Carborane-Based Compounds: Potential and Emerging Applications in Medicine

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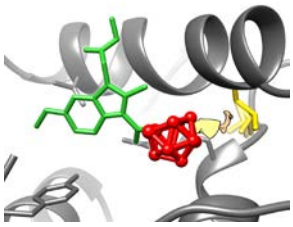
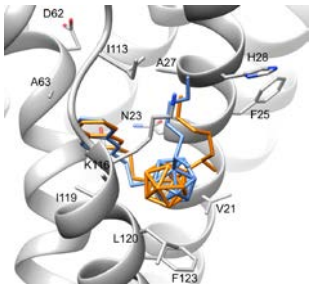
Since the discovery of polyhedral carboranes more than fifty years ago, their potential for various applications has been unlocked. Mainly, their use as pharmacophores is due to their remarkable biological stability and hydrophobicity. The cage framework of these clusters can be easily modified with a variety of substituents both at the carbon and at the boron atoms. It has been shown that the implementation of the carboranyl moiety, as a phenyl mimetic, in biologically active molecules results in compounds that can exhibit improved biological stability and activity in comparison to their generic paradigms. However, up to now, the use of carboranes as pharmacophores is limited to just a few examples.[1] Our research focuses on several types of enzyme inhibitors, such as cyclooxygenase (COX) or lipoxygenase (LOX) inhibitors.



A highly coveted approach in the design of novel nonsteroidal anti-inflammatory drugs that are applied in the treatment of various inflammatory processes is achieving cyclooxygenase (COX) 2 selectivity. By implementing a carboranyl moiety in the structures of known COX inhibitors more selective and robust COX-2 inhibitors were obtained.[2]

5-Lipoxygenase (5-LOX) is an enzyme of the extracellular matrix and plays a role in increased metastasis and angiogenesis. Numerous reports show the overexpression of 5-LOX in several cancer cell lines. For the activation of 5-LOX, the 5-LOX-activating protein (FLAP) is necessary.[3] Therefore, inhibition of 5-LOX or FLAP could inhibit tumour growth and angiogenesis. Replacement of phenyl rings in selected 5-LOX inhibitors by carboranes resulted in a similar enzymatic inhibitory behaviour but markedly increased cytotoxicity against several melanoma and colon cancer cell lines.[4]



Selected examples also for other biological targets[5] will be presented.

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