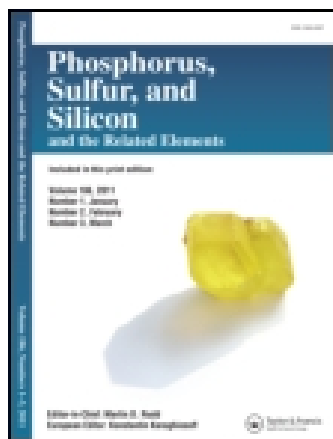


This article was downloaded by: [Selcuk Universitesi]

On: 25 December 2014, At: 20:43

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number:
1072954 Registered office: Mortimer House, 37-41 Mortimer
Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
<http://www.tandfonline.com/loi/gpss20>

Asymmetric Synthesis of Aminophosphonic Acids

Marian Miko Zajczyk , Piotr Źwa & Józef Drabowicz

^a Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences , 90-363 żódź, Sienkiewicza 112, Poland

^b Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences , 90-363 żódź, Sienkiewicza 112, Poland

^c Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences , 90-363 żódź, Sienkiewicza 112, Poland

Published online: 17 Mar 2008.

To cite this article: Marian Miko Zajczyk , Piotr Źwa & Józef Drabowicz (1999) Asymmetric Synthesis of Aminophosphonic Acids, *Phosphorus, Sulfur, and Silicon and the Related Elements*, 144:1, 157-160, DOI: [10.1080/10426509908546206](https://doi.org/10.1080/10426509908546206)

To link to this article: <http://dx.doi.org/10.1080/10426509908546206>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

Terms & Conditions of access and use can be found at [http://
www.tandfonline.com/page/terms-and-conditions](http://www.tandfonline.com/page/terms-and-conditions)

Asymmetric Synthesis of Aminophosphonic Acids

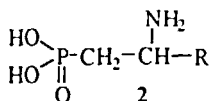
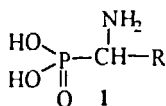
MARIAN MIKOŁAJCZYK*, PIOTR ŁYŻWA and
JÓZEF DRABOWICZ

*Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences,
90-363 Łódź, Sienkiewicza 112, Poland*

A new synthesis of chiral α - and β -aminophosphonic acids is described which involves a highly diastereoselective addition of phosphite and phosphonate anions to enantiopure sulfinimines.

Keywords: aminophosphonic acids; sulfinimines; asymmetric synthesis

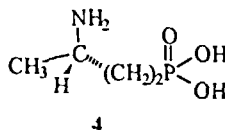
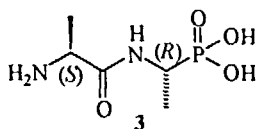
Aminophosphonic acids **1** and **2**, the phosphonic analogues of naturally occurring aminoacids, are attracting increasing interest, mainly due to their interesting biological properties.^[1]



* Fax: (048-42) 684-71-26

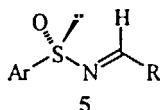
Some of these compounds have been reported to show antibacterial, antibiotic and antiviral properties as well as pesticidal, insecticidal and herbicidal activity. Therefore, they have found diverse industrial applications, eg. in pharmaceuticals and agrochemicals.

The bioactivity of aminophosphonic acids strongly depends on their structure, and especially on the chirality at the stereogenic α - and β -carbon atom. Thus, for example the (*S*, *R*) diastereomer of alafosfalin (**3**) shows significant activity against Gram-positive microorganisms, whereas the other diastereomers are less potent. Similarly, the (*S*) enantiomer of 2-amino-4-phosphonobutanoic acid (**4**) is 20-40 times more active than the (*R*)-form in the suppression of glutamate mediated neurotransmission.

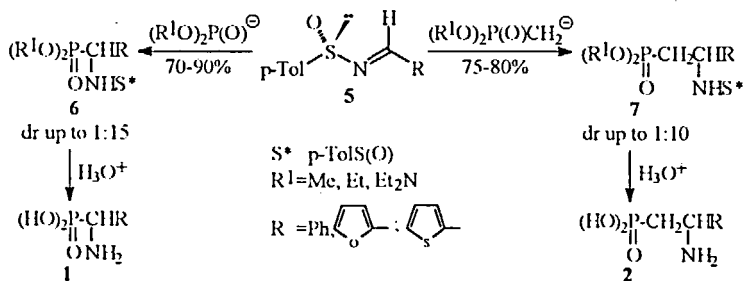


For these reasons, the number of syntheses of chiral, non-racemic aminophosphonic acids have been devised during the past two decades.^[2] Among them the asymmetric additions of dialkyl or trialkyl phosphites to chiral imine derivatives were found to be a very useful approach. However, in contrast to the widely investigated α -aminophosphonic acids, the synthetic approaches to chiral, racemic and enantiomeric β -aminophosphonic acids are few in number and of limited applicability.

Searching for a simple, general and efficient method for the synthesis of optically active α - and β -aminophosphonic acids **1** and **2** we turned our attention to enantiomerically pure sulfinimines **5** as chiral auxiliaries.



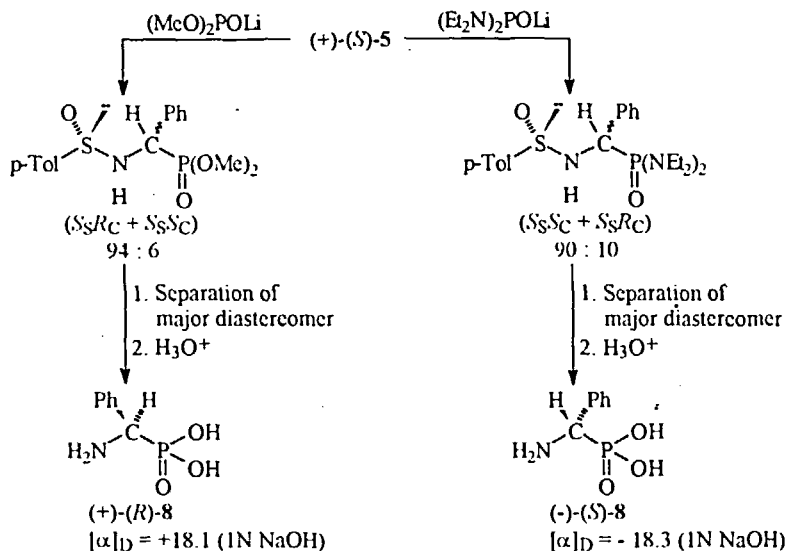
In addition to their ready availability^[3] they contain an arylsulfinyl moiety as a powerful stereodirecting group inducing high diastereoselectivity and an activated carbon-nitrogen double bond prone to attack by nucleophilic reagents.



It was found that the imine **5** react with dialkyl phosphite anions^[4] and dialkyl phosphonate carbanions^[5] to give corresponding diastereomeric adducts **6** and **7** in high yields and good diastereoselectivity (Scheme 1).

The major diastereomers of N-sulfinylaminophosphonates **6** and **7** were isolated by flash chromatography and converted to the corresponding free α - and β -aminophosphonic acids **1** and **2** by heating under reflux for 7 h in a mixture of glacial acetic acid and hydrochloric acid (36% aq).

It is interesting to point out that the addition dialkyl phosphite and diamido phosphite anions to (+)-(*S*)-sulfinimine **5** showed the contrasting stereochemical outcome leading to α -aminobenzylphosphonic acids **8** with opposite chirality at the α -carbon atom (Scheme 2).



SCHEME 2

References

- [1] For a comprehensive review on the biological activity of aminophosphonic acids see: P. Kafarski and B. Lejczak, *Phosphorus, Sulfur and Silicon*, **1991**, 63, 193.
- [2] For comprehensive reviews, see: D. Dhawan and D. Redmore, *Phosphorus and Sulfur*, **1987**, 32, 119; V.P. Kukhar, V.A. Soloshonok and V.A. Solodenko, *Phosphorus, Sulfur and Silicon*, **1994**, 92, 239.
- [3] F.A. Davis, R.E. Reddy, J.M. Szewczyk, G.V. Reddy, P.S. Portonowo, H. Zhang, D. Fanelli, H. Zhang, R. Thimma Reddy, P. Zhou and P.J. Carroll, *J.Org.Chem.*, **1997**, 62, 2555.
- [7] [4] M. Mikołajczyk, P. Łyżwa and J. Drabowicz, *Tetrahedron: Asymmetry*, **1997**, 8, 3991.
- [5] M. Mikołajczyk, P. Łyżwa, J. Drabowicz, M.W. Wieczorek and J. Błaszczyk, *Chem.Commun.*, **1996**, 1503.