

The Laboratory for Organic and Inorganic Chemistry

Final PhD Seminar

Monday, June 19th at 11:30 in the Seminar Room

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Gandelman Group

On the Topic of:

**New approaches in synthesis of chiral
halogen containing compounds**

New approaches in synthesis of chiral halogen containing compounds

Organohalides are important building blocks in organic synthesis. Previously in our group we developed efficient, robust, and general approach to geminal dihaloalkanes via decarboxylative iodination.^[1] Having an efficient synthetic method in hand, we examined application of these polyfunctional compounds as electrophiles in Suzuki cross-coupling reactions. Namely, we demonstrated selective two-step one pot sequential cross-coupling of 1,1-(chloro)iodoalkanes to prepare chiral secondary alkanes.^[2] Interestingly, the first cross-coupling process chemoselectively furnished secondary alkyl chlorides; however, it was obtained as a racemic mixture of products.

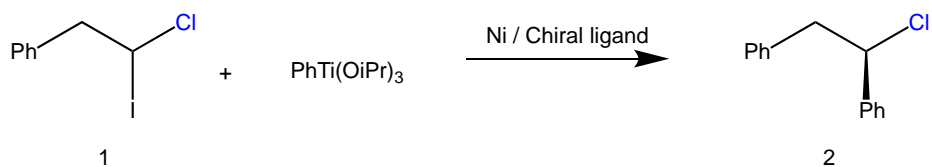
My PhD research is inspired by these previous results. By using titanium(IV) nucleophiles, we succeeded to obtain chiral chlorides from 1,1-(chloro)iodoalkanes by Ni-catalyzed cross-coupling reaction. Although the enantioselectivity of the process was moderate (up to 63% ee), it represents a first example of asymmetric synthesis of chiral chlorides via cross-coupling reaction. Further improvements of this process are under progress in our lab.

My research is also focused on the development of new approaches to the catalytic asymmetric synthesis of fluoroalkanes. Organic fluorides have found broad and spectacular applications in various fields of chemistry and chemical materials including pharmaceuticals, drug discovery and agrichemicals.

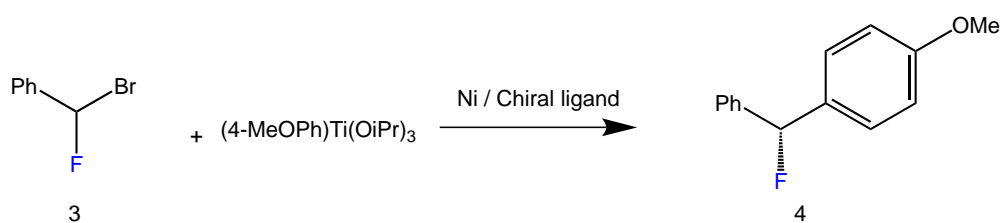
We have prepared geminal (bromo)fluoroalkanes and examined them as electrophiles in cross-coupling reactions with organotitanium nucleophiles. The reaction proceeds with excellent yield and good enantioselectivity. Based on this approach, we have developed a straightforward method to the synthesis of chiral fluorinated benzhydryls which are of interest as potentially bioactive motifs.

Lastly, we have designed and developed a novel approach to the synthesis of α -CF₃-substituted ethers via Ni-catalyzed reductive cross-coupling reaction. This approach allowed for high functional group tolerance and atom-economy comparing to previously demonstrated Hiyama cross-coupling method. The target compounds could be synthesized with excellent yield and high enantioselectivity. Preliminary investigation of the mechanism of this reaction revealed a ligand dependent mechanism under our reaction conditions.

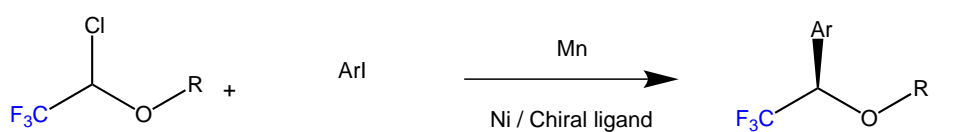




70% yield, 63% ee



91% yield, 80% ee



up to 92% yield, 94% ee

[1] *Adv. Synth. Catal.* **2011**, 353, 1438 – 1442.

[2] *Chem. Sci.* **2016**, 7, 2762–2767.

