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Synthesis and MMP inhibition studies of novel triazolylmethyl aziridines and azetidines

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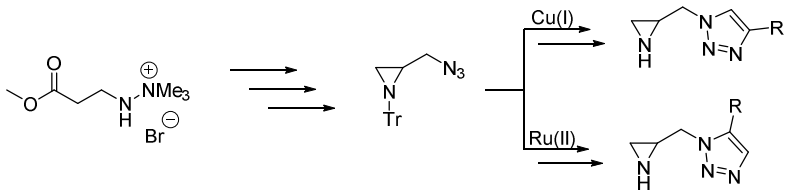
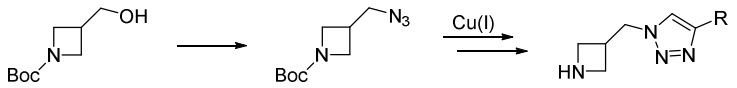
Matrix metalloproteinases (MMPs) are zinc-dependent endopeptidases that are responsible for cleavage of extracellular matrix proteins such as collagen, gelatin, elastin and casein. Because of their effect on both physiological and pathological processes, MMPs have become interesting targets for treatment of cancer. In addition, it is known that MMP-2 has the most important impact to tumour growth [1].

We have previously reported promising results for aziridine derivatives with 1,4-disubstituted 1,2,3-triazole in the side chain as a new class of MMP-2 inhibitors [2,3]. Hence, we describe here an expansion of aziridine series by preparing both 1,5- and 1,4-disubstituted 1,2,3-triazole derivatives. Also azetidine-triazole conjugates were prepared.

The syntheses were realized by transition metal catalyzed azide-alkyne cycloaddition reactions (CuAAC or RuAAC) with good to excellent yields. It is the first time when RuAAC has been used with aziridine containing substrates.





The products acting as selective MMP-2 inhibitors were found among aziridine 1,4-disubstited 1,2,3-triazole conjugates bearing relatively lipophilic side chain.

References

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