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A competition assay for diols using 9-(*N*,*N*-diethanolaminomethyl)anthracene and phenylboronic acid

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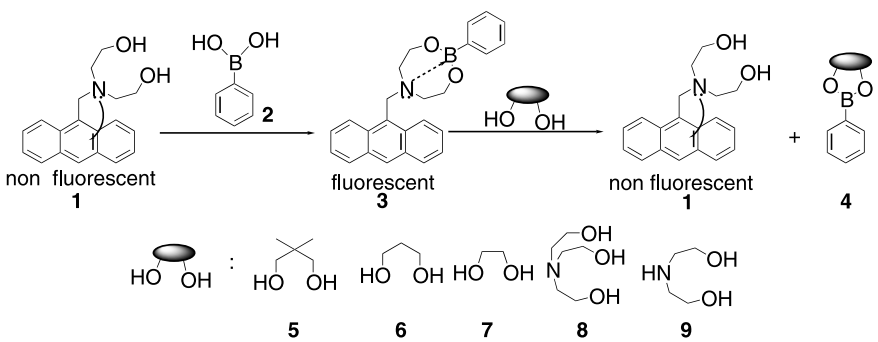
Abstract—9-(*N*,*N*-Diethanolaminomethyl)anthracene and phenyl boronic acid can be used in a competition assay for diols in chloroform. © 2002 Published by Elsevier Science Ltd.

Over the last few years we have been interested in developing molecular sensors using boronic acids.[1–4] The systems we are developing contain a receptor and reporter (fluorophore or chromophore) as part of a discrete molecular unit. This is however not the only approach towards boronic acid based sensors. Anslyn has recently demonstrated that boronic acid receptors and a separate reporter unit can be used in competitive assays.[5–7] A competitive assay requires that the receptor and reporter (typically a commercial dye) associate under the measurement conditions. The receptor–reporter complex is then selectively dissociated by the addition of the appropriate guests. When the reporter dissociates from the receptor a measurable response is produced.

We are interested in such competitive systems because they reduce the synthetic complexity of the receptor. In a recent communication 9-(*N*,*N*-diethanolaminomethyl)anthracene **1** has been used as a fluorescent sensor for boronic acids in methanol.[8] We were interested in using compound **1**, but, our reinvestigation showed that **1** does not bind with phenylboronic acid **2** in methanol.[9] This result was somewhat surprising since Hall and ourselves have recently used diethanolamine based polymers to bind with boronic acids.[10,11] However, the loading of diethanolamine based polymers is achieved in THF, which is a non-protic polar solvent.

During our reinvestigation we discovered that chloroform was an excellent solvent in which to form a stable complex between **1** and phenylboronic acid **2**. This led us to believe that we could yet develop a competitive sensor for diols using compound **1**, but in chloroform and not methanol (Scheme 1).

The fluorescence titration of **1** (1.0×10^{-6} mol dm^{-3}) with phenylboronic acid **2** was carried out in chloroform. The fluorescence intensity of **1** increased with added



Scheme 1. Proposed species in chloroform.

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phenylboronic acid **2** (Fig. 1). The fluorescence intensity change is due to formation of a cyclic boronate ester (complex **3**) with a strong B–N bond. The stability constant K was 361±6 mol^{-1} dm^3 ($r^2=1.00$) determined using standard curve fitting.[4]

The fluorescence titrations of **3** ([**1**]$=1.0\times10^{-6}$ mol dm^{-3} in the presence of [**2**]$=1.0\times10^{-2}$ mol dm^{-3}) with five different diols (2,2-dimethylpropylene glycol **5**, propyleneglycol **6**, ethyleneglycol **7**, triethanolamine **8**, and diethanolamine **9**) were carried out in chloroform (Fig. 2). The fluorescence intensity decreases with increasing concentration of diol. The fluorescence intensity change shows that the added diols can compete with fluorescent sensor **1** for the phenylboronic acid **2**. The decrease in fluorescence intensity has the following selectivity order: **5**>**9**>**8**>**7**>**6**.

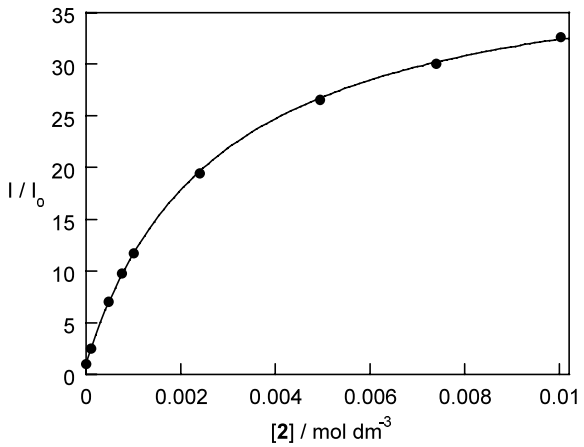


Figure 1. Relative fluorescence intensity of **1** (1.0×10^{-6} mol dm^{-3}) with different concentration of **2** (0–1.0×10^{-2} mol dm^{-3}) in chloroform. λ_{ex} 370 nm, λ_{em} 417 nm.

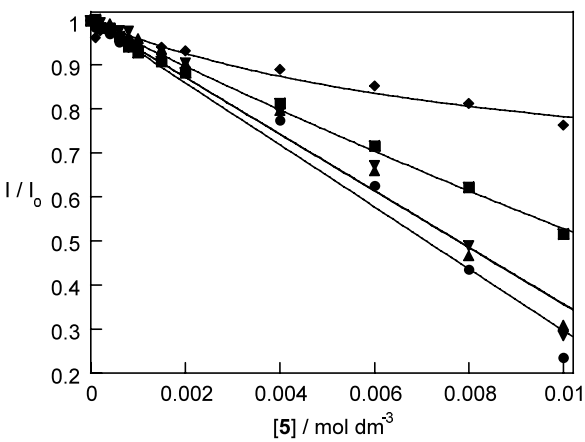


Figure 2. Relative fluorescence intensity of **1** (1.0×10^{-6} mol dm^{-3}) with different concentrations of diols (0–1.0×10^{-2} mol dm^{-3}) in the presence of **2** (1.0×10^{-2} mol dm^{-3}) in chloroform. (●) **5**, (◆) **6**, (■) **7**, (▲) **8**, (▼) **9**, λ_{ex} 370 nm, λ_{em} 417 nm.

Fig. 3 shows the titration of **1** with phenylboronic acid **2** in the presence of diol (1.0×10^{-2} mol dm^{-3}). The fluorescence intensity of **1** increases with added phenylboronic acid **2**. The increase in fluorescence intensity mirrors the order in Fig. 2 (**6**>**7**>**8**>**9**>**5**). The fluorescence change is caused by phenylboronic acid **2** binding with a diol, and inhibiting the formation of a complex between **1** and phenylboronic acid **2**.

To confirm these observations, we recorded the ^1H and ^{13}C NMR of **1** with and without phenylboronic acid **2** and also the ^{11}B NMR of phenylboronic acid **2** with **1**, **1**+**5** and **5** in $CDCl_3$. The data obtained are summarised in Tables 1 and 2.

The ^{11}B NMR provides the clearest evidence that a complex is formed in chloroform. The boron signal of phenylboronic acid **2** appears at 32.27 ppm and shifts to 15.90 ppm on addition of **1**, indicating that the boron changes hybridisation from sp^2 to sp^3.[12] The boron signal of phenylboronic acid **2** with **1** and **5** appears at 29.00 ppm, the signal is similar to that for the complex formed between phenylboronic acid **2** and **5** at 29.72 ppm. The observed shift from 15.90 to 29.00 ppm is due to a change from complex **3** (sp^3) to complex **4** (sp^2). Also, in the ^{13}C NMR the methylene next to the oxygen of **1** shifts by 3.03 ppm on addition of phenylboronic acid **2**, but when **5** is also added the shift is only 0.13 ppm. The ^1H NMR of **1** is also informative; the spectrum becomes broad on addition of phenylboronic acid **2**, however, the spectra of **1**+**2**+**5** is sharp. All of these NMR measurements indicate that in chloroform **1** and phenylboronic acid **2** form a fluorescent complex **3**, this complex is then broken by the addition of diols (**5**–**9**) to produce complex **4**.

In conclusion we have developed a new competitive PET sensor system for diols using **1** in chloroform.

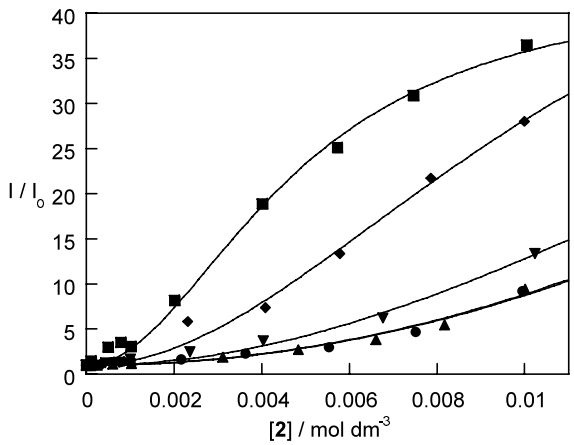
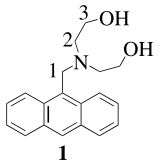


Figure 3. Relative fluorescence intensity of **1** (1.0×10^{-6} mol dm^{-3}) with different concentrations of **2** (0–1.0×10^{-2} mol dm^{-3}) in the presence of diols (1.0×10^{-2} mol dm^{-3}) in chloroform. (●) **5**, (◆) **6**, (■) **7**, (▲) **8**, (▼) **9**, λ_{ex} 370 nm, λ_{em} 417 nm.

Table 1. ^{1}H and ^{13}C NMR of **1** in $CDCl_3$ (shift on addition of **2** and **2**+**5**)



1

	Assignment	**1** (ppm)	**1**+**2** (ppm)	**1**+**2**+**5** (ppm)
^{1}H (ppm) (300.2 MHz)	1	4.69	–[a]	4.70 (+0.01)
	2	2.80	–[a]	2.80 (±0.00)
	3	3.52	–[a]	3.53 (0.01)
^{13}C (ppm) (75.5 MHz)	1	51.55	51.52 (−0.03)	51.61 (+0.06)
	2	55.85	55.99 (+0.14)	55.87 (+0.02)
	3	59.65	62.68 (+3.03)	59.78 (+0.13)

[a] Proton spectra too broad to assign.

Table 2. ^{11}B NMR (96.3 MHz) of **2** in $CDCl_3$ (shift on addition of **1**, **1**+**5** and **5**)

2 (ppm)	**1**+**2** (ppm)	**1**+**2**+**5** (ppm)	**2**+**5** (ppm)
32.27	15.90 (−16.37)	29.00 (−3.27)	29.72 (−2.55)

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