Preparation of 6-Aryl- and 6-Heteroarylpurines by [2+2+2]-Cyclotrimerizations

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The aim of my project was to synthesize new potentially biologically active arylpurines by transition metal catalyzed or mediated [2+2+2]-cyclotrimerization reactions. This approach should enable to assemble various structural motives attached to the purine skeleton. The main targets were 6-arylpurines.

6-Arylpurine derivatives have diverse types of a biological activity: some substituted 6-arylpurine bases are antagonists of corticotropin-releasing hormone or possess antimycobacterial and antibacterial activity, while 6-arylpurine ribonucleosides are potent cytostatics. These facts explain, why it is worth being interested in synthesis of this class of compounds.

Until now 6-arylpurines have been mostly prepared by cross-coupling reactions of 6-halopurines with various organometallic compounds, but this approach is limited by factors like availability, reactivity and stability of the corresponding arylmetals.

The synthetic strategy used in my project was based on a transition metal catalyzed or mediated cyclotrimerization of alkynes. Generally, these methods enable to assemble aromatic and heteroaromatic compounds from easily accessible starting materials (alkynes, nitriles) under neutral reaction conditions. Advantage of the cyclotrimerization reactions is in capability of connecting variously substituted alkynes into highly substituted arenes. In the same manner can be prepared substituted pyridines by cocyclotrimerizations of alkynes with nitriles.

My project was divided into the following three sections: a) catalytic cyclotrimerization of 6-alkynylpurines with diynes, b) stoichiometric cycloaddition of zirconacyclopentadienes with 6-alkynylpurines, and c) catalytic cocyclotrimerization of 6-diynylpurines with nitriles. Essential part of this project was testing of biological activity of the obtained products with respect to the cytostatic activity.