Pergamon

Tetrahedron Letters, Vol. 35, No. 14, pp. 2201-2204, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0297-B

Attempts to Change the Color of Dye Molecules by Saccharides

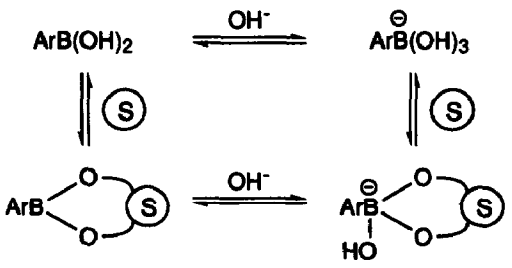
Takeshi Nagasaki, Hideyuki Shinmori, and Seiji Shinkai*

Department of Organic Synthesis, Faculty of Engineering,
Kyushu University, Fukuoka 812, Japan

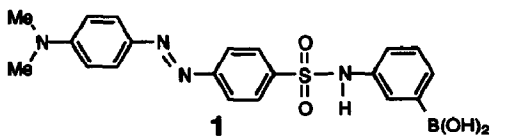
Abstract: Azobenzene derivatives bearing a phenylboronic acid moiety changed their colors in response to added saccharides. On the basis of detailed spectral studies the color change was ascribed to deaggregation of dye molecules induced by complexation with these saccharides.

The color of flowers attracts vision of the human and makes their heart peaceful. How does nature create such beautiful colors? The survey of the past literatures teaches us that an anthocyanin dye family is used in most flowers and the subtle change in the color tone is controlled by intermolecular and/or intramolecular interactions of saccharides covalently-bound to the anthocyanin dye.[1,2] The purpose of the present research is to reproduce such a saccharide-induced color change in a totally artificial system. Recently, it was shown that boronic acids serve as an efficient "covalent-bond-forming interface" for saccharides.[3-7] It thus occurred to us that the color of boronic-acid-appended dye molecules would be readily controllable by added saccharides. Three possible but mechanistically-different strategies come to our mind: (a) as shown in Scheme 1, neutral sp^2 borons change to anionic sp^3 borons on the addition of saccharides, so that the saccharide-binding can affect the π-conjugation system in dye molecules, (b) in most cases dye molecules aggregate in aqueous solution, so that the color change can be readily induced when added saccharides affect the association-dissociation equilibrium, and (c) synergistic effects of (a) plus (b). In this paper we report the synthesis and the evaluation of **1** and **2** to assess the feasibility of strategy (b).

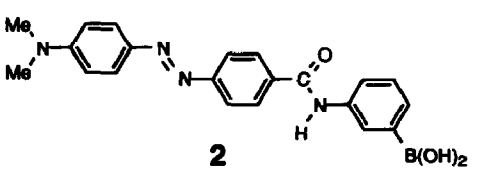
Compounds **1** and **2** were synthesized from *m*-aminophenylboronic acid and the corresponding acid chloride in a water-dioxane (3:11 v/v) mixed solution in the presence of $NaHCO_3$: **1**, mp 152-154 °C, yield 60%;



Scheme 1: (S) denotes monosaccharide



1



2

2, mp 251-253 °C, yield 30%. These products were identified by IR and ^{1}H NMR spectral evidence and elemental analysis.

We measured the absorption spectra of **1** (1.00×10^{-5} M) in water:DMF = 300:1 v/v at 25 °C and pH 10.5 where boronic acids can bind saccharides efficiently. A concentration (10^{-6} M ~ 10^{-5} M) vs. absorbance plot satisfied the Lambert-Beer's law and the λ_{max} (470 nm) was not so different from that in DMF (446 nm). The results suggest that **1** does not aggregate in aqueous solution. The photo-titration of **1** established that the amide proton (RSO_2NHR') is dissociated at around pH 10.4 to give the anionic species. Hence, **1** shows the high solubility in aqueous solution. At neutral pH region, on the other hand, **1** precipitated.

Compound **2** was soluble even at neutral pH region. The photo-titration in water:DMF = 300:1 v/v at 25 °C proved the pK_a of the boronic acid to be 8.7 in the absence of saccharides and 5.6 in the presence of 0.10 M D-fructose (data not shown here). We thus chose pH 6.9 where a large difference in the absorption spectra would be induced by the saccharide addition. The concentration-dependence of **2** did not obey the Lambert-Beer's law and gave a new peak at 385 nm at higher concentrations. The spectral shape changed when DMF was added to the aqueous solution (Fig. 1). The results indicate that **2** does aggregate in this medium. We thus added several monosaccharides, expecting that complexation between **2** and monosaccharides induces deaggregation of **2**. Very interestingly, *the color of the solution changed from yellow to orange*: the corresponding absorption spectra are shown in Fig. 2. The λ_{max} at 385 nm disappears as the λ_{max} at 472 nm increases and an isosbestic point exists at 391 nm. Particularly, the absorption spectrum in the presence of D-fructose is very similar to that in the presence of the SDS (100 mM) micelle in which **2** is dispersed discretely.

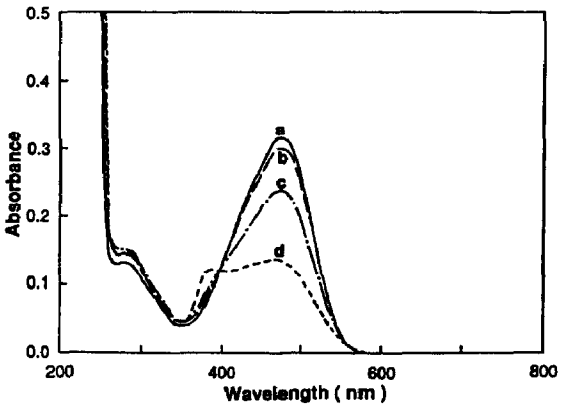


Fig. 1. Absorption spectra of **2** (1.00×10^{-5} M) at 25 °C and pH 6.9 (0.10 M phosphate): water:DMF (v/v) = 5:1 (a), 10:1 (b), 20:1 (c), and 300:1 (d).

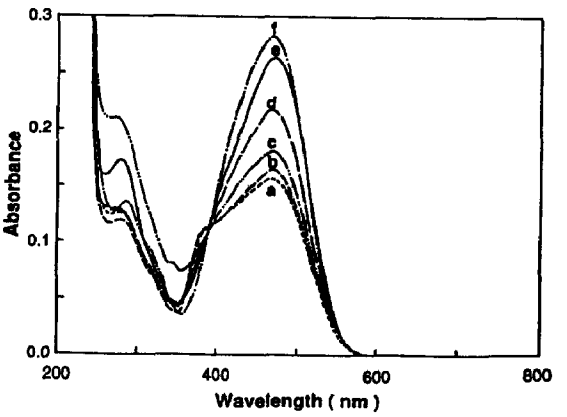


Fig. 2. Absorption spectra of **2** (1.00×10^{-5} M) at 25 °C and pH 6.9 (0.10 M phosphate): water:DMF = 300:1 v/v: no saccharide (a), [saccharide] = 0.10 M D-glucose (b), D-mannose (c), D-arabinose (d), D-fructose (e), and no saccharide in the presence of the SDS (100 nm) micelle (f).

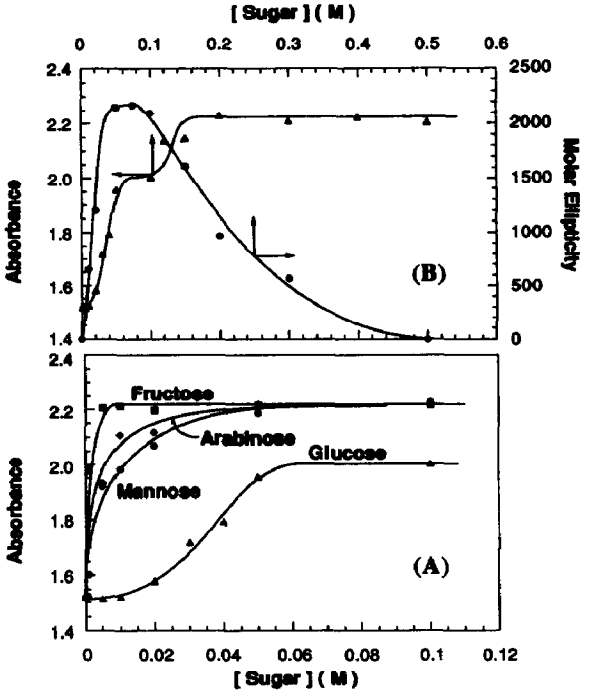


Fig. 3. (A) Plots of [saccharide] vs. OD_{472} at [2] = 1.00 x 10^{-3} M at 25 °C and pH 10.5 (0.10 M carbonate) in water:DMF = 30:1 v/v: (B) plots of [D-glucose] vs. OD_{472} and θ_{501} at [2] = 1.00 x 10^{-3} M at 25 °C and pH 10.5 (0.10 M carbonate) in water:DMF = 30:1 v/v. The cell with 1mm length was used.

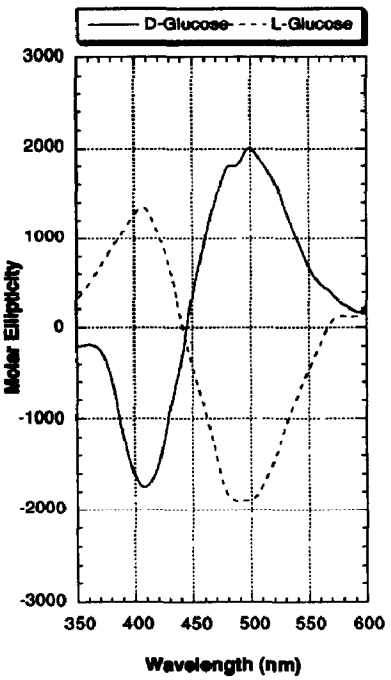
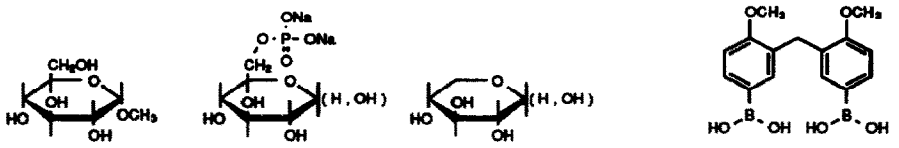


Fig. 4. CD spectra of **2** (1.00 x 10^{-3} M) at 25 °C and pH 10.5 (0.10 M carbonate) in water:DMF = 30:1 v/v: [glucose] = 0.10 M.

Figure 3A shows plots of monosaccharide concentration vs. OD_{472}. The magnitude of the spectral change is exactly in line with the order of association constants for simple boronic acids: that is, D-fructose > D-arabinose > D-mannose > D-glucose.[8] The result, together with those described above, supports the view that the color change is related to deaggregation of monosaccharides induced by the saccharide-binding which makes **2** more hydrophilic. Strangely, D-glucose shows a biphasic concentration-dependence. The sigmoidal dependence is frequently seen when the auto-accelerative process is involved in the concerned system. We noticed that at intermediary concentration region the D- and L-glucose complexes become CD (circular dichroism)-active (Fig. 3B) and give a pair of symmetrical exciton coupling bands (Fig. 4). The CD-activity was not observed for other three monosaccharides. Since the exciton coupling appears when two dipoles interact asymmetrically at the excited state, the finding supports the formation of a 2:1 **2** / glucose complex.[9] This means that with increasing glucose concentration the CD-active 2:1 complex is initially formed, which is gradually changed to the CD-silent 1:1 complex. When glucose forms the 2:1 complex, 1,2-diol and 4-OH•5-CH_2OH are used for complexation.[4,7] The CD-activity was not observed for glucose analogs **3-5**, indicating again that the origin of the CD-activity is the formation of the 2:1 complex.



3 4 5 6

It is not yet clear why only glucose can form the CD-active 2:1 complex to give the exciton coupling. We previously studied the monosaccharide recognition with diboronic acid **6** to form cyclic 1:1 complexes.[4] Among several monosaccharides, glucose gave the exceptionally large affinity with **6**.[4] The facile ring formation suggests that glucose has a special configuration which can orient two phenylboronic acids to the same direction.[10] In **2**, therefore, the formation of the 2:1 complex is stabilized by intramolecular hydrophobic interactions between two bound dye molecules and the CD-activity arises from the interaction of these two dipoles at the excited state.

In corollary, the present study demonstrated for the first time that by imitating the coloration of flowers in nature the color of dye molecules can be changeable by saccharides.

References

1. For a recent comprehensive review see S. Misumi, *Kagaku To Kogyo* (*Chem. Chem. Ind.*), **46**, 756 (1993).
2. T. Goto and T. Kondo, *Angew. Chem. Int. Ed. Engl.*, **30**, 17 (1991).
3. L. K. Mohler and A. W. Czarnic, *J. Am. Chem. Soc.*, **115**, 2998 (1993).
4. K. Tsukagoshi and S. Shinkai, *J. Org. Chem.*, **56**, 4089 (1991); Y. Shiomi, M. Saisho, K. Tsukagoshi, and S. Shinkai, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2111.
5. S. Shinkai, K. Tsukagoshi, Y. Ishikawa, and T. Kunitake, *J. Chem. Soc., Chem. Commun.*, **1991**, 1040; R. Ludwig, K. Ariga, and S. Shinkai, *Chem. Lett.*, **1993**, 1413.
6. K. Kondo, Y. Shiomi, M. Saisho, T. Harada, and S. Shinkai, *Tetrahedron*, **48**, 8239 (1992).
7. T. D. James, T. Harada, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1993**, 857.
8. K. Yoshino, M. Fukuda, and Y. Mori, Paper presented at the 58th Annual Meeting of the Chemical Society of Japan, 1989, Kyoto.
9. We attempted the determination of the stoichiometry by a molar ratio method or a continuous variation method but failed bacause of the small association constant and the complexity arising from the aggregation.
10. Efforts to determine the structure of the 2:1 **2** / glucose complex in D_2O by ^1H NMR spectroscopy are currently continued but seem difficult so far.

(*Received in Japan* 29 *November* 1993)