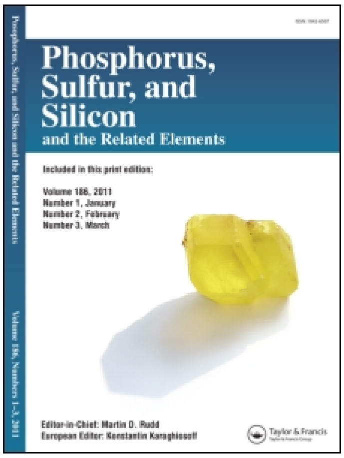


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Biosynthesis of 2-Amino-1-Hydroxy-Ethyl-Phosphonic Acid In Acanthamoeba Castellanii

Friedrich Hammerschmidt[a]
[a] Institut für Organische Chemie der Universität Wien, Wien, Währinger Straβe, Austria

To cite this Article Hammerschmidt, Friedrich(1987) 'Biosynthesis of 2-Amino-1-Hydroxy-Ethyl-Phosphonic Acid In Acanthamoeba Castellanii', Phosphorus, Sulfur, and Silicon and the Related Elements, 30: 3, 575 — 578

To link to this Article: DOI: 10.1080/03086648708079130

URL: http://dx.doi.org/10.1080/03086648708079130

Phosphorus and Sulfur, 1987, Vol. 30, pp. 575–578
Photocopying permitted by license only

BIOSYNTHESIS OF 2-AMINO-1-HYDROXY-ETHYLPHOSPHONIC ACID IN ACANTHAMOEBA CASTELLANII

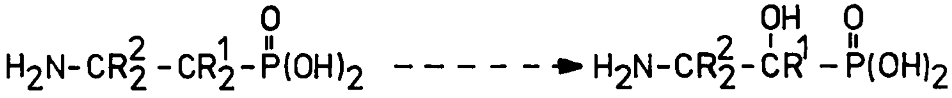
FRIEDRICH HAMMERSCHMIDT
Institut für Organische Chemie der Universität
Wien, A-1090 Wien, Währinger Straße 38, Austria

Abstract The 2-amino-1-hydroxy-ethylphosphonic acid in Acanthamoeba castellanii (Neff) is biosynthesized by hydroxylating 2-amino-ethylphosphonic acid with removal of the C-1 pro-S hydrogen and replacing it by OH with retention of configuration.

INTRODUCTION

There are two natural products with a P-C-bond and a hydroxy-group on C-1: 2-amino-1-hydroxy-ethylphosphonic acid[1] (OH-AEP) 2 and the phosphonic acid of fosfazinomycins.[2]

The OH-AEP is most likely produced by hydroxylating either 2-amino-ethylphosphonic acid (AEP) 1 or phosphonoacetaldehyde.[3] $(1,1\text{-}^2H_2)$-, $(2,2\text{-}^2H_2)$- and (1-^2H)-AEP were prepared and added to the growth medium (1 mg/ml) of Acanthamoeba castellanii (Neff), which produces both AEP and OH-AEP. These two compounds were isolated from the amoeba and the isotopic composition was determined by MS.



$$H_2N\text{-}CR^2_2\text{-}CR^1_2\text{-}\overset{O}{\overset{\|}{P}}(OH)_2 \dashrightarrow H_2N\text{-}CR^2_2\text{-}\overset{OH}{\overset{|}{C}}R^1\text{-}\overset{O}{\overset{\|}{P}}(OH)_2$$

			d_0	d_1	d_2(%)
1a	$R^1={}^2H, R^2=H$	2a	9	91	
b	$R^1=H, R^2={}^2H$	b	17	46	37
c	$R^1_2=H+{}^2H$	c	53	47	

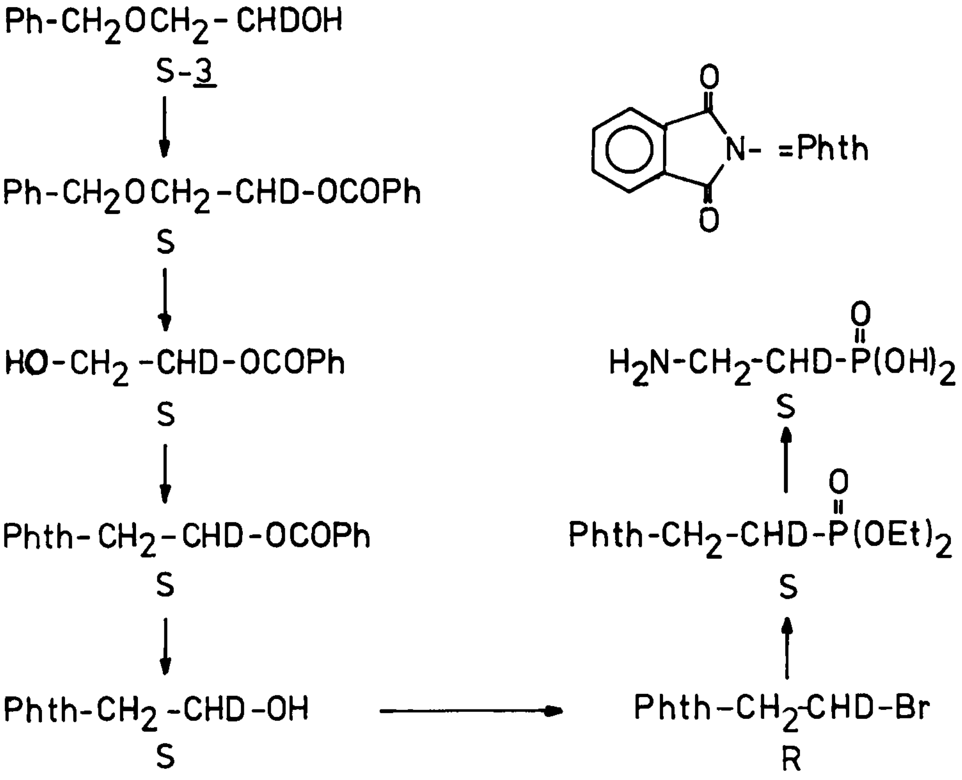
The AEP is taken up by the amoebas and incorporated into OH-AEP with virtually no kinetic isotope effect. The presence of doubly deuterated OH-AEP on feeding $(2,2\text{-}^2H_2)$-AEP 1b suggests direct hydroxylation of AEP. Oxygen-18 from $^{18}O_2$ is incorporated into the OH of OH-AEP.

To study the stereochemical course of the hydroxylation, chirally labelled AEP was prepared and the absolute configuration of OH-AEP was determined.

SYNTHESIS OF (R)- and (S)-(1-^2H)-AEP

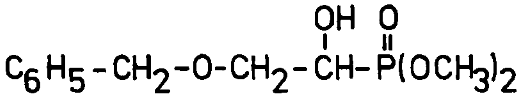
(S)-2-Benzyloxy-(1-^2H)-ethanol 3 was prepared by HLAD[4] catalyzed reduction of the corresponding deuterated aldehyde. It was used as starting material for the synthesis of (R)- and (S)-(1-^2H)-AEP given in scheme 1. The overall yield for the seven steps was 65 %. The ^2H of (S)-AEP (90% e.e.) is lost on hydroxylation, the ^2H of (R)-AEP (84% e.e.) is retained. Therefore the C-1 pro-S hydrogen of AEP is removed by the hydroxylase. The e.e.-value can be increased to about 95% for both chirally labelled AEP by using reaction flasks treated with trimethylsilylchloride/pyridine for the Arbusow-reaction.

SCHEME 1



ABSOLUTE CONFIGURATION OF OH-AEP

Racemic 1-hydroxyphosphonate 4 was resolved with a chiral lactol.[5] The S configuration is assigned to (+)-4 on the basis of a X-ray analysis. (R)-(-)-4 was transformed to (R)-OH-AEP which is identical with the natural product.



$$C_6H_5\text{-}CH_2\text{-}O\text{-}CH_2\text{-}\overset{\overset{OH}{|}}{C}H\text{-}\overset{\overset{O}{\|}}{P}(OCH_3)_2$$

(±)-4

The hydroxylation occurs with retention of configuration at C-1 of AEP.

Further studies will concentrate on the biosynthesis of the phosphonic acid of fosfazinomycins A and B.

REFERENCES

1. E. D. Korn, D. G. Deaborn, H. M. Fales and E. A. Sokoloski, *J. Biol. Chem.* 248, 2257 (1973).
2. T. Ogita, S. Gunji, Y. Fukazawa, A. Terahara, T. Kinoshita and H. Nagaki, *Tetrahedron Lett.* 24, 2283 (1983).
3. M. Horiguchi and H. Rosenberg, *Biochim. Biophys. Acta* 404, 333 (1970).
4. J. B. Jones and I. J. Jakovac, *Can. J. Chem.* 60, 19 (1982).
5. Ch. R. Noe, *Chem. Ber.* 115, 1576 and 1591 (1982).