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DIZAJN I SINTEZA MANOZILIRANIH FEROCENSKIH DERIVATA DESMURAMIL-PEPTIDA

DESIGN AND SYNTHESIS OF MANNOSYLATED FERROCENE DERIVATIVES OF DESMURAMYL PEPTIDES

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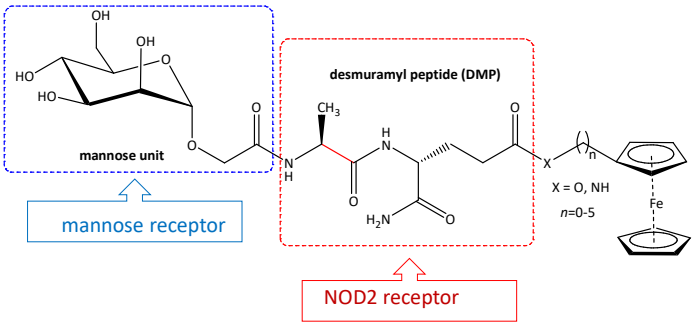
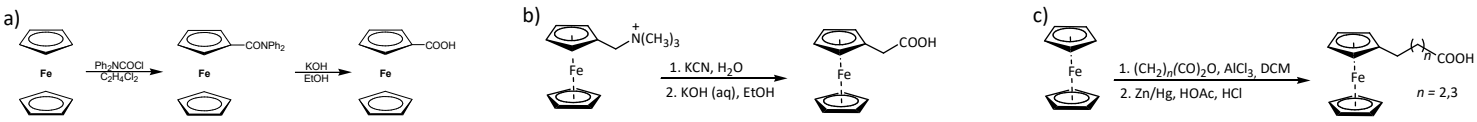
INTRODUCTION

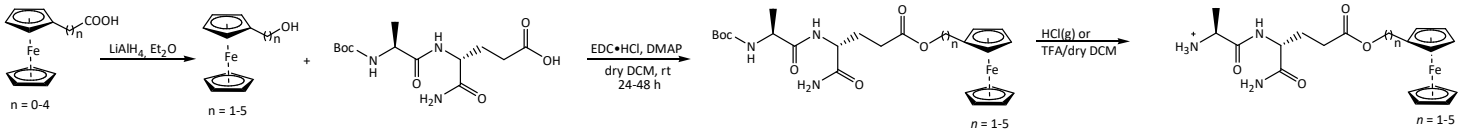
Muramyl dipeptide (MDP, *N*-acetylmuramyl-L-alanyl-D-isoglutamine) is the smallest peptidoglycan fragment capable to trigger the immune response. MDP acts as a pathogen-associated molecular pattern and activates the NOD2 receptor [1]. The main parameter for the improvement of NOD2 agonistic properties is increased lipophilicity. Mannose receptors presented on immunocompetent cells are pattern-recognition receptors, as well as NOD2, and consequently they can affect the immune reactions [2]. Therefore, we present the design and synthesis of mannosylated desmuramyl peptides containing ferrocene lipophilic substituents attached at D-isoglutamine of dipeptide pharmacophore through ester or amide bond. Alkyl spacers of different lengths are inserted between peptide and ferrocene unit to further increase lipophilicity of the synthesized compounds.



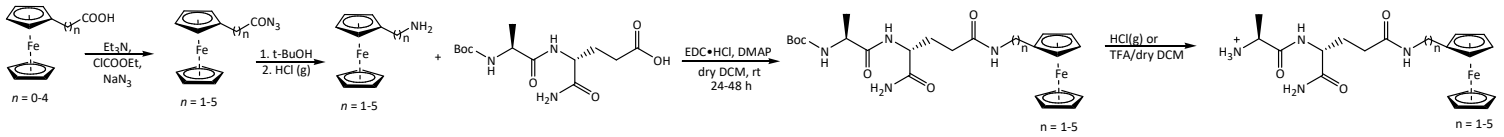
DESIGN AND SYNTHESIS



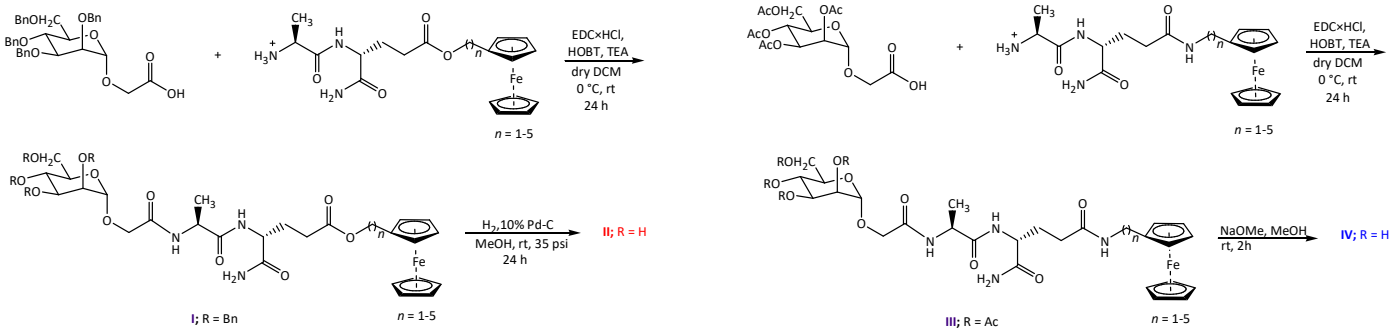
Scheme 1. Preparation of ferrocene acids



Scheme 2. Preparation of desmuramyl peptides containing ester ferrocene substituent



Scheme 3. Preparation of desmuramyl peptides containing amide ferrocene substituent



Scheme 4. Mannosylation of ferrocene desmuramyl peptides

CONCLUSION

Efficient synthetic routes for the preparation of mannosylated ferrocene derivatives of desmuramyl peptides have been developed in order to evaluate the immunomodulating properties of synthesized compounds in different *in vitro* models.

References:
[1] A. Maršavelski, M. Paurević, R. Ribić, *Org. Biomol. Chem.* 19(32) (2021) 7001.
[2] R. Ribić, M. Paurević, S. Tomić, *Croat. Chem. Acta* 92 (2019) 153.

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