Organobismuths – A Powerful Pnictogen in Modern Organic Synthesis

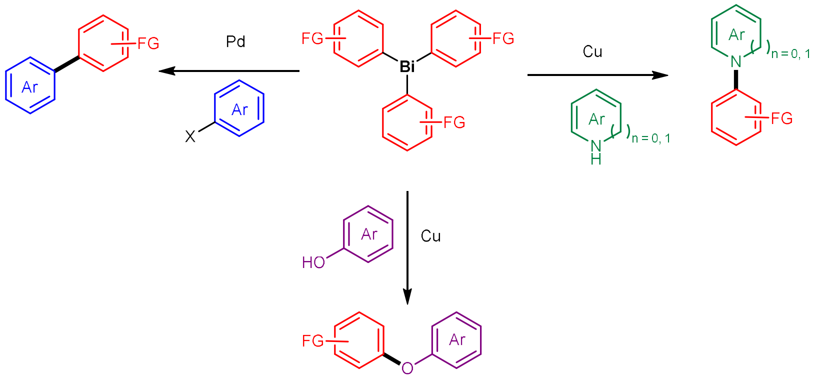
Reported by Zachary M. Firestein November 2, 2021

Classical Uses of Bismuth Reagents

The use of bismuth reagents in organic synthesis has been an underexplored area of study until just the last few decades. Classically utilized as a Lewis acid additive, inorganic Bi(III) salts have found applications in the activation of carbonyl compounds, while Bi(V) compounds have been used to enable oxidations and serve as industrial catalysts in the production of feedstock chemicals. In the 1980s, Barton demonstrated an arylation utilizing organobismuth(V) compounds that afforded aryl ethers, while Wada and Dubac pursued Barbier-type allylations utilizing organobismuth(III) reagents.[1] At the end of that decade, Suzuki investigated bismothonium salts and ylides that could serve as competent electrophiles and carbene precursors, respectively, but this work did not map on to a great deficit in the chemical space of that time.[2] When compared to their phosphonium counterparts, few advances have been made in recent years.

Cross-Coupling *via* Bismuthanes for Orthogonal C, N, O Arylation and Alkylation

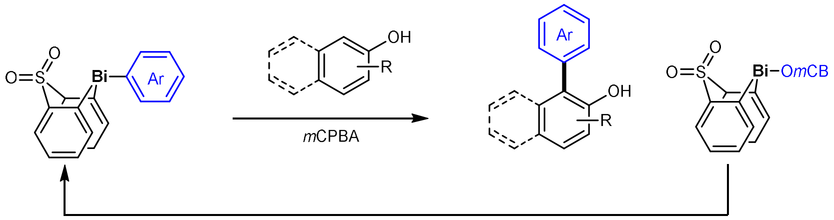
More modern techniques utilizing organobismuth reagents have been developed that have added to a vast chemical lexicon of cross-coupling reactions. Stemming largely from Barton's arylations involving organobismuth(V) complexes, similar modes of reactivity could be found using triarylbismuthanes as transmetallating agents in palladium and copper-based cross couplings (**Scheme 1**).[3] Triarylbismuthanes are conveniently prepared from inexpensive precursors, are air, moisture, and column stable, and can demonstrate a wide range of functional group tolerance. Utilizing copper mediated Barton or Ullman type couplings, O- and *N*-arylations are shown on an array of phenols and aliphatic alcohols, as well as a variety of heterocyclic amines. Switching to a Pd(0) conditions similar to Suzuki-Miyaura, sp^2-sp^2 couplings can be accomplished without the use of boronic acids. Additionally, sp^3-S coupling has recently



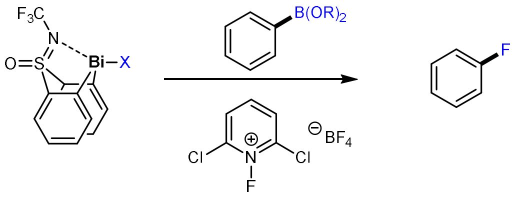
Scheme 1 – *C*-, *N*-, and *O*-Arylation *via* Triarylbismuthane Reagent been demonstrated for the first time utilizing trialkylbismuthanes, and a Liebeskind-Srogl type cross-coupling has been accomplished to convert benzazole-2-thiones to the corresponding 2-arylbenzazoles by Pd(0) catalysis with a copper additive.[4,5]

Tethered Organobismacycles – Catalysis and Modular Arylation

A valid concern for any chemist seeking to utilize arylbismuthanes for use in organic synthesis is the atom economy of the reagents themselves. Cornella's lab has recently developed a new type of modular bismacycle that seeks to ameliorate this issue (**Scheme 2**).[6] Utilizing a tethered diaryl backbone, a single transferrable aryl group can be loaded on to a Bi(III) precursor. This aryl bismacycle is capable of *ortho*-arylation of phenols and naphthols, and the byproduct is recyclable back to the precursor. Some preliminary mechanistic studies have shown that this arylation proceeds *via* an $\mathrm{S_E}$Ar-type mechanism, which is highlighted by its orthogonality to traditional cross-coupling methods through aryl halides. Inspired by others, Ball and coworkers sought out the use of organobismuth complexes as a capable main-group catalyst, and a rationally designed bismacycle was developed for the catalytic fluorination of aryl boronic esters (**Scheme 3**).[7]



Scheme 2 – Cornella's Modular Bismacycle for *ortho*-arylation



Scheme 3 – Ball's Organobismuth Fluorination Catalyst

References

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