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New vitamin B_{12} derivatives activates sGC

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Background

Protoporphyrin IX (PPIX) was shown to strongly activate *in vitro* the soluble guanylate cyclase enzyme (sGC), which makes it an interesting drug candidate for treatment of hypertension [1,2]. In order to overcome the problem of PPIX poor bioavailability (especially in the case of oral administration), we decided to exploit the specific uptake pathway of vitamin B_{12}, which was frequently used for delivering biologically active substances from the digestive system into the body cells. To this end, we embarked on the synthesis of a series of hybrid molecules, containing PPIX and vitamin B_{12} moieties, linked *via* chains of different length and chemical character [3].

Methods and results

Our synthetic approach is based on the synthesis of linking molecules containing a primary -NH_2 group and -N_3 or alkyne group at the other end. Amine functionality allows us to connect these linkers to vitamin B_{12}, and to PPIX, finally, the union of the two parts is possible using Cu-catalyzed azide alkyne cycloaddition (the "click reaction") [4].

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