Visual sensing of fluoride ion and saccharides utilizing a coupled redox reaction of ferrocenylboronic acids and dye molecules

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F⁻ and saccharides which feature specific affinity with the boronic acid group can be detected *visually* by the redox reaction between ferrocenylboronic acid derivatives and dyes with the appropriate redox potentials.

It is known that reversible redox properties of ferrocene derivatives are useful for indicating molecular recognition events[1,2] and for their use as switches to control the rate of mass transport across membranes.[3] We recently demonstrated that the redox active ferrocenylboronic acid **1** has excellent selectivity in the electrochemical recognition of F⁻ in the presence of other halides and common anions.[4] We also found that chiral ferrocenylboronic acid **2** bearing an intramolecular tertiary amine can bind saccharides at neutral pH and the complexation can be conveniently monitored by electrochemistry.[5] The results imply that the complex formation of the boronic acid group with F⁻ or saccharides (Scheme 1) affects the redox potential of the ferrocene–ferrocenium redox couple. Here, it occurred to us that these complexation events may be *visually* detectable by skilfully combining with appropriate dye molecules. Complexation which develops a negative charge on the boron atom in **1** or induces deprotonation of the tertiary amino group in **2** should make $E_{1/2}$ more negative; if the $E_{1/2}$ of the dye is slightly more negative than that of the ferrocenyl group, then the dye is reduced only when F⁻ or saccharides are bound to the ferrocene moiety.

Compound **1** was purchased from Tokyo Kasei Kogyo Co., Ltd. The synthesis of **2** has been described previously.[5] The voltammograms were recorded at 25 °C with a BAS-100B/W electrochemical analyser using a single compartment cell fitted with a glassy carbon working electrode, a platinum wire counter electrode and a Ag/AgCl reference electrode.

The pH dependence of $E_{1/2}$ for **1** and methylene blue (**3**) is shown in Fig. 1. The $E_{1/2}$ value of **1** is pH-independent at pH 1.0–7.0 whereas that of **3** decreases with increasing pH in this range. We chose pH 3.0 for the measurements where the $E_{1/2}$ difference is about 250 mV. Our previous study[4] suggests that this difference can be reduced by F⁻ complexation.
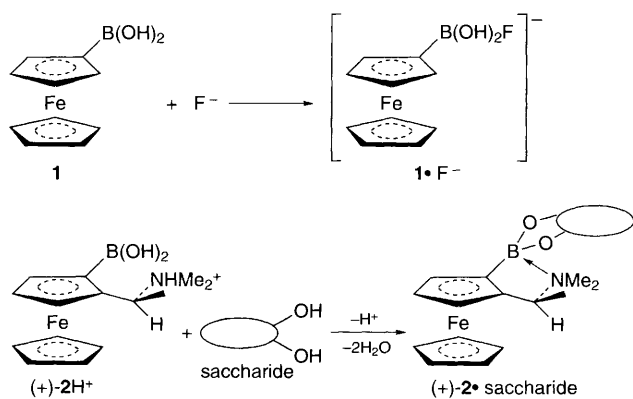
Fig. 2 shows plots of $E_{1/2}$ for **1** and **3** *versus* [F⁻]. It is seen from Fig. 2 that the $E_{1/2}$ of **3** is nearly [F⁻]-independent up to [F⁻] = 10⁻² mol dm⁻³. On the other hand, the $E_{1/2}$ of **1** is [F⁻]-independent at [F⁻] < 2.0 × 10⁻³ mol dm⁻³ whereas the decrease in $E_{1/2}$ begins at [F⁻] > 2.0 × 10⁻³ mol dm⁻³ and the peak splits into two at [F⁻] > 3.0 × 10⁻² mol dm⁻³. The lower $E_{1/2}$ of **1** becomes comparable with that of **3** at [F⁻] *ca.* 3 × 10⁻² mol dm⁻³.

The reduction of **3** to its leuco form was followed by monitoring the disappearance of the absorption maximum at 665 nm. As shown in Fig. 3 (○ for [**1**]/[**3**] = 10), the absorbance begins to decrease at [F⁻] *ca.* 4 × 10⁻³ mol dm⁻³ and reaches zero at [F⁻] = 3.0 × 10⁻² mol dm⁻³. Although the $\Delta E_{1/2}$ is still 200 mV at this F⁻ concentration, the redox reaction can take place because of the concentration difference (*i.e.* [**1**] > [**3**]). When the concentration of **1** is increased (▲ for [**1**]/[**3**] = 50), the absorbance begins to decrease at the lower F⁻ concentration. Hence, it becomes possible to *visually* detect the F⁻ concentration by the reduction of **3** by **1**, that is, by the
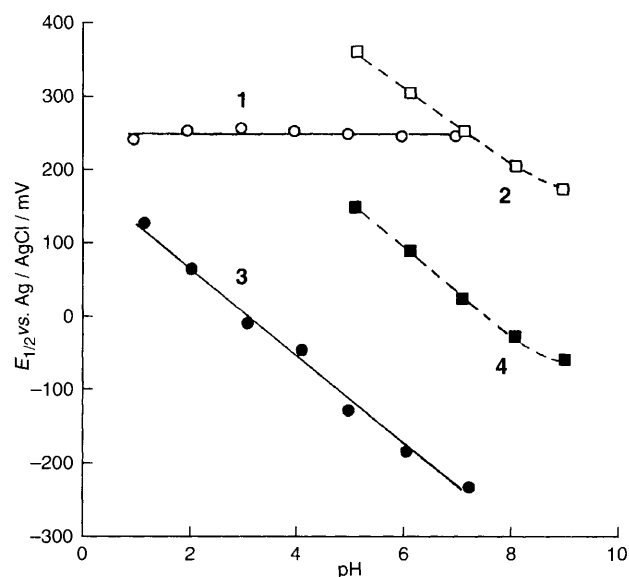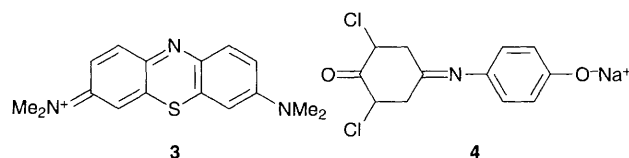

Fig. 1 pH Dependence of $E_{1/2}$: 25 °C, I = 0.1 mol dm⁻³, [**1**] = [**4**] = 1.0 × 10⁻⁴ mol dm⁻³, [**2**] = 1.0 × 10⁻³ mol dm⁻³, [**3**] = 1.0 × 10⁻³ mol dm⁻³. pH was adjusted with 0.20 mol dm⁻³ citrate buffer (**1** and **3**) or 0.10 mol dm⁻³ phosphate buffer (**2** and **4**). The Osteryoung method was used with 25 mV sweep amplitude, 15 Hz sweep frequency and 4 mV step.
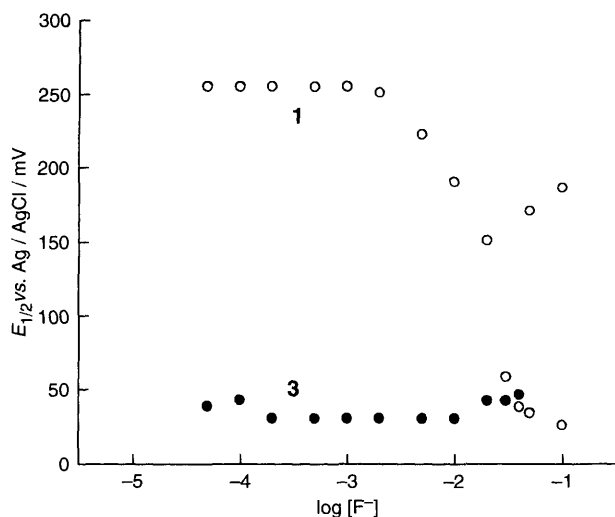

Scheme 1

Fig. 2 Plots of $E_{1/2}$ for **1** and **3** versus [F⁻] at pH 3.0 (0.20 mol dm⁻³ acetate buffer). When an unavoidable pH change was induced by the addition of a large amount of NaF, it was adjusted to 3.0 with aqueous conc. HCl. Other conditions are as in Fig. 1.
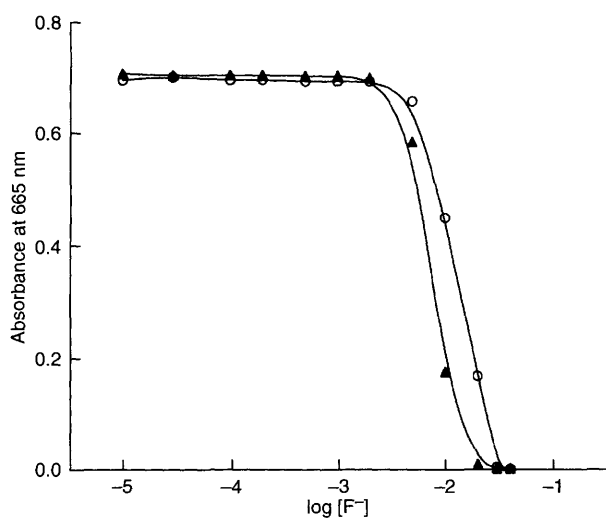

Fig. 3 Reduction of **3** by **1** in the presence of F⁻: [**3**] = 1.0 × 10⁻⁵ mol dm⁻³, [**1**] = 1.0 × 10⁻⁴ (○) or 5.0 × 10⁻⁴ mol dm⁻³ (▲)

disappearance of the blue colour of the solution. It has been established that $E_{1/2}$ of **1** is scarcely affected by the presence of other halides and common anions.[4] Consequently in this study, the absorbance at 665 nm in the presence of **1** and **3** was scarcely affected (< 5%) by the addition of Cl⁻, Br⁻, SO_4^{2-}, HPO_4^{2-} or SCN⁻. This implies that one can selectively detect F⁻ in the presence of these common anions.

The saccharide concentration is also detectable on a similar basis. As shown in Fig. 1, $E_{1/2}$ for **2** shows a similar pH dependence as that for 2,6-dichloroindophenol (**4**), the $E_{1/2}$ difference being about 220 mV. If the saccharide complexation which occurs according to Scheme 1 can lower the $E_{1/2}$ of **2** to a value comparable with that of **4**, then reduction of **4** by the **2**-saccharide complex should take place. Measurements were carried out at pH 7.0 (0.10 mol dm⁻³ phosphate buffer) where **2** can efficiently bind saccharides[5,6] and the reaction was followed by monitoring the disappearance of the absorption maximum at 605 nm. Plots of A_{605} versus saccharide concentration are illustrated in Fig. 4 for D-mannitol and D-sorbitol which are known to have a relatively large affinity towards **2**.[5] It is seen from Fig. 4 that the absorbance begins to decrease from ca. 5 × 10⁻² mol dm⁻³ for D-mannitol and ca. 6 × 10⁻³ mol dm⁻³ for D-sorbitol. Hence, one can accurately estimate
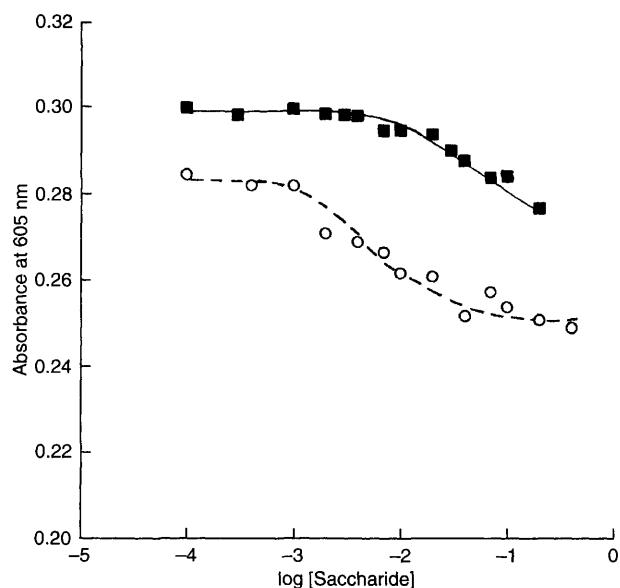
Fig. 4 Reduction of **4** by **2** in the presence of saccharides: [**2**] = 2.0 × 10⁻³ mol dm⁻³, [**4**] = 2.0 × 10⁻⁵ mol dm⁻³ at pH 7.0 (0.10 mol dm⁻³ phosphate buffer); D-mannitol (■) or D-sorbitol (○)

saccharide concentrations using the calibration curves in Fig. 4.†

In conclusion, the present study demonstrated that F⁻ and saccharides which feature specific affinity with the boronic acid group can be detected by the redox reaction between ferrocenyl-boronic acid derivatives and dyes with appropriate redox potentials. We believe that this concept is very novel and important in the following: (*i*) selective F⁻ detection and sensitive saccharide detection, which are difficult using other methods, is possible, (*ii*) concentrations can be conveniently determined by colour changes and (*iii*) different dyes with different colours can be used if the $E_{1/2}$ of ferrocenylboronic acid is modified by introduction of appropriate substituents.

Footnote

† Our previous study on the electrochemical detection of saccharides by (+)-**2** indicated that it has a moderate chiral recognition ability for sorbitol.[5] The present coupled redox reaction system is somewhat inferior to the electrochemical method in experimental precision and not so suitable to strict discussion about chiral recognition.

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