# Dihydropyrrolo[1,2-*b*]pyrazoles:

## Synthesis of new derivatives and their biological evaluation

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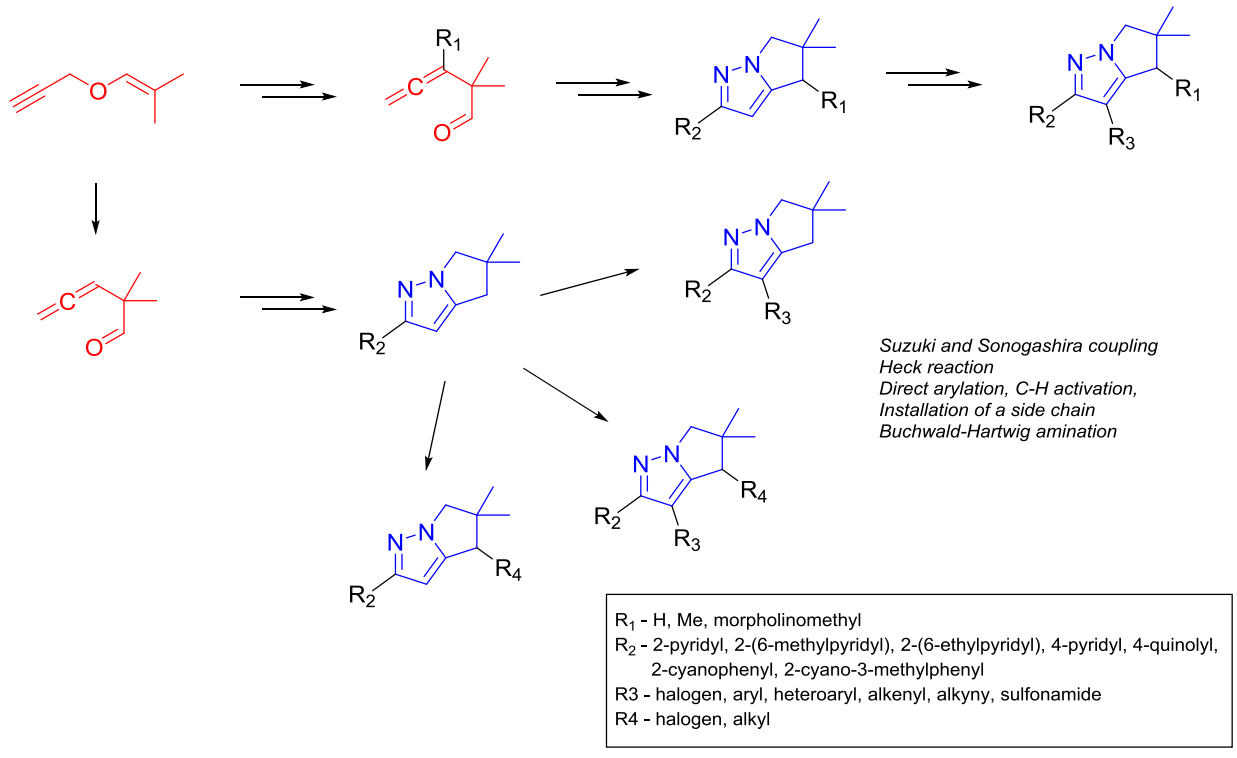
During the last two decades, compounds with dihydropyrrolo[1,2-*b*]pyrazole (DPP) core showed promising biological activity. Sawyer published series of papers dealing with this field of organic chemistry.[1-5] These DPP derivatives are inhibitors of transforming growth factor β type I (also known as ALK5) of kinase receptor domain. TGF-β plays an important role in many pathological states including inflammation, fibrosis, cancer, asthma and cardiovascular diseases.[6-11]

In my talk I will present our recent work aimed at synthesis of some analogues of these compounds with DPP core bearing 2-pyridyl, 2-(6-methylpyridyl), 2-(6-ethylpyridyl), 4-pyridyl, 4-quinolinyl, 2-cyanophenyl or 2-cyano-3-methylphenyl moiety at position 2. Homoallenyl aldehyde (with H, alkyl or amine substitution at position 3), synthesized according to our improved procedure,[12] is a key intermediate for the creation of DPP core. Various palladium catalyzed coupling reactions (Suzuki, Sonogashira, Heck, direct arylation and C-H activation) are shown in the following schemes. Conditions for substitution of position 4 were discovered and they will be discuss as well. Based on some docking studies a series of compounds were selected for biological screening. In few cases, these tests shown a selective activity as inhibitors of ALK5 kinase (the best compound around 100 nM) and for some other derivatives lower activity in inhibition of CDK2/E was also observed. Biological testing of some recently prepared compounds is ongoing and it will be also discuss in my talk.




Scheme 1.

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