Palladium(II) Catalysis

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A New Direction in C–H Alkenylation: Silanol as a Helping Hand**

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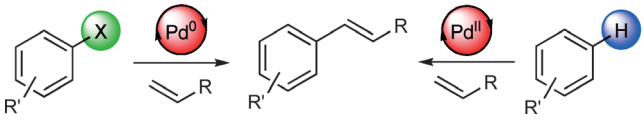
alkenylation · C–H activation · cross-coupling · directing groups · silicon

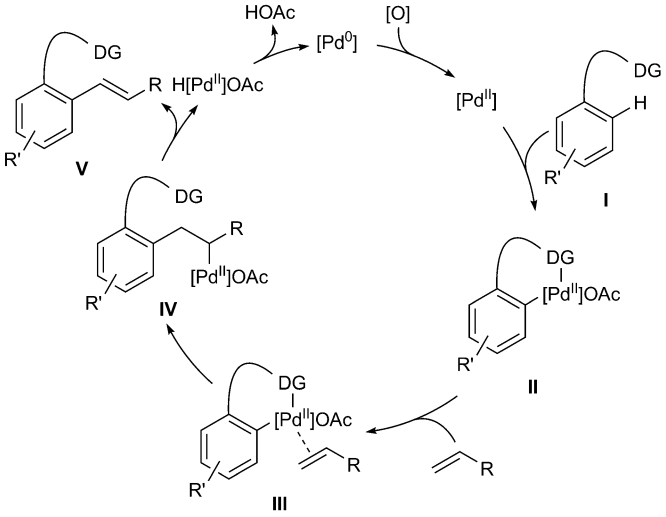
On the tide of progress towards sustainable chemistry,[1] the palladium(II)-catalyzed alkenylation of unfunctionalized arenes through C–H activation is currently garnering tremendous attention because laborious arene prefunctionalization like that required for the palladium(0)-catalyzed Mizoroki–Heck reaction[2] would be or is now no longer required (Scheme 1).[3]



Scheme 1. C–X versus C–H alkenylation (X = halide or triflate).

To selectively address just one out of several C–H bonds is, however, challenging. A directing group[4,5] largely resolves the issues of both regiocontrol and monoselective alkenylation by bringing the transition metal into the proximity of the targeted C–H bond. The palladated arene formed in the directed C–H activation (**I**→**II**, Scheme 2) then enters the generally accepted Mizoroki–Heck mechanism (**II**→**III**→**IV**→**V**). Prominent directing groups employed are aniline-derived amides,[4b] pyridines,[4c] amines,[4d] and carboxylic acids,[4e] but there are limitations in terms of synthetic usefulness. The development of directing groups that either serve as linchpins for subsequent functional-group manipulations or are easy to remove is therefore welcome.

The laboratories of Miura and Carretero reported such C–H alkenylations with the aid of removable directing groups,[6] and Cui and Wu made use of the dual ability of *N*-oxides to act as a directing group and at the same time as an oxidant.[7] The Yu group demonstrated "remote C–H activation" for C–H bonds that are five or six bonds away from the directing atom.[8] This approach offers in a way more flexibility as the carbon skeleton might be constructed prior to the actual cross-coupling.



Scheme 2. Proposed catalytic cycle of the palladium(II)-catalyzed *ortho*-directed C–H alkenylation ([O] = external oxidant and DG = Lewis basic directing group).

The same research group was recently able to extend this strategy to an unprecedented ligand-promoted hydroxy-directed C–H alkenylation (Scheme 3).[9] Even though palladium is known not to be particularly oxophilic, the tertiary hydroxy group functions as a neutral ligand to form a palladium(II) intermediate that is sufficiently electrophilic to activate the C–H bond with perfect regioselectivity (cf. **II** in Scheme 2 with DG = OH). However, the reaction stops at the alkenylation stage in only a few cases, and a palladium(II)-catalyzed oxidative cyclization is usually observed.

All the above-mentioned directing groups are usually covalently connected to the arene through a carbon atom and are therefore part of the molecule's carbon framework. In an alternative approach, a silicon tether offers an expedient twist with several advantages, namely, easy installation, "traceless" cleavage, and conversion into different functional groups. Based on the seminal work of Itami and Yoshida,[10] silicon-tethered pyridines have already been used in directed C–H functionalizations.[11] The combination of Yu's hydroxy-directed C–H alkenylation (Figure 1, left) with the silicon chemistry paved the way to a new family of silanol-based directing groups. The laboratories of Gevorgyan[12] (Figure 1, right) and shortly thereafter Ge[13] (Figure 1, middle) reported

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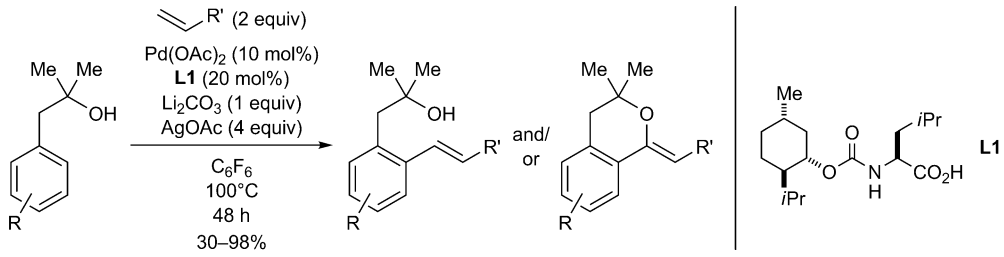


Scheme 3. Hydroxy-directed C–H alkenylation.

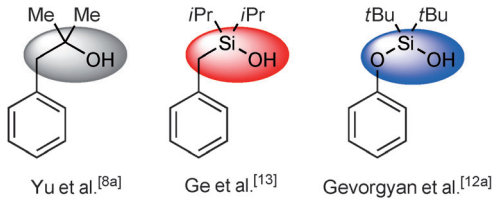
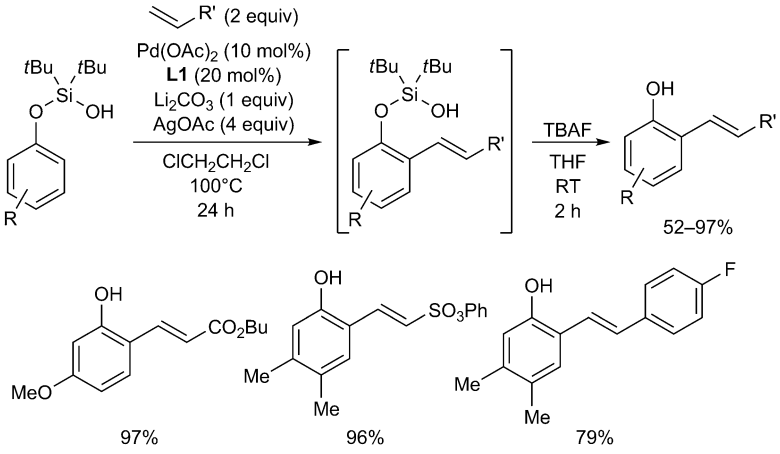


Figure 1. C–OH and Si–OH directing groups.

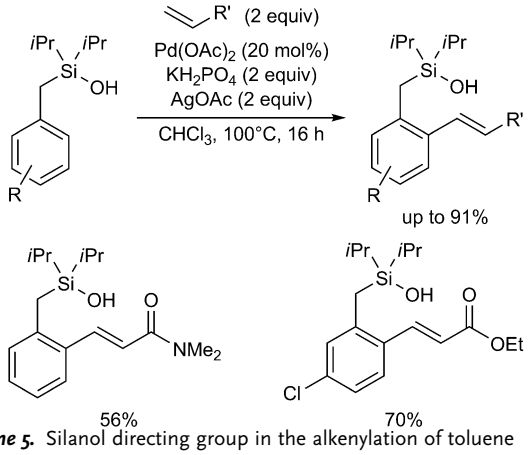
independently the use of Si–OH groups as an alternative to the C–OH group in directed oxidative C–H alkenylation.

Gevorgyan et al. equipped phenols with a silanol group (Scheme 4). They adopted Yu's reaction setup, and the palladium(II)-catalyzed alkenylation proceeded in good to excellent yields; subsequent cyclization was not seen at all.[12] The silanol group was removed with tetrabutylammonium fluoride (TBAF) in a "semi-one-pot" approach to afford *ortho*-alkenylated phenols. Owing to the steric demand of the silicon atom decorated with two *tert*-butyl groups, the regioselectivity was perfect even for unsymmetrically substituted phenols. Not surprisingly, electron-rich arenes and electron-poor alkenes were the optimal combination.

Ge et al. described a ligand-free palladium(II)-catalyzed alkenylation of toluene-derived silanols in a related paper (Scheme 5).[13] Yields are generally good, and the scope ranges from electron-rich to -poor arenes; electron-rich alkenes showed low reactivity. Smooth "deprotection" of the alkenylated benzylic silanols yielded the parent toluenes, again in a one-pot procedure (not shown). Demonstration as



Scheme 4. Silanol directing group in the alkenylation of phenols.



Scheme 5. Silanol directing group in the alkenylation of toluene derivatives.

to whether these benzylic silanols participate in Hiyama–Denmark-type cross-couplings will be the next logical step.

These recent developments in the topical area of direct/directed C–H functionalization nicely showcase the benefits of more versatile directing groups. It is clear though that stoichiometric use of such tools is only justifiable as long as known catalytic systems are not completely selective themselves.

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