

C-H bond activation by metal carbene

C-H bonds, alongside with C-C bonds, are the most common chemical bonds that constitute organic molecules. C-H bonds are ubiquitous and they are also very stable. The replacement of the hydrogen atom of the C-H bond with other atom, for example fluorine atom, will significantly change the property of the compounds and possibly afford functionalized organic molecules that are highly useful in the production of medicines or materials. However, because of their inertness, to break C-H bonds usually needs harsh reaction conditions, such as high temperature, strong acid or base, as well as long reaction time. In many cases the other functional groups in a complex molecule cannot tolerate such harsh conditions. More challenging problem is the selectivity. Because organic molecules normally contain many C-H bonds of very similar chemical properties, to selectively break certain C-H bond and functionalize it is a daunting task for a synthetic organic chemist.

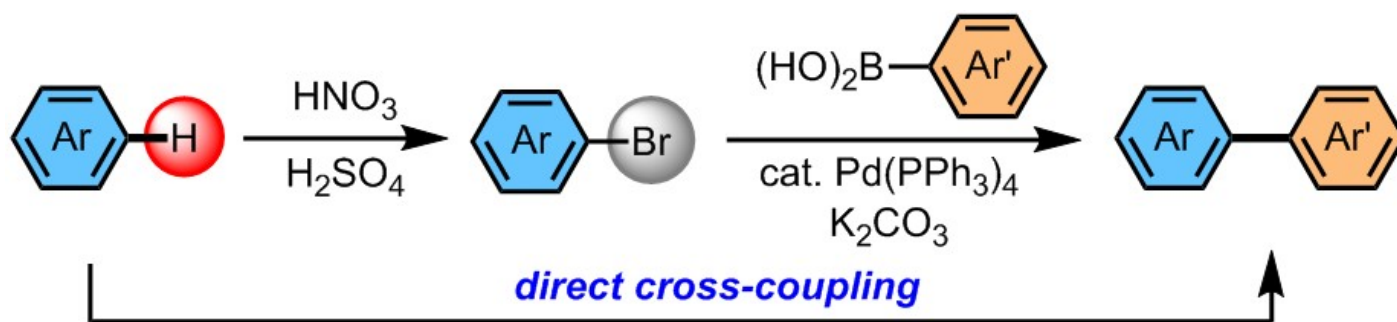


Fig. 1. Production of biphenyl derivatives.

The traditional method to achieve the functionalization of inert C-H bond is to first convert it into a relatively active chemical bond, normally under harsh or rigorous conditions. From the intermediate containing the active chemical bond it would be possible to further synthesize various useful organic molecules by conventional methods. For example, to convert substituted benzene into biphenyl derivatives, one of the methods based on traditional chemical transformation is to first convert substituted benzene into the corresponding bromobenzene through bromination. Subsequently, Suzuki-Miyaura cross-coupling (2010 Nobel prize) with arylboronic acid with palladium catalyst would produce the target molecule. Such transformation, even though highly reliable, requires laborious operations and may produce large amount of pollutants. Obviously, direct C-H bond cross-coupling would be highly desirable (Fig. 1).

To achieve such goal, one has to overcome the obstacles related to the low reactivity and poor selectivity of the C-H bonds. One of the currently widely practiced approaches is to use a directing group, which is pre-installed in the substrate, to coordinate to the transition metal of the catalyst. The metal break the C-H bond in a selective manner to general carbon-metal bond, which is further converted into the target chemical bond, such as C-C bond.

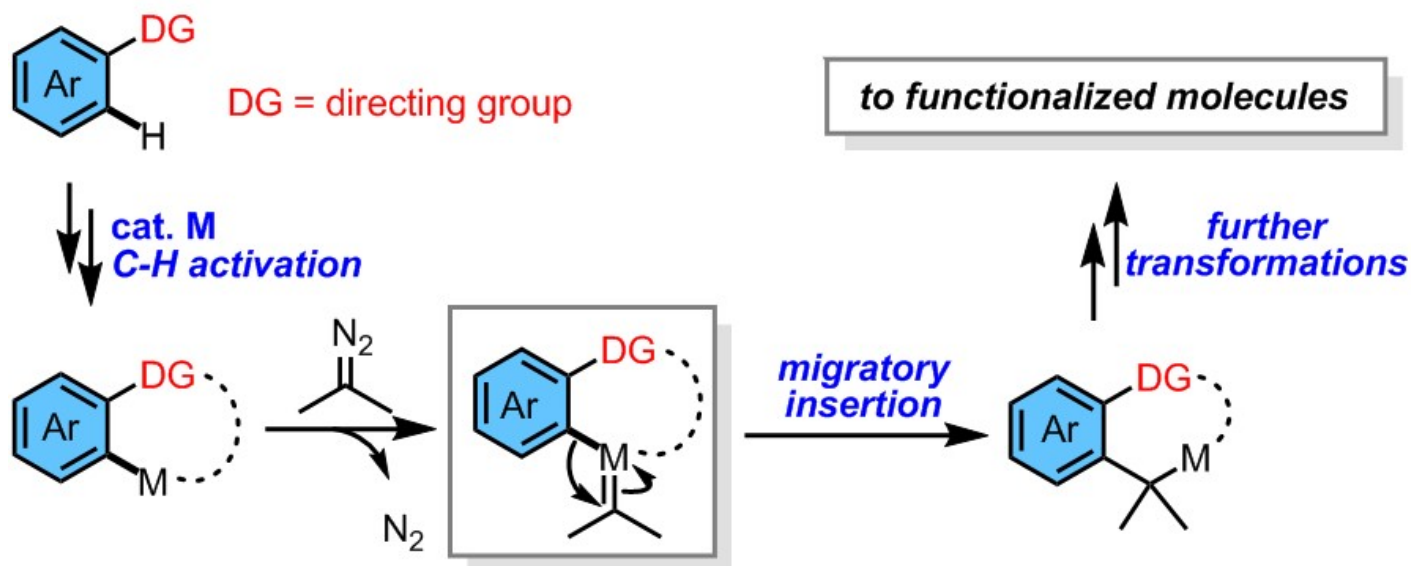


Fig. 2. C-H bond functionalization based on metal carbene migratory insertion.

On the other hand, metal carbenes represent a type of important reactive intermediates in organic chemistry. They are particularly useful in C-C bond forming transformations. In general, diazo compounds are the metal carbene precursors. In the past decade, the metal carbene chemistry has merged with transition-metal-catalyzed cross-couplings, the indispensable transformations for constructing C-C bonds, providing a new type of cross-coupling reactions. Mechanistically, the reactions involve metal carbene migratory insertion as the common key steps in the C-C bond formation. This type of reactions has recently applied to C-H bond functionalizations. As shown in Fig. 2, with the assistance of a directing group, the aromatic C-H bond is broken to generate an organometallic intermediate. This intermediate reacts with diazo substrate to generate a metal carbene species through extrusion of nitrogen gas. Subsequently, migratory insertion occurs to generate a new organometallic species, which further undergo transformations such as protonation, β -H elimination, C-N bond formations and so on, leading to various functionalized molecules. This feature article summarizes the recent developments in this emerging area.

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