Synthetic Strategies of Novel Betulin-1,2,3-Triazole Conjugates

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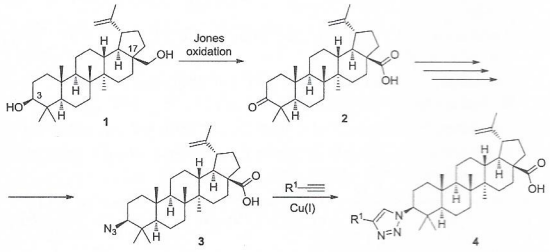
INTRODUCTION

Betulin is a naturally occurring triterpene found in the outer layer of birch bark. Since these tree species is very commonly found in Latvia and betulin is easy to isolate, our research group has taken interest in the synthesis and biological properties of its derivatives. In addition, betulin itself has shown anti-HIV-activity and certain cytotoxicity [1].

RESULTS AND DISCUSSIONS

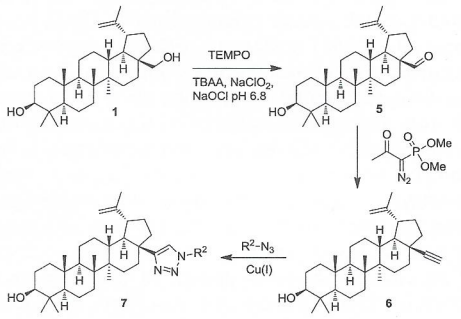
Herein, we report an approach towards the synthesis of triazole conjugates with betulin, namely, in positions C(3) and C(17).

Betulin (**1**) was used as a starting material and was extracted from the birch bark. The synthesis process started with Jones oxidation of betulonic acid (**2**) and was continued by its reductive amination [2] to 3-deoxy-3-aminobetulinic acid as a diastereomeric mixture. 3-Deoxy-3-azidobetulinic (**3**) acid was synthesized as a precursor of the final product in the subsequent diazotransfer reaction (Scheme 1).



Scheme 1. General route for the preparation of betulinic acid-1,2,3-triazole conjugates.

The key intermediate of the second synthetic strategy was betulinaldehyde (**5**). Reaction with Ohira-Bestmann reagent transformed the aldehyde group to terminal alkyne (**6**). Next, CuAAC reactions with various azides gave target compounds **7** (Scheme 2).



Scheme 2. General route for the preparation of 1,2,3-triazole conjugates in the betulin at C(17).

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