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Palladium(II)-Catalyzed Arylation of Unactivated C(sp^3)-H Bonds by Using 2,1,3-Benzoselenadiazole-4-amine as Directing Ligand

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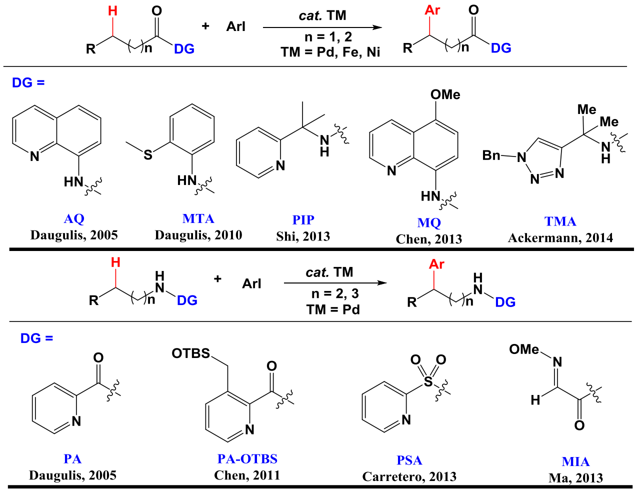
ABSTRACT

A modified bidentate directing ligand derived from 2,1,3-benzoselenadiazole (BSeD) was designed and synthesized. It exhibited high regioselectivity in the catalytic activation of unactivated C(sp^3)-H bonds with aryl iodides in the presence of palladium catalyst in yields up to 94%.

Activation and functionalization of C-H bonds to form C-C or C-X (X=O, N, S… etc.) bonds has been one of the most hot spots in the research field of organic synthesis.[1] Excellent synthetic methods based on the functionalization of C(sp^2)-H bonds of arenes and heteroarenes have been becoming readily available.[2] In the induction of this trend, the selective functionalization of C(sp^3)-H bonds to construct stereogenic centers and create complex structures would be an important and useful advance.[3] While providing straightforward and operationally economical solutions for target-oriented synthesis, C(sp^3)-H functionalization could also significantly expand current strategies for diversity-oriented synthesis in medicinal chemistry research.[4] Compared with C(sp^2)-H bond activation, however, the catalytic functionalization of C(sp^3)-H bonds,[5,6] especially unactivated methylene C(sp^3)-H bonds, remains an important fundamental challenge.

Because of the potential competing β-hydride elimination from cyclometallates, C(sp^3)-H bonds activation is somewhat limited to the functionalization of *tert*-butyl groups. On the other hand, methylene C−H bonds are significantly more resistant to Pd insertion than primary C−H bonds because they are more sterically hindered.[7] Therefore, a number of ligand directing strategies[7,8] have been successfully developed for C(sp^3)-H activation.[9] For example, the seminal work of Daugulis and co-workers on the palladium-catalyzed arylation of secondary C(sp^3)-H bonds with 8-aminoquinoline-derived *N,N*-bidentate directing group[10] has inspired several research groups to use this type of auxiliary to develop a diverse collection of novel C(sp^3)-H functionalization reactions (Scheme 1).[11] Continually, an elegant example of ligand-enabled C-H arylation of methylene C(sp^3)-H bonds was reported by Yu and coworkers.[12] Moreover, this chemistry has been successfully applied in the total synthesis of natural products such as pipercyclobutanamide.[13]



Scheme 1 Some Examples of Pd-catalyzed direct C(sp^3)–H activation assisted by bidentate auxiliaries.

On the other hand, 2,1,3-benzoselenadiazole (BSeD) compounds have served as common and important structural motifs, which are widely found in conjugated polymers, organic solar cells, fluorescent colorants, and bioactive indicators (Figure

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