



Calix[4]arene Based α -Aminophosphonates: Novel Carriers for Zwitterionic Amino Acids Transport.

Igor S. Antipin^{a*}, Ivan I. Stoikov^a, Evgueni M. Pinkhassik^b, Nataly A. Fitseva^a,
Ivan Stibor^b, Alexander I. Konovalov^a

^aDepartment of Organic Chemistry, Kazan State University, Kremlevskaja 18, 420008 Kazan, Russia

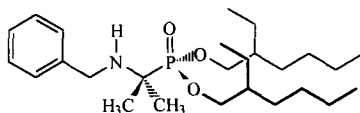
^bDepartment of Organic Chemistry, Institute of Chemical Technology, Technicka 5, 16628 Prague, The Czech Republic

Abstract: a series of calix[4]arene based α -aminophosphonates were synthesized by the Kabachnik-Fields reaction of the calixarene-diamine (either at lower or upper rim), diethyl phosphite and a carbonyl compound (acetone or cyclohexanone). These compounds exhibited remarkable selectivity as carriers for the membrane transport of the zwitterionic form of aromatic amino acids.

© 1997 Elsevier Science Ltd.

Molecular recognition of biorelevant molecules constitutes an important problem in organic chemistry.¹ In particular, great attention has been drawn to the transport of amino acids and their derivatives.² Amino acids exist as strongly solvated zwitterions in neutral aqueous solutions and their extraction and transport through the lipophilic membranes is very difficult. Although a number of synthetic receptors binding either ammonium or carboxylate moieties has been reported,³ only a few examples of zwitterionic amino acids transport are known.^{4,5}

α -Aminophosphonates possess an array of potential binding sites for both ammonium (phosphoryl group, nitrogen lone pair) and carboxylate (N-H bond) moieties. Recently we have described the transport of amino acids through a liquid membrane supported on a polymer film induced by α -aminophosphonate **1**.⁵



1

Using a chiral α -aminophosphonate as carrier the certain enantioselectivity of amino acids transport can be achieved.⁶

One attractive way to create new selective receptors is a functionalization of available natural or synthetic macrocycles by the suitable functional groups which are properly arranged in receptor for the achievement of effective interaction with the substrate. The calix[4]arene framework is a rigid scaffold and provides the lipophilicity to the whole molecule. 1,3-diaminocalix[4]arenes fixed in *cone* conformation were chosen as the starting platform because tweezer-like structure is likely to combine the appropriate binding mode with the lack of steric hindrance.

The synthesis of **3** and **4** was performed by the Kabachnik-Fields reaction⁷ of 1,3-bis(aminoethoxy)-calix[4]arene **2**⁸ with diethylphosphite and corresponding carbonyl compound (Scheme 1):