEt_3)PdMeCl)_2$ (65.4 mg, 0.12 mmol, 0.5 equiv) in THF (5 mL) was added. The resulting yellow suspension quickly became a light yellow solution with a fine precipitate. It was stirred at room temperature for 1 h and then filtered through Celite. The solvent was then removed under reduced pressure until ca. 1 mL remained. To this was added pentane, and the resulting suspension was allowed to stand at −40 °C overnight. After 12 h, the product, a beige solid, was collected by filtration (39 mg, 0.08 mmol, 32% yield).

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(14) McGuinness, D. S.; Cavell, K. J. *Organometallics* **2000**, *19*, 4918−4920.

(15) The ^1H NMR spectrum is unchanged after 1 week at room temperature in C_6D_6.

(16) (a) McGuiness, D. S.; Saendig, N.; Yates, B. F.; Cavell, K. J. *J. Am. Chem. Soc.* **2001**, *123*, 4029−4040. (b) Nielsen, D. J.; Magill, A. M.; Yates, B. F.; Cavell, K. J.; Skelton, B. W.; White, A. H. *Chem. Commun.* **2002**, 2500−2501.