Electrochemical Saccharide Recognition by a Phenylboronic Acid-Terminated Redox Active Self-Assembled Monolayer on a Gold Electrode

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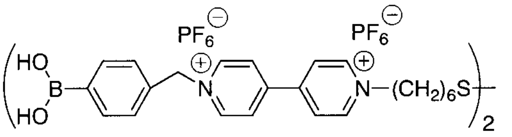
Phenylboronic acid-terminated viologen-carrying alkyl disulfide (**1**) and a reference compound **2** were designed and synthesized. Self-assembled monolayers of **1** on gold electrodes were found to function as a highly sensitive saccharide sensor in aqueous solution.

The interaction of phenylboronic acids and compounds with *vic*-diols can be detectable in water by several methods including fluorescence spectroscopy[1] and an electrochemical technique[2]. Our goal is to design and construct self-assembled monolayers of a phenylboronic acid-carrying electroactive compound on an electrode that performs electrochemical communication with saccharides in aqueous solution. For this purpose, we synthesized 1,1''-(dithiodi-6,1-hexanediyl)bis[1'-(4-dihydroxyboryl)phenylmethyl-4,4'-bipiridinium] tetrakis(hexafluorophosphate) (**1**). Recently, Olliff and co-workers[3] prepared a self-assembled monolayer (SAM) of a phenylboronic acid-terminated alkanethiol on a gold electrode and examined the response to nicotinamide adenine dinucleotide by means of surface plasmon resonance measurements. Kitano and co-workers[4] described sugar recognition by a phenylboronic acid-carrying SAM on a gold colloid or a gold electrode detected, respectively, by UV–vis absorption change and by cyclic voltammetry using an electroactive marker. Here we describe first electrochemical saccharide sensing with a redox active phenylboronic acid-terminated SAM on a gold electrode.

The synthesis of **1** is as follows. 4-(1,3-Dioxa-2-boranyl) benzyl bromide[5] was reacted with 4,4'-bipyridyl in CH_3CN at refluxed temperature for 13 h to produce 4-(4-pyridyl)-*N*-(4-(1,3-dioxa-2-boranyl)benzyl)pyridinium bromide, which was reacted with 6-thiobenzoyloxy-1-bromohexane in DMF at 60 ˚C for 48 h, followed by hydrolysis with concd HCl and then ion exchange with potassium hexafluorophosphate. Compound **1**[6] was obtained as a white solid. 1,1''-(Dithiodi-6,1-hexanediyl)bis(1'-benzyl-4,4'-bipiridinium) tetrakis(hexafluorophosphate), **2**[7], a reference compound of **1**, was synthesized by a similar procedure.



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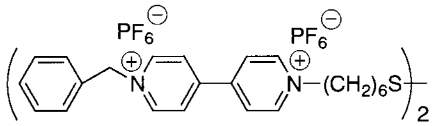

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A mirror-polished polycrystalline gold disk electrode (BAS Co., geometrical area: 2.01 mm^2) was immersed in 1.0 mmol dm^{-3} of **1** (or **2**) in methanol for 24 h and then rinsed with methanol and then with 0.1 mol dm^{-3} potassium hexafluorophosphate aqueous solution. Cyclic voltammogram (CV) measurements (BAS-100BW) for the obtained electrodes (**1**-SAM/Au and **2**-SAM/Au) were carried out in 0.1 mol dm^{-3} potassium hexafluorophosphate aqueous solution (pH 10.5) containing given concentration of a saccharide at 23 ± 1 °C in argon atmosphere using a gold wire and a saturated calomel electrode (SCE) as the counter and the reference electrodes, respectively.

Typical CVs for a **1**-SAM/Au electrode is shown in Figure 1. A **2**-SAM/Au electrode gave similar CVs (data not shown). The formal potentials for the first reduction/reoxidation of the viologen moiety in **1** and **2** obtained from the CVs were –495 and –500 mV, respectively. Both cathodic and anodic peak current of the CVs for **1**-SAM/Au (Figure **1**) and for **2**-SAM/Au (data not shown) at a scan range of 25–200 mV/s increased linearly with the increase of scan rates, indicating that the electron transfer of the surface confined species with the electrode governs the electrochemistry. The surface coverage of **1** and **2** calculated from the CVs were $(1.3 \pm 0.2) \times 10^{-10}$ and $(1.4 \pm 0.2) \times 10^{-10}$ mol cm^{-2}, respectively.[8]

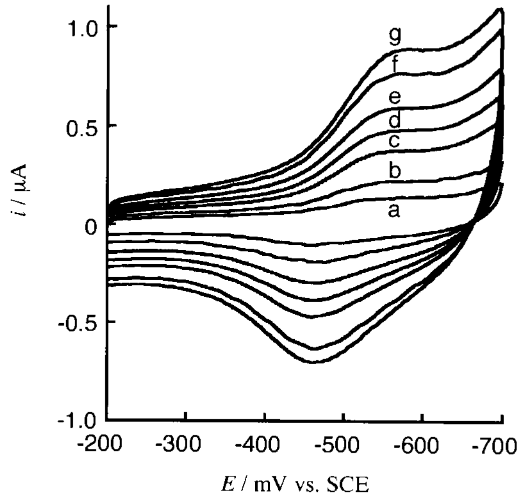

Figure 1. Cyclic voltammograms for a SAM of **1** on an gold electrode in 0.1 M KPF_6 aqueous solution. Scan rates in mV s^{-1} are (a) 25, (b) 50, (c) 75, (d) 100, (e) 125, (f) 150 and (g) 200.

Figure **2** shows CVs for a **1**-SAM/Au in the absence or presence of 0.1 mol dm^{-3} xylose in aqueous solution. The presence of xylose causes the shift of the formal potential to negative direction by 18 mV. This shift might be explained by the

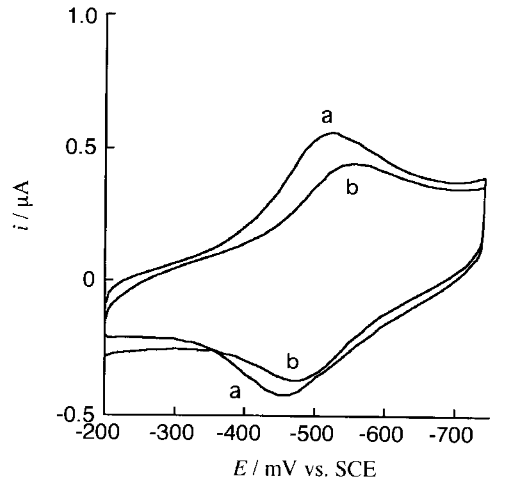

Figure 2. Cyclic voltammograms for a SAM of **1** on a gold electrode in 0.1 M KPF_6 aqueous solution in the absence (a) and presence (b) of xylose (0.1 mol dm^{-3}). Scan rate, 100 mV s^{-1}.

stronger binding of the saccharide with the oxidized form of **1** than the reduced form. On the contrary, no such shift in the formal potential was observed for a **2**-SAM/Au electrode. CVs at **1**-SAM/Au electrodes were measured in the presence of given concentrations of galactose, fructose, mannose, glucose, xylose, α-methylglucoside and methyl-β-xylopyranoside, and the observed shifts in $E^{0'}$ were plotted as a function of saccharide concentration in Figure 3. Interesting features observed are as follows. i) **1**-SAM/Au electrodes exhibited a response for xylose, mannose and fructose at the concentration range of 10^{-6}–10^{-3} mol dm^{-3}. ii) CV response of the electrode was also occurred to α-methylglucoside, a compound possessing no 1,2-diol moiety. This might be due to the binding of the phenylboronic acid moiety in **1** with the 4- and 6-hydroxy groups in α-methylglucoside. iii) The electrode had a response to methyl-β-xylopyranoside, a compound that has no binding site with phenylboronic acid, at the relatively higher concentrations. Possible hydrogen bonding between the phenylboronic acid moiety in **1** with the 2,3-and 4-hydroxy moieties in methyl-β-xylopyranoside may explain the shift.

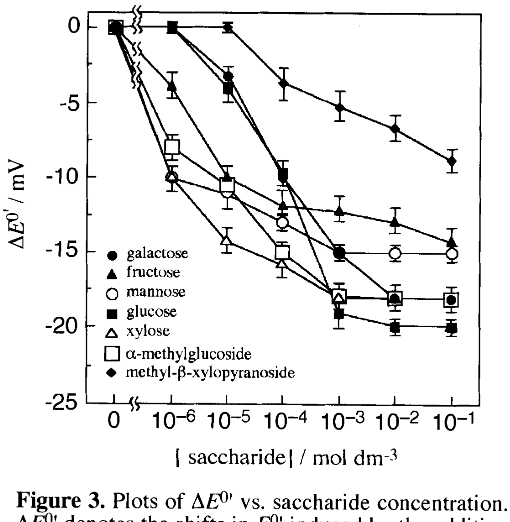

Figure 3. Plots of $\Delta E^{0'}$ vs. saccharide concentration. $\Delta E^{0'}$ denotes the shifts in $E^{0'}$ induced by the addition of saccharides for SAMs of **1** on gold electrodes. Details see the text.

In conclusion, we have found, for the first time, that phenylboronic acid-terminated redox active SAMs on gold electrodes respond to a variety of saccharides at relatively low concentration (ppm order). Intense effort is currently underway in our laboratory to reveal fully the characteristics of **1**-SAMs/Au electrodes including the mechanism of the observed potential shift in the CVs and explore potential applications of the electrodes as highly sensitive sensors for biological oligo- and poly(saccharides).

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References and Notes

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6 mp >300 °C. Anal. Found: C, 40.10; H, 4.01; N, 4.02%. Calcd for $C_{46}H_{56}N_4O_4B_2F_{24}P_4S_2$: C, 39.6; H, 4.04; N, 4.02%. IR (KBr): 3400 (OH), 3058 (CH, Ar), and 2942 (CH) cm^{-1}. ^1H NMR (200 MHz, CD_3CN, TMS); δ 1.3–1.8 (m, 16H, $SC(CH_2)_4CN^+$), 2.70 (m, 4H, SCH_2), 4.60 (t, 4H, CH_2N^+), 5.84 (s, 4H, N^+CH_2Ph), 6.43 (s, 4H, OH), 7.49 (d, 4H, ArH), 7.88 (d, 4H, ArH), 8.37 (m, 8H, PyH), 8.89 (d, 4H, PyH), 8.98 (d, 4H, PyH).

7 mp >300 °C. Anal. Found: C, 38.93; H, 4.31; N, 4.41%. Calcd for $C_{46}H_{54}N_4F_{24}P_4S_2 \cdot 5.7H_2O$: C, 39.19; H, 4.68; N,3.97%. IR (KBr): 3139 (CH, Ar), and 2931 (CH) cm^{-1}. ^1H NMR (200 MHz, DMSO-d_6, TMS); δ 1.30 (m, 8H, $SC_2(CH_2)_2C_2N^+$), 1.63 (m, 4H, $SCCH_2C_4N^+$), 1.95 (m, 4H, $SC_4CH_2CN^+$), 2.70 (m, 4H, SCH_2), 4.65 (t, 4H, CH_2N^+), 5.94 (s, 4H, N^+CH_2Ph), 7.47 (d, 6H, ArH), 7.61 (d, 4H, ArH), 8.75 (m, 8H, PyH), 9.36 (d, 4H, PyH), 9.52 (d, 4H, PyH).

8 The surface roughness factor determined by the anodic oxidation of chemisorbed iodine on bare Au electrodes was ca. 1.4, whose value was used to calculate the surface coverage. Detailed for the anodic oxidation of chemisorbed iodine, see: J. F. Rodriguez, T. Mebrahtu, and M. P. Soriaga, *J. Electroanal. Chem.*, **233**, 283 (1987).