IL-28

Phosphinic acid-based enzyme inhibitors

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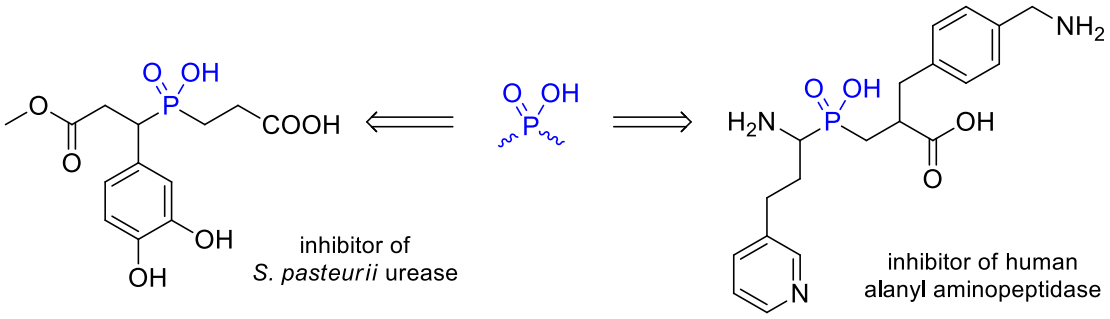
The phosphinic acid functionality has emerged an invaluable scaffold for the construction of biologically active compounds, in particular, enzyme inhibitors. The utility of phosphinates originates from favorable structural and physicochemical properties, and synthetic feasibility. Compared with the more explored phosphonic acids, the main advantages of phosphinic counterparts involve: (1) enhanced steric and electronic similarities to the enzymatic substrates in the high energy transition states and (2) the opportunity of two-directional structural optimization.

Current achievements concerning preparation and applications of phosphinic acids as inhibitors of hydrolases will be presented. Synthetic approaches to catechol- and cinnamate-based inhibitors of ureases [1], and dipeptide analog inhibitors of metalloaminopeptidases [2], with the activity of the target compounds, will be discussed in further details.



Scheme 1. Exemplified phosphinic acid inhibitors of bacterial ureases and metalloaminopeptidases.

Acknowledgments. The work is supported by the National Science Centre, Poland, Grant No. 2018/31/B/NZ6/02017.

References

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[2] S. Vassiliou, E. Węglarz-Tomczak, Ł. Berlicki, M. Pawełczak, B. Nocek, R. Mulligan, A. Joachimiak, A. Mucha, *J. Med. Chem.*, **2014**, *57*, 8140-8151.