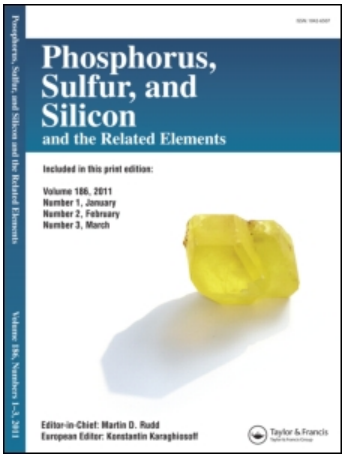


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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

To cite this Article Kolodyazhnyi, O. I. , Vovk, A. I. , Mischenko, I. M. , Tanchuk, V. Yu. , Kachkovskii, G. A. , Sheiko, S. Yu. and Kukhar, V. P.(2008) 'α-(N-Benzylamino)benzylphosphonic Acids: Stereoselectivity of Binding to Prostatic Acid Phosphatase', Phosphorus, Sulfur, and Silicon and the Related Elements, 183: 2, 648 — 649
To link to this Article: DOI: 10.1080/10447310701795984
URL: http://dx.doi.org/10.1080/10447310701795984

Phosphorus, Sulfur, and Silicon, 183:648–649, 2008

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10447310701795984

Taylor & Francis
Taylor & Francis Group

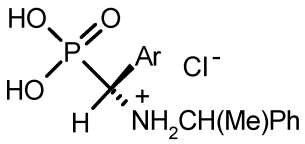
α-(N-Benzylamino)benzylphosphonic Acids: Stereoselectivity of Binding to Prostatic Acid Phosphatase

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

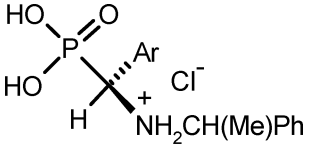
The stereoselectivity of the binding of α-(N-benzylamines)benzylphosphonic acids to the human prostatic acid phosphatase was studied. The mechanisms of stereaspecificity of prostatic acid phosphatase inhibition by α-(N-benzylamino)benzylphosphonic acids are discussed.

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]



(RS)-**1a**, *(RS)*-**2a**



(SR)-**1b,** *(SR)*-**2b**

Ar = Ph (**1a,b**); Ar =4-C_6H_4OMe (**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*)-enatiomer. 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. Guliaiko, 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).