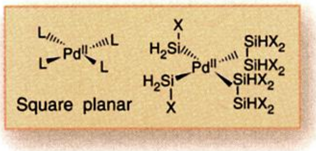
species (see the first figure). Surprisingly, their compound does not have an electronegative ligand, but a silicon one. This feature makes it organometallic at least in spirit, because Si is the nearest chemical relative of carbon.



The geometry typically found for Pd(II) and the Pd(II) model of the present compound. L, ligand on Pd; X, nonhydrogen substituent on silicon.

To assign an integer oxidation state to an atom in a compound can be difficult, however. It requires clear-cut situations with a well-defined number of bonds between atoms. Consider the hypothetical species PdH_6, which contains Pd(VI). H–H bond formation could in principle give $Pd(H_2)H_4$ with oxidation state Pd(IV), $Pd(H_2)_2H_2$ with Pd(II), and $Pd(H_2)_3$ with Pd(0). Each time we replace two M–H bonds by a neutral H_2 ligand, the oxidation state of Pd decreases by two.

Oxidation state ambiguity (*6*) can arise in organometallic species because they often show structures with partial bonds. A structure partway between PdH_6 and $Pd(H_2)H_4$—for example, with a long H···H bond—leads to one such ambiguity. The same can happen if we replace the M–H bonds by $M–SiX_3$ and consider formation of $X_3Si–SiX_3$ ligands, although such a ligand has never previously been seen.

The new compound described by Chen *et al.* is frozen partway between the $Pd(SiX_3)_6$ and $Pd(X_3Si–SiX_3)_2(SiX_3)_2$ forms. Two Si···Si distances in the ligand sphere (dashed in the first figure) are about 2.5 Å, too close to be considered nonbonding but too far to be pure Si–Si bonds. The compound thus has some Pd(VI) and some Pd(II) character. The limiting Pd(II) form (see the second figure) has the square planar geometry typical of Pd(II). Which model is most appropriate, Pd(VI) (first figure) or Pd(II) (second figure), will require further study. But both are unprecedented. Changing the X groups on Si should push the compound toward one or the other limiting structure. This a likely topic for future work.

Chen *et al.*'s work not only opens up what may be a wide field of such high valent organometallic compounds and of Si–Si complexes but allows us to consider Pd(VI) and Si–Si complexes as intermediates in certain catalytic reaction mechanisms. The work also justifies a half-serious comment (*7*) once made by J. C. Bailar of the University of Illinois (1904–1991), an early pioneer in the area. Bailar quipped that the advent of organometallic chemistry had simplified the lives of students because they no longer had to learn the permitted valence states of the metals: It could be safely assumed that for organometallic compounds all valence states were now possible.

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PERSPECTIVES: SYNTHETIC CHEMISTRY

The Key to Successful Organic Synthesis Is...

William D. Jones

The ability to selectively form carbon-carbon bonds between organic fragments has been crucial to the development of synthetic organic chemistry. Complex molecules held together largely by carbon-carbon bonds can be synthesized through careful planning and execution of a series of chemical reactions that build up the desired structure step by step. This approach is used, for example, in the chemical synthesis of natural product molecules for use in the pharmaceutical industry.

Existing methods are not perfect, however, and complex synthetic routes may be required to reach a desired product. New methodologies for the formation of carbon-carbon bonds therefore continue to be important. On page of 305 of this issue, Cho *et al.* report such a new methodology. They catalytically convert aromatic compounds into precursors that can facilely form bonds between unsaturated carbon centers (*1*). The method is versatile and selective and promises to be widely used in organic synthesis.

Three methods have proven particularly valuable for the formation of bonds between unsaturated carbon atoms (see left panel in the figure). Heck coupling is typically used to join alkenes with halide-functionalized benzene (aryl halides) or alkenes (vinyl halides) with a palladium catalyst. Stille coupling is also catalyzed by palladium; here, a tin compound, trialkyltin, carries one of the two organic units that are to be joined. Suzuki coupling is similar to Stille coupling, except that a borylate group, $B(OR)_2$, is used instead of trialkyltin to carry the aryl or vinyl group.

These methods have gained widespread use because they can be applied to a wide range of reactions and do not form undesired side products (*2*). They have proven to be superior to earlier methods in the syntheses of several organic compounds (*3–5*). The particularly successful Suzuki coupling (*6*) has been adapted to solid-phase synthesis (*7*), two-phase catalysis (*8*), and industrial applications (*9*) and has led to breakthroughs in the synthesis of polyarylene polymers (*10*).

All of these couplings, however, require one or both of the coupling partners to carry a functional group (halogen, trialkyltin, or borylate). This can require additional reaction steps in the preparation of the starting materials.

Smith and co-workers and Hartwig and co-workers have reported progress toward overcoming this problem. Using transition metal compounds as catalysts, they have prepared aryl and alkyl borylates that can be used in Suzuki couplings of unfunctionalized arenes and alkanes (*11*, *12*). Smith and co-workers showed that several unfunctionalized arenes could be catalytically converted to borane derivatives by activating the aromatic C–H bond and substituting with boron. Cho *et al.* now report several major steps beyond this previous work.

First, their new iridium-based catalyst system gives high yields and high turnovers. The catalyst (see right panel in the figure) is readily synthesized from commercially available starting materials in one step. In the presence of a chelating phosphine (dppe), it can convert arenes with fluoro-, chloro-, and even bromo-substituents to the arylboronate products. The reaction is highly selective for meta substitution (two atoms removed from the halogen group, see the figure), while the halogen group re-

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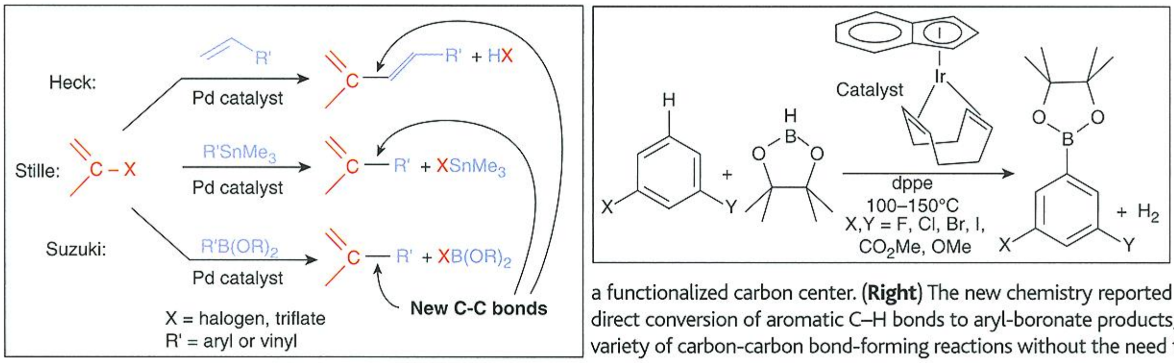

A versatile route to carbon-carbon bonds. (Left) Catalytic formation of carbon-carbon bonds can be accomplished with palladium (Pd) catalysts, but prior methodologies require the existence of a functionalized carbon center. **(Right)** The new chemistry reported by Cho *et al.* (*1*) allows direct conversion of aromatic C–H bonds to aryl-boronate products, which can be used in a variety of carbon-carbon bond-forming reactions without the need for functionalization.

mains intact. Esters and ethers also do not interfere with the reaction. It is remarkable (and fortunate) that no aryl halide-aryl boronate coupling is observed even though both species are present in the reaction mixture.

Second, "tandem reactivity" has been demonstrated by performing the iridium-based borylation of aryl halides in the presence of a palladium catalyst. The iridium catalyst first borylates the aryl halide to give a halo- and boryl-substituted arene. This difunctional arene then undergoes palladium-catalyzed Suzuki coupling with itself, resulting in the formation of a polyphenylene material. This method is likely to increase further the scope for industrial applications of Suzuki coupling.

Third, a further iridium catalyst, derived from the first, can perform borylation of the highly reactive aryl iodides while leaving the aryl-iodine bond intact. The ability to selectively produce aryl boronates with iodide functionality should greatly extend the range of applicability of the Suzuki reaction.

Finally, the authors make a strong case for the presence of Ir(III)/Ir(V) species as intermediates. Further studies will be required, however, to elucidate the detailed mechanism of the arene borylation reaction.

Cho *et al.* describe an important new route to aromatic precursors to carbon-carbon bond formation. The reactions are quite general and selective and are likely to find widespread application in a variety of synthetic processes. The catalysts permit the direct conversion of arene C–H bonds to reactive C-BX$_2$ intermediates without the necessity of initial functionalization of the C–H bond and represent an efficient means for building up organic frameworks in complex molecules.

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PERSPECTIVES: CELL BIOLOGY

Slick Recruitment to the Golgi

Vytas A. Bankaitis

The Golgi complex is the central protein sorting station of the cell. Here, proteins destined for secretion are segregated into vesicles and are transported to the cell surface. As part of its trafficking duties, this organelle must execute a complicated program of vesicle formation and recycling. Vesicle biogenesis first requires the coordinated recruitment to Golgi membranes of the proteins that direct vesicle formation. Complexes of these proteins form vesicle budding machines that transform Golgi membranes with low surface curvatures into highly curved structures. Subsequently, the closely apposed Golgi membrane lipid bilayers positioned at the necks of nascent vesicles resolve in a fission reaction that liberates cargo-laden vesicles from the organelle. The intricacies of this process become particularly pronounced at the trans-Golgi network (TGN) from which are formed distinct vesicle populations destined for the plasma membrane, secretory vesicles, or lysosomes.

How are the TGN membrane domains that are involved in the formation of different vesicle populations segregated? What are the cues for recruiting particular proteins to specific areas of the TGN? What other components must be brought to these domains so that vesicle assembly can be initiated? How are vesiculation reactions limited so that Golgi integrity is preserved? The incisive work of Baron and Malhotra (*1*) on page 325 of this issue yields some fascinating insights. These investigators make a compelling case that diacylglycerol (DAG), a signal-transducing lipid, is essential for recruitment of a vesicle biogenesis factor, protein kinase D (PKD), to mammalian cell TGN membranes so that a specific class of transport vesicle can be formed. These findings uniquely connect a lipid with a protein kinase that participates directly in the budding of TGN-derived vesicles.

PKD consists of two cysteine-rich domains (C1a and C1b), a pleckstrin homology (PH) domain, and a catalytic domain (see the figure). The connection between PKD and the Golgi arose from analyses of how ilimaquinone (a natural product of marine sponges) affects wholesale vesiculation of the Golgi in mammalian cells. Baron and Malhotra discovered that ilimaquinone hyperstimulates PKD, resulting in the inappropriate elevation of Golgi-derived vesicle formation (*2*). In contrast, a reduction in PKD activity results in failure of Golgi tubules to undergo fission and resolution into transport vesicles (*3*). Thus, PKD regulates TGN vesicle formation.

How does cytosolic PKD engage the TGN? Although PKD has a PH domain, this module is not involved in its recruitment by the TGN. Rather, Baron and Malhotra present several lines of biochemical evidence supporting the notion that the C1a domain of PKD binds to DAG and that this binding is a prerequisite for PKD's recruitment to the Golgi. Moreover, they show that compromising DAG production by treating cells with pharmacological agents such as fumonisin B1 or propanolol

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