

Calix[4]arene Phosphonates - Recognition of Amino Alcohols in Water

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ABSTRACT: *The water-soluble calix[4]arenes based cavitands were obtained in good yield by introduction of phosphonic acids groups at the upper rim; we describe the design, synthesis, and formation of the complexes with ephedrine, norephedrine, and noradrenaline hydrochloride in the phosphate buffer at pD 7.3. © 2004 Wiley Periodicals, Inc. Heteroatom Chem 15:155–161, 2004; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10229*

INTRODUCTION

Calix[4]arenes have become an interesting platform for further synthetic elaboration into host molecules [1,2]. A lot of work has been done to modify either the lower or the upper rim positions to create host molecules mainly for the attraction of simple cations, anions, and small organic molecules [3]. However, water solubility is required for in vivo application of appropriately functionalized host [4]. Water soluble calixarenes, in most cases, have been achieved by the introduction of charged functional groups like carboxylic, sulfonic, and phosphonic or phosphoric. After the first reports of Ungaro [5] and Shinkai [6], a variety of new compounds have been obtained and their binding properties in aqueous solution have been demonstrated, which was summa-

rized in review [7]. In our opinion the introduction of phosphonate groups into the calix[4]arene seems to be the most promising approach. In contrast to the carboxylate or sulfonate group, the phosphonate group can be easily modified with preservation of hydrophilic properties.

Kalchenko [8] has described water soluble calix[4]arenes bearing one, two, or four protonizable dihydroxyphosphoryl groups at the lower rim, and their salt formation with L-(–)- α -phenylethylamine and (1*S*,2*R*)-(+)-ephedrine. These salts in deuteromethanol solution at room temperature exist as tight ion pair. However, increasing the temperature or addition of deuterated water leads to appreciable dissociation of the ion pairs. On the other hand, Coleman [9] reported a series of amphiphilic calix[4]arenes having four hydrophobic acyl chains at the upper rim as well as two hydrophilic dihydroxyphosphoryloxy groups at the lower rim self-assemble at the air-water interface as stable Langmuir monolayers. Calix[4]arenes substituted at the upper rim by hydroxyethoxyphosphoryl groups and their self-assembly to capsules with tetra-cationic counterparts in polar solvents has been recently described by Schrader [10]. Unfortunately the 1:1 complexes were often insoluble in water and in some cases precipitated even from methanol. Calix[4]arenes bearing α -amino or α -hydroxyphosphonic acid fragments were also described. Their self-assembly [11] and transport [12] of bioactive guest through cell membrane were reported.

As one can see, the amphiphilic calix[4]arenes bearing phosphonic acids groups at the lower or upper rim can form salts with amines, self-assemble

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