ABSTRACT

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Bisphosphonates (BPs) are limited in therapeutical use because of their poor bioavailability after oral administration. Typically less than 1% is absorbed. Second limitation of treatment connected with BPs is the incidence of upper gastrointestinal tract irritation (2-10% cases). The aim of this work was the synthesis of new derivatives of aminobisphosphonate alendronate (ALN) with improved pharmacological properties which could be potentially used as a prodrug. ALN is used in clinical practice primarily to treat postmenopausal osteoporosis.

The synthetic route leading to protected aminobisphosphonate derived from ALN was revised and optimized for large scale synthesis. The products of this route were needed for continuation in the preparation of new derivatives.

Copper catalyzed ''click'' reaction of terminal alkyne and azidoBP was used with different starting materials to get a new possible prodrugs. Reaction of propargyl alcohol and azidoBP with Cu powder as a catalyst was successful and led to heterocyclic derivative of protected BP which is the important model compound for further studies.

Additionally, the new design of conjugation of protected BP with deoxycholic acid was suggested in order to get new possible compound. Finally, novel deoxycholic acid-protected ALN conjugate was synthesized. However, complete deprotection of both synthesized final products wasn't realized.

Main benefits of presented work are the experimental part and the proposed synthetic routes as well as review of mechanism of action and traditional uses and novel applications of BPs. Nevertheless, the topic of synthesis of new derivatives of BPs is really vast and remains opened for further development.