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Porphyrin phosphonates: novel anionic receptors for saccharide recognition

Vladimír Král,* Oleksandr Rusin, Jana Charvátová, Pavel Anzenbacher Jr. and Jaroslav Fogl

Institute of Chemical Technology, Department of Analytical Chemistry, Technická 5, 166 28 Prague, Czech Republic

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Abstract

Novel porphyrin phosphonates (**1**–**3**) exhibit binding of alkyl pyranosides in organic media (receptor **1**), monosaccharides, selected disaccharides in water (receptors **2** and **3**); effective binding for D(−) fructose, D(+) maltose and α-D-lactose were found; association constants for **1** (in acetonitrile) and for **2** and **3** (in water) are of the order 10^4 M^{-1}.

Keywords: porphyrins; receptors; saccharides.

The recent literature describes numerous host systems that utilize sterically well organized receptors for recognition of biologically important substrates.[1] The design of these systems utilizes the combination of different noncovalent binding modes. Remarkable effort has been devoted to the design of saccharide receptors.[2,3] These studies focused on diverse aspects of carbohydrate recognition such as stereo- and enantioselectivity, binding in polar solvents and easy detection of the binding events.

Porphyrin phosphonates represents a novel group of compounds with interesting binding properties, where P=O groups play a vital role as they are known to be strong hydrogen bond acceptors. Several examples of synthetic receptors containing P=O groups have been published in connection with sugar recognition.[4–8] Design of our receptor is based on a combination of a UV and fluorescence signal unit (porphyrin) together with two or four binding units (phosphonates) (Fig. 1). We have recently developed a general synthetic utilization of porphyrin bromomethyl derivatives for preparation of polycationic porphyrin derivatives.[9] Another approach, described here, is application of bromomethylporphyrins for preparation of phosphonate esters of diphenyl and tetraphenylporphyrins. The porphyrin bromomethyl derivatives were heated with an excess of trialkylphosphyte according to the Arbuzov procedure with following hydrolysis of benzylphosphonate esters. This synthetic protocol represents an easy access to

* Corresponding author.

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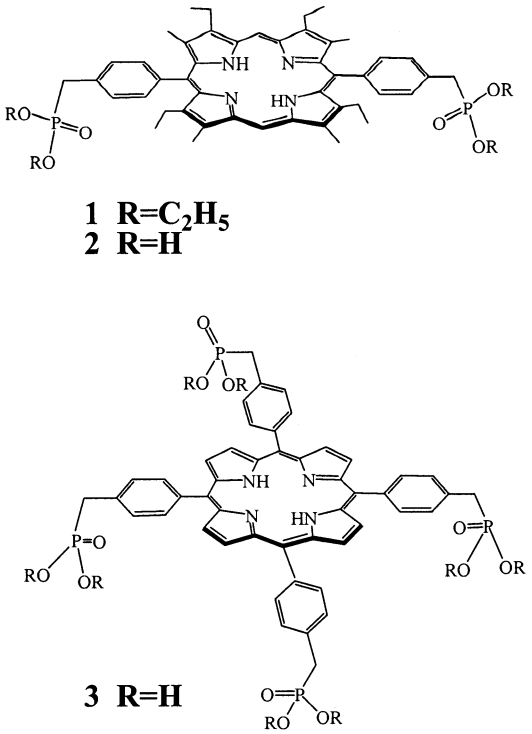
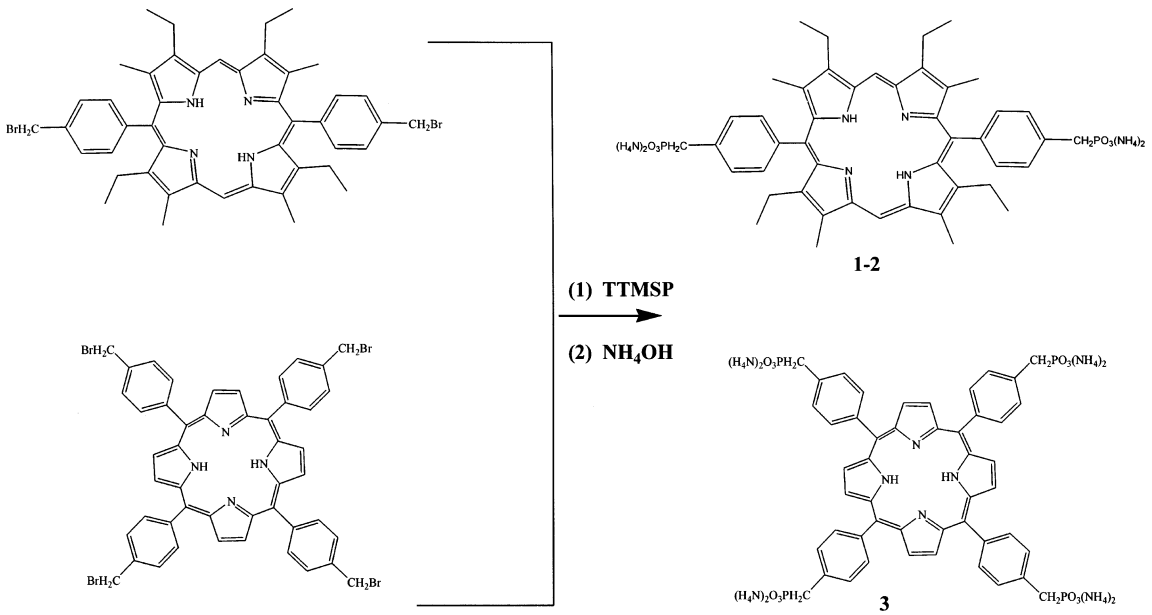


Figure 1. Porphyrin phosphonate diethyl ester **1** ($R = C_2H_5$) and porphyrin phosphonate **2**–**3** ($R = H$)

water-soluble porphyrin phosphonates (Scheme 1). Their saccharide binding properties are presented here.



Scheme 1. Strategy for synthesis of the porphyrin phosphonates **1**–**3** according to Arbuzov's procedure: (1) tris-trimethylsilylphosphite (TTMSP), 120°C, 24–28 h; (2) NH_4OH (aq), 100°C, 1 h

Binding studies of the novel receptor **1** were carried out in acetonitrile with octyl glycopyranosides: octyl-α-D-gluco- and octyl-α-D-galactopyranoside. Several mono-, di- and trisaccharides were used for the complexation study of the water-soluble receptors **2** and **3**.

An increase of sugar concentration caused intensity changes at the Soret band and Q-bands in the optical spectra of all hosts. The UV–vis measurements showed no shift of the Soret peak maxima (Fig. 2). The complexation was analyzed by least-squares curve-fitting, assuming a 1:1 complex formation.

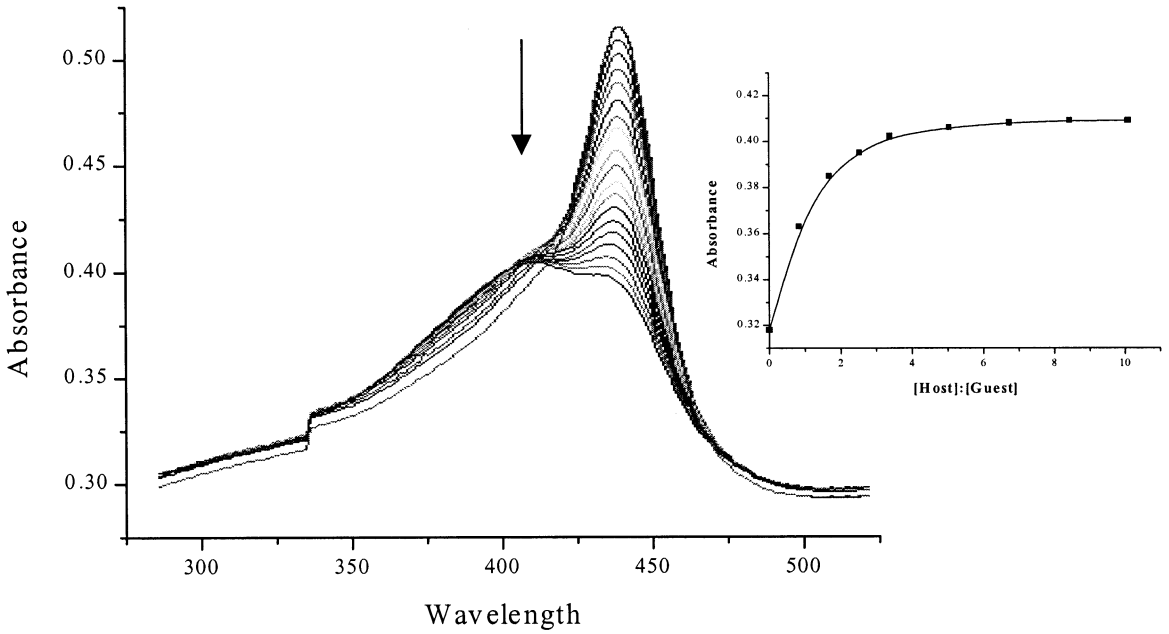


Figure 2. Typical UV–vis titration experiment. Spectral UV–vis changes upon the incremental addition of α-D-glucose to **2** in water. $\lambda_{max} = 428$ nm

Table 1 summarizes binding constants calculated for the receptors **1**–**3**. The UV–vis spectroscopic method indicates preferable binding of **1** to the octyl-α-D-glucopyranoside in comparison with octyl-β-D-galactopyranoside. Interaction UV–vis studies of **2** and **3** to mono- and disaccharides showed stronger binding to D-trehalose, D-maltose and α-D-lactose. Additional evidence for the saccharide binding mode in solution came from ^{1}H and ^{31}P NMR spectra. ^{1}H NMR spectra showed signals at δ 2.22, 4.65 and 4.94 ppm, which belong to hydroxylic pyranoside protons. A model complexation experiment of octyl-α-D-glucopyranose with the receptor **1** in equimolar ratio in $CDCl_3$ at 25°C showed broadening and downfield shift of the OH saccharide signals. The downfield chemical shift of 0.21 ppm for ^{31}P NMR spectra of the complex of **1** with octyl-α-D-glucopyranoside under the same conditions was also observed.

Interaction of the α-D-glucose at 25°C with **2** (equimolar ratio) in DMSO-d_6 caused broadening of the proton signals corresponding to glycoside OH and the CH-1 (δ 6.28 and 6.63 ppm, respectively). Signals from saccharide aliphatic protons were insignificantly influenced by complexation. The downfield chemical shift of 2.6 ppm in the ^{31}P NMR spectra for the 2-glucose complex (1:1) in water was observed, compared with 19.7 ppm for the starting compound **2**.

Table 1
Association constants for binding of saccharides with receptors **1**–**3** in water followed by UV–vis titration[a]

Saccharide	Association constant (K_a), 10^4 [M^{-1}]		
	1	**2**	**3**
Octyl-α-D-glucopyranoside	5.11		
Octyl-α-D-galactopyranoside	3.30		
D(+) Galactose		1.35	1.97
α-D-Glucose		1.90	1.76
α-D-Arabinose		1.38	1.50
D(+) Mannose		1.40	1.20
D(−) Fructose		1.33	1.18
D(−) Ribose		0.60	0.78
D-Trehalose		1.94	2.12
D(+) Maltose		2.17	2.42
α-D-Lactose		2.13	2.50

[a] In a 1 cm square quartz cuvette was placed 1.3×10^{-5} M solution of macrocycle **1** in acetonitrile or **2** and **3** in H_2O containing 5% of MeOH (v/v). A known amount of saccharide was added in increments (0–100 equiv.; concentration of receptor in cuvette is constant). The absorbance changes at Soret band (**1** at 398 nm, **2** at 428 nm and **3** at 440 nm) were measured (room temperature), and data evaluated with the aid of the least squares curve fitting. The K_a was calculated for 1:1 complexes. The reproducibility of the K_a values was $\pm 10\%$ in triplicate runs.

The interaction of saccharides with porphyrin phosphonates was also monitored by infrared spectroscopy. The shift of saccharide OH bond resonance from 3351 to 3369 cm^{-1} for 1-octyl-α-D-glucopyranoside complex (equimolar ratio) was monitored. The change of saccharide C–O bond resonances (1074–1078 cm^{-1} and 1020–1031 cm^{-1}, respectively) was also observed. The interaction of **2** with α-D-glucose is also characterized by the shift of resonance of saccharide OH bonds from 3390 to 3408 cm^{-1}, and the shift and broadening of the C–O bond signal from 1025 to 1071 cm^{-1}. The broadening of the resonance signal for P=O grouping at 1250 cm^{-1} was also observed simultaneously with the shift resonance for a simple P–O bond from 1180 to 1158 cm^{-1}.

All spectroscopic data prove that hydrogen bonds between the phosphonate and vicinal diol segment of the saccharide play a decisive role in porphyrin phosphonate–saccharide complexation. A binding mode between macrocyclic phosphonates and saccharides has been recently proposed.[4–10] Receptor **1** showed a stronger interaction with alkyl glucopyranoside than galactopyranoside. Porphyrin phosphonates **2** and **3** tend to bind to oligosaccharides especially to D(+) maltose and α-D-lactose. In conclusion, these synthetic receptors may serve for developing saccharide sensor systems.

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