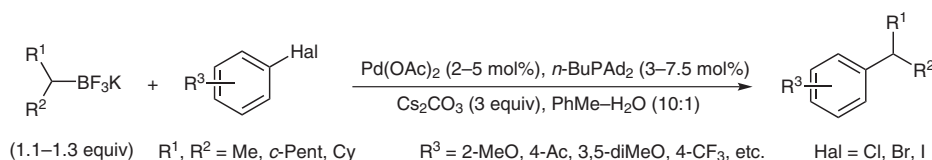


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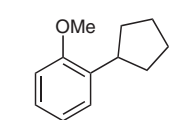
Efficient Cross-Coupling of Secondary Alkyltrifluoroborates with Aryl Chlorides – Reaction Discovery Using Parallel Microscale Experimentation

J. Am. Chem. Soc. **2008**, *130*, 9257-9259.

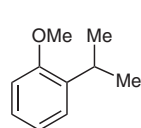
Cross-Coupling of Secondary Alkyltrifluoroborates with Aryl Chlorides



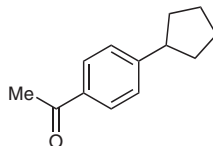
Selected examples:



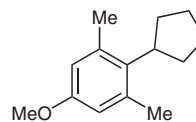
X = Cl, 87% yield



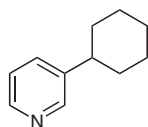
X = Cl, 78% yield



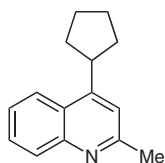
X = Cl, 51% yield



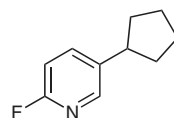
X = Br, 77% yield



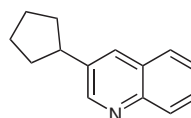
X = Cl, 87% yield



X = Cl, 88% yield



X = Cl, 77% yield



X = Br, 87% yield

Significance: This valuable synthetic method demonstrates the usefulness of the parallel microscale experimentation approach in the development of new methodology in synthetic chemistry. Conditions for a smooth Pd-catalyzed cross-coupling between secondary alkyltrifluoroborates and aryl or heteroaryl chlorides have been found after the screening of a number of phosphine ligands. The parallel microscale experimentation is proved to be a very promising method of investigation in synthetic chemistry that will find more and more applications not only in industry, but also in the academic research.

Comment: The experimentation was performed in 10 mmol scale in a 96-plate reactor, and 12 ligands were screened for each substrate, so that the optimization required much less time compared to standard optimization technique. The cross-coupling of isopropyl organometallics is often complicated by the formation of a linear product. As it is shown by the given experimental data, this side reaction takes place to a various extent with different substrate–catalyst pairs and the results are often difficult to predict. That makes a fast screening procedure for cross-coupling reactions quite desirable.

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