

Complexation of amino acids derivatives in water by calix[4]arene phosphonic acids

Joanna Dziemidowicz · Dariusz Witt ·
Janusz Rachoń

Received: 19 September 2007 / Accepted: 26 February 2008 / Published online: 4 April 2008
© Springer Science+Business Media B.V. 2008

Abstract Series of the calix[4]arene phosphonic acids with various substituents at the lower rim was synthesized. Complexing properties of these receptors towards methyl esters of six amino acids strongly depended on the calix[4]arene conformation flexibility. The complex formation processes were monitored using ^1H NMR spectroscopy (deuterated phosphate buffer at pD 7.3, 22 °C) and association constant values were evaluated. Inherently mobile calix[4]arene molecule **3** occurred in *cone* conformation in aqueous solution turned out to be more effective in complexation of the basic amino acids methyl esters compared to the rigid **2** and flexible **4**. Mixed 1:2 and 2:1 (host–guest) complexes were observed for compound **1** with all amino acids methyl esters.

Keywords Amino acids · Association constants · Calix[4]arenes · Molecular recognition in water · Phosphonic acids · Supramolecular chemistry · Complex formation

Introduction

Calix[4]arenes [1] are easily available through the base-induced condensation of *p*-alkylphenols with formaldehyde. Moreover, because of their susceptibility to the chemical modifications and ipso facto access to the unique architecture

of four conformers (*cone*, *partial cone*, *1,2-alternate*, *1,3-alternate*) they are often used as scaffolds for a creation of the new, sophisticated molecules with designed solubility and binding properties [2]. The supramolecular complex forming ability of the calix[4]arenes with charged or neutral molecules through the weak noncovalent interactions (e.g. hydrogen bonds, electrostatic interactions, van der Waals forces, π – π , and π –cation interactions) depends on the nature and number of the interacting groups as well as their mutual structural fitting [3]. Especially in polar solvents where solvophobic effect plays a crucial role, the aromatic cavity present in the calixarene molecule with the accompaniment of other functional groups may become very useful. Since molecular recognition of amino acids in natural environment involves multiple non-covalent interactions, the multivalent macrocyclic receptors created to this aim have to be equipped with the array of the properly arranged substituents in order to ensure effective interactions with the multifunctional guest molecules. Such selective artificial receptors offer better insight into mechanisms of interactions between biomolecules [4] and can be used for analytical purposes as well [5].

Since the non-covalent phosphate–ammonium interactions play a key role in living systems for many critical molecular recognition processes, we were interested in the complexation properties of the calix[4]arene-phosphonic acids towards the ammonium type compounds. Previously, we reported the molecular recognition of the aromatic and aliphatic amines and 1,2-amino alcohols by a macrocyclic host **1** in phosphate buffered D_2O at pD 7.3 [6]. The results have shown dependence of the binding strength on a guest geometry, the protonated form of the amino group has also appeared important. This prompted us to investigate the inclusion properties of the host **1** towards amino acids derivatives. We were extremely interested in a subject of

J. Dziemidowicz · D. Witt · J. Rachoń (✉)
Department of Organic Chemistry, Chemical Faculty, Gdansk
University of Technology, Narutowicza 11/12, 80-952 Gdansk,
Poland
e-mail: rachon@chem.pg.gda.pl

J. Dziemidowicz
e-mail: dziemidowicz@wp.pl