

SYNTHESIS OF ENEDIYNE PEPTIDOMIMETICS BY PASSERINI REACTION

SINTEZA ENEDIJSKIH PEPTIDOMIMETIKA PASSERINIJEVOM REAKCIJOM

Mladena Glavaš, Matija Gredičak, Ivanka Jerić

Division of Organic Chemistry and Biochemistry, Ruđer Bošković Institute, Bijenička cesta 54, 10000 Zagreb, Croatia

E-mail: mglavas@irb.hr

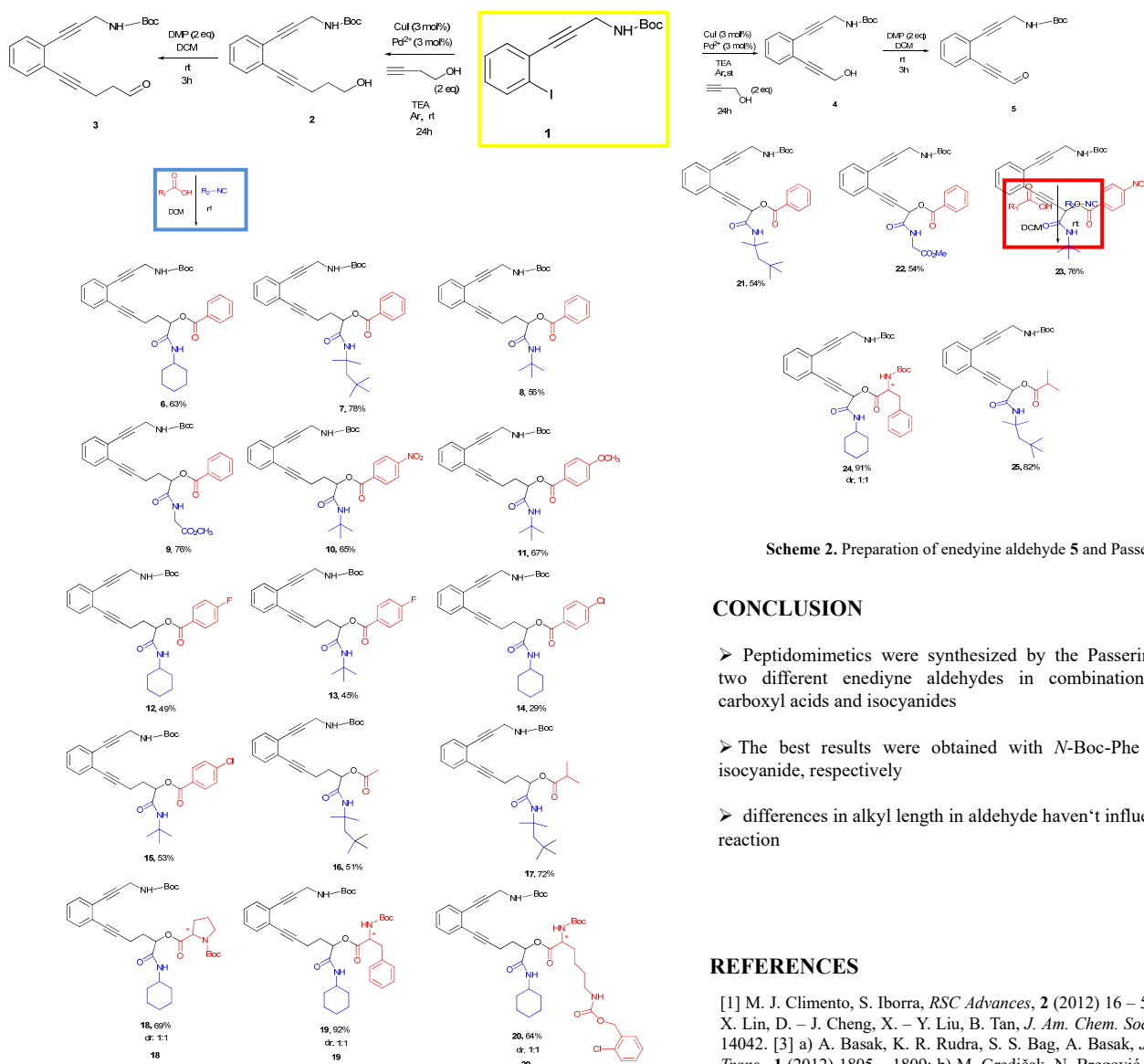
INTRODUCTION

Chemical synthesis performed through one-pot mode represents a significant area of organic chemistry. [1] Such reactions, known as multicomponent reactions comprise three or more starting reagents and give a single product. The main advantage of multicomponent reactions are an easy access to libraries of complex and structurally diverse compounds starting from relatively simple components. Isocyanide-based multicomponent reactions, e.g. Passerini and Ugi reactions are of special importance, because they provide diverse peptide-like compounds. The Passerini reaction involves coupling of an aldehyde, a carboxylic acid and an isocyanide in a nonpolar solvent. [2]

Herein, we report the synthesis of enediyne peptidomimetics by the Passerini reaction. Enediyne structural motif found in natural products with anticancer activity was shown to induce β -turn conformation when incorporated into peptides. [3] Therefore, we prepared two aldehydes comprising aromatic enediyne moiety and used them in the Passerini reaction with aromatic or aliphatic acids and commercially available isocyanides.

SYNTHESIS

Enediyne aldehydes **22** and **23** were prepared by the Sonogashira reaction of **21** with propargyl alcohol or 3-buten-1-ol, and subsequent oxidation with Dess-Martin periodinane (Scheme 1 and Scheme 2). The Passerini reaction was performed in dichloromethane at room temperature with 2.1 or 3.1 equiv. of acid and isocyanide.



Scheme 2. Preparation of enediyne aldehyde **5** and Passerini products **21** – **25**.

CONCLUSION

➤ Peptidomimetics were synthesized by the Passerini reaction from two different enediyne aldehydes in combination with different carboxylic acids and isocyanides

➤ The best results were obtained with *N*-Boc-Phe and cyclohexyl isocyanide, respectively

➤ differences in alkyl length in aldehyde haven't influence on Passerini reaction

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Scheme 1. Preparation of enediyne aldehyde **3** and Passerini products **6** – **20**.