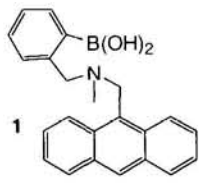
Selective Fluorescence Signalling of Saccharides in Their Furanose Form

Christopher R. Cooper and Tony D. James*
The University of Birmingham, School of Chemistry, Edgbaston, Birmingham B15 2TT, UK

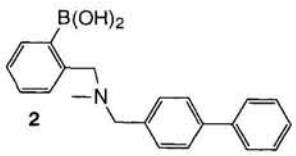
(Received June 1, 1998; CL-980421)

A boronic acid binding site and biphenyl fluorophore has been used to create a fluorescent PET (photoinduced electron transfer) sensor for saccharides in aqueous solution at pH 7.77. Formation of five or six membered cyclic boronate esters can be "read out" by the relative fluorescence intensity.

The development of fluorescent receptors for saccharides has attracted much attention.[1] The interaction of boronic acid and amine[2] has been used to create photoinduced electron transfer (PET)[3,4] sensory systems for saccharides. When saccharides form cyclic boronate esters with boronic acids, the acidity of the boronic acid is increased.[5] The stronger acid-base interaction modulates the PET from the amine (acting as a quencher) to anthracene (acting as a fluorophore). These compounds show increased fluorescence at neutral pH through suppression of the photoinduced electron transfer from nitrogen to anthracene on saccharide binding.[2] This work originated though our desire to investigate the factors influencing the strength of the B-N interaction and fluorescence signalling process. It is our belief that a better understanding of these fundamental interactions will lead to improved saccharide selective fluorescent sensors. Therefore, we decided to investigate what influence the fluorophore has on the efficiency of the photoinduced electron transfer process.



1



2

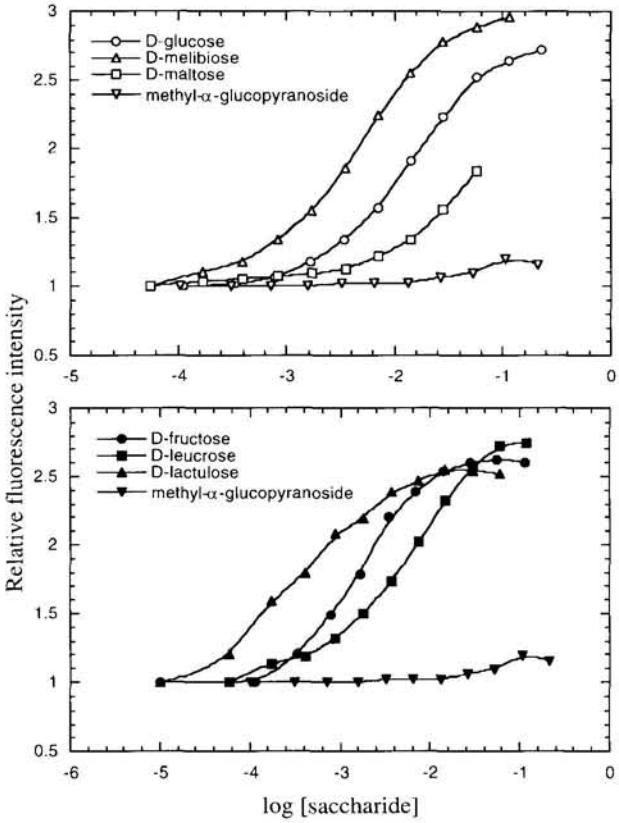


Figure 1. Saccharide concentration *vs* relative fluorescence intensity profile for **1** at pH 7.77 in 33% (w/w) methanol/water: excitation at 370 nm, emission at 418 nm.

For this study compound **1** was prepared according to literature procedure[2e], and compound **2** was prepared by an analogous route.

These two fluorescent systems were chosen because they have significantly different emission wavelengths 418nm and 318nm respectively. These differences in spectroscopic properties correlate with a larger HOMO-LUMO gap for the biphenyl system. Because the HOMO of the biphenyl is lower in energy than that of the anthracene a "stronger" B-N interaction will be required to suppress the photoinduced electron transfer from nitrogen on saccharide binding. Figure 1 shows selected saccharide titrations with compounds **1** and Figure 2 shows selected saccharide titrations with compounds **2** both systems are at pH 7.77 in 33% (w/w) methanol/water.[6]

From these titration curves it can be seen that with an anthracene fluorophore all the saccharides produce the same level of fluorescence recovery on saccharide binding, but with a biphenyl fluorophore maltose and leucrose do not cause the same level of fluorescence recovery as that observed with fructose, glucose, lactulose and melibiose. Compounds **1** and **2** show no fluorescence recovery with methyl-α-D-glucopyranoside, indicating that the 4,6-hydroxyls of pyranosaccharides do not contribute to the fluorescence increases observed with these saccharides. Within the group of saccharides studied all the saccharides except maltose and leucrose can equilibrate between pyranoside and furanoside forms under neutral aqueous conditions (Figure 3).

The observed fluorescence intensity is modulated by the strength of the B-N interaction. The fluorescence results obtained with compound **1** (anthracene) do not give any information about the relative strength of the B-N interaction, since in all cases high fluorescence recovery is observed. The fluorescence results with compound **2** (biphenyl) imply that a cyclic boronate ester formed with a furanose-(1,2)-diol results in a strong B-N interaction (high fluorescence recovery) and the cyclic boronate ester formed with a pyranose-(1,2)-diol results in a weak B-N interaction (low fluorescence recovery).

These results indicate that mono boronic acids bind

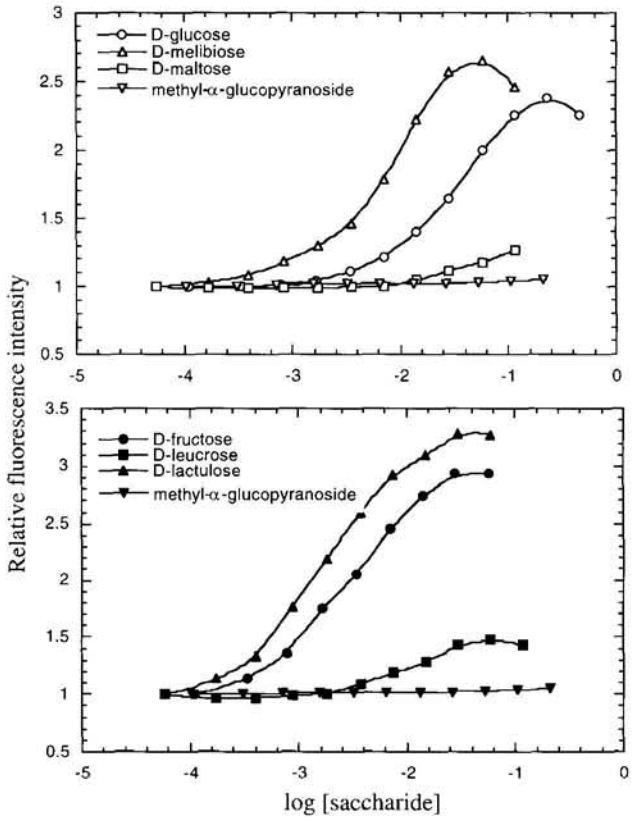


Figure 2. Saccharide concentration *vs* relative fluorescence intensity profile for **2** at pH 7.77 in 33% (w/w) methanol/water: excitation at 270 nm, emission at 318 nm.

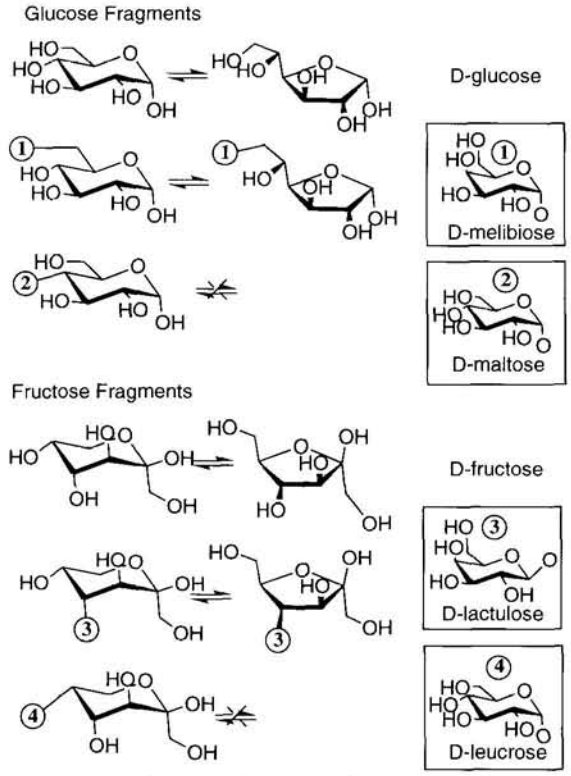


Figure 3. Pictoral representation of potential pyranose to furanose isomerisation of saccharides.

preferentially with saccharides in the furanose form. These results compliment the recent NMR work of Norrid and Eggert, who have shown that in neutral and basic conditions phenylboronic acid preferentially binds with the 2,3 hydroxyls of fructofuranose[7a] and the 1,2-hydroxyls of glucofuranose.[7b]

The fluorescent properties of compound **2** make it possible to detect monosaccharides in the presence of 1,4-linked polysaccharides. 1,4-Linked polysaccharides are conformationally fixed as pyranosides; therefore, they do not cause a large fluorescence increase on binding with compound **2**. Whereas, monosaccharides can isomerise from the pyranose to the furanose form in aqueous solution, and binding of compound **2** with the furanose form of the monosaccharide results in a large fluorescence increase. We believe this sensor could be used to monitor the disappearance of saccharide monomers in saccharide polymerisation reactions.

TDJ wishes to acknowledge the Royal Society for support through the award of a University Fellowship. CRC wishes to acknowledge the School of Chemistry for support through the award of a School Studentship.

References

1 a) G. Deng, T. D. James, and S. Shinkai, *J. Am. Chem. Soc.*, **116**, 4567 (1994) and references cited therein. b) J. Yoon and A. W. Czarnik, *J. Am. Chem. Soc.*, **114**, 5874 (1992). c) G. T. Morin, M. P. Hughes, M-F. Paugam, and B. D. Smith, *J. Am. Chem. Soc.* **116**, 8895 (1994) and references cited therein.

2 a) T. D. James, K. R. A. S. Sandanayake, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1994**, 477. b) T. D. James, K. R. A. S. Sandanayake, and S. Shinkai, *Angew. Chem., Int. Ed. Engl.*, **33**, 2207 (1994). c) T. D. James, K. R. A. S. Sandanayake, and S. Shinkai, *Nature*, **374**, 345 (1995). d) T. D. James and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1995**, 1483. e) T. D. James, K. R. A. S. Sandanayake, R. Iguchi, and S. Shinkai, *J Am. Chem. Soc.*, **117**, 8982 (1995). f) T. D. James, P Linnane, and S Shinkai, *Chem. Commun.*, **1996**, 281. g) T. D. James, K. R. A. S. Sandanayake, and S. Shinkai, *Angew.Chem., Int. Ed. Engl.*, **35**, 1910 (1996). h) C.R. Cooper and T. D. James, *Chem Commun*, **1997**, 1419.

3 R. A. Bissel, A. P. de Silva, H. Q. N. Gunaratna, P. L. M. Lynch, G. E. M. Maguire, C. P. McCoy, and K. R. A. S. Sandanayake, *Top. Curr. Chem.*, **168**, 223 (1993).

4 A. W. Czarnik, "Fluorescent Chemosensors for Ion and Molecular Recognition," ACS Books, Washington (1993).

5 J. P. Lorand and J. D. Edwards. *J. Org. Chem.*, **24,** 769 (1959).

6 D. D. Perrin and B. Dempsey, "Buffers for pH and Metal Ion Control Ch. 6," Chapman and Hall, London (1974)

7 a) J. C. Norrid and H. Eggert, *J. Chem. Soc., Perkin 2*, **1996**, 2583. b) J. C. Norrid and H. Eggert, *J. Am. Chem. Soc.*, **117**, 1479 (1995).