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α -(N-Benzylamino)benzylphosphonic Acids: Stereoselectivity of Binding to Prostatic Acid Phosphatase

O. I. Kolodyazhnyi^a; A. I. Vovk^a; I. M. Mischenko^a; V. Yu. Tanchuk^a; G. A. Kachkovskii^a; S. Yu. Sheiko^a; V. P. Kukhar^a

^a Institute of Bioorganic Chemistry and Petrochemistry, NAS of Ukraine, Kyiv, Ukraine

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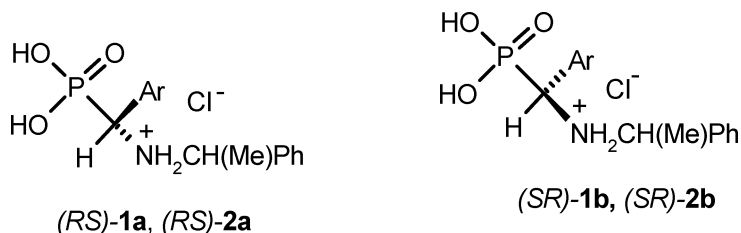
O. I. Kolodyazhnyi, A. I. Vovk, I. M. Mischenko, V. Yu. Tanchuk, G. A. Kachkovskii, S. Yu. Sheiko, and V. P. Kukhar

Institute of Bioorganic Chemistry and Petrochemistry, NAS of Ukraine, Kyiv, Ukraine

The stereoselectivity of the binding of α -(N-benzylamines)benzylphosphonic acids to the human prostatic acid phosphatase was studied. The mechanisms of stereospecificity of prostatic acid phosphatase inhibition by α -(N-benzylamino)benzylphosphonic acids are discussed.

Keywords α -(N-benzylamino) benzylphosphonic acids; prostatic acid phosphatase inhibitors; stereospecificity of phosphatase inhibition

α -(N-Benzylamino) benzylphosphonic acids have been shown to be a potent inhibitors exhibiting high specificity toward acid phosphatase from human prostate.¹ On the previous ICPC we have reported the asymmetric synthesis of (*R*)- and (*S*)- α -(N-benzylamino)-benzylphosphonic acids and (1*R*2*S*)-, (1*S*2*R*)-aryl[(1-phenylethyl)amino]methylphosphonic acids (**1a,b** and **2a,b**) of high enantiomeric purity.^{2,3}



Ar = Ph (**1a,b**); Ar = 4-C₆H₄OMe (**2a,b**)

Address correspondence to O. I. Kolodyazhnyi, Institute of Bioorganic Chemistry and Petrochemistry, NAS of Ukraine, 1, Murmanskaya str, 02660, Kyiv-94, Ukraine. E-mail: oikol123@bpci.kiev.ua

Continuing these investigations, we have tested the activities of enantiomerically pure α -(N-benzylamino)benzylphosphonic acids against human prostatic acid phosphatase. As expected, (*R*)- α -(N-benzylamino)benzylphosphonic acid demonstrated higher affinities for the enzyme than (*S*)-enantiomer. However, (1*R*2*S*)-phenyl[(1-phenylethyl)amino]methylphosphonic acid **1a** was found to be 40 fold weaker inhibitor than its (1*S*2*R*)-analogue **1b**. Experimentally tested phosphonic acids **1a,b** and **2a,b** have been docked computationally to the active centre of this enzyme. Implications of theoretical results to mechanisms of stereospecificity of prostatic acid phosphatase inhibition by α -(N-benzylamino)benzylphosphonic acids are discussed.

REFERENCES

- [1] S. A. Beers, C. F. Schwender, D. A. Loughney, E. Malloy, K. Demarest, and J. Jordan, *Bioorg. Med. Chem.*, **4**, 1693 (1996).
- [2] O. I. Kolodiazhnyi, S. Sheiko, I. Guliako, and E. Grishkun, *Phosphorus, Sulfur, Silicon, and the Related Elements*, **177**, 2269 (2002).
- [3] G. A. Kachkovskii, N. V. Andrushko, S. Yu. Sheiko, and O. I. Kolodyazhnyi. *Russ. J. Gen. Chem.*, **11**, 1735 (2005).