Synthesis of Sugar-containing Polymers by Self-condensation with Diboronic Acid

Masafumi Mikami and Seiji Shinkai*

Chemirecognics Project, ERATO, Research Development Corporation of Japan, Aikawa 2432-3, Kurume, Fukuoka 830, Japan

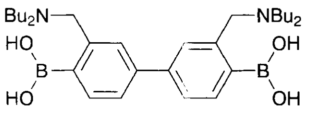
Self-condensation of 3,3′-bis(*N,N*-di-n-butylaminomethyl)biphenyl-4,4′-diboronic acid and saccharides yields polymers containing saccharides in the main chain: they show unique CD spectroscopic properties which reflect the chirality of saccharides.

Recently, we and a few other groups proposed to use boronic acids as a saccharide-binding functional group.[1-7] Since one boronic acid reacts with two OH groups, we expected that the polycondensation reaction of diboronic acid and monosaccharide should yield a sugar-containing linear polymer. To test this hypothesis we synthesized **1**. Compound **1** was designed taking the following factors into account: (*i*) the biphenyl skeleton is employed to detect the induced chirality of the main chain by CD spectroscopy,[4] (*ii*) two boronic acids are introduced into 4,4′-positions to suppress the formation of an intramolecular 1 : 1 adduct with saccharides,[4] (*iii*) a boronic acid-diol complex is stabilized by coordination of an intramolecular tertiary amine[8] and (*iv*) four n-butyl groups are attached to enhance the solubility in organic solvents. Monoboronic acid **2** was used as a reference compound.

Compound **1** was synthesized from 4,4′-diamino-3,3′-dimethylbiphenyl according to Scheme 1. The product (mp > 300 °C) was identified by IR, ^{1}H NMR and MS evidence and elemental analysis. Compound **2** was synthesized from 4-bromo-2-methylaniline according to Scheme 2. The product (mp 132–136 °C) was identified by the same methods.

Equimolar amounts of **1** and saccharide (20 mmol dm^{-3} each) were dissolved in anhydrous dichloromethane and the reaction mixture was refluxed for 1.5–6 h in the presence of molecular sieves 4Å. At the initial state of the reaction the system is heterogeneous. As the reaction proceeds, the solution becomes clear and homogeneous. The molecular mass was estimated by a light-scattering method (Otsuka Electronics DLS-700). The CD spectra were measured with a JASCO J-720 CD spectrometer.

As shown in Fig. 1, an equimolar mixture of **1** and L-fucose gave one positive maximum (277 nm) and two negative minima (252 and 230 nm) in the CD spectra and the intensities increase with increasing molecular mass. Since one of the two absorption maxima (268 nm) in the absorption spectra is consistent with the cross-over wavelength ($\lambda_{\theta=0}$ 262 nm) in the CD spectra, the positive maximum and the negative minimum at longer wavelength region can be regarded as an exciton-coupling band.



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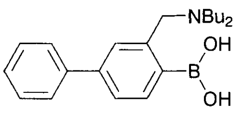

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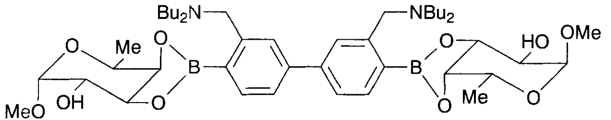

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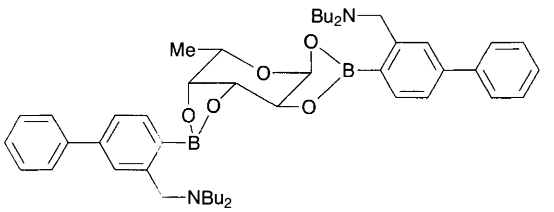

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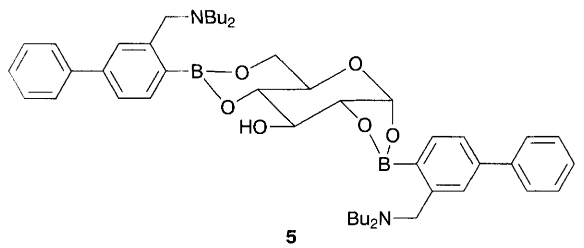

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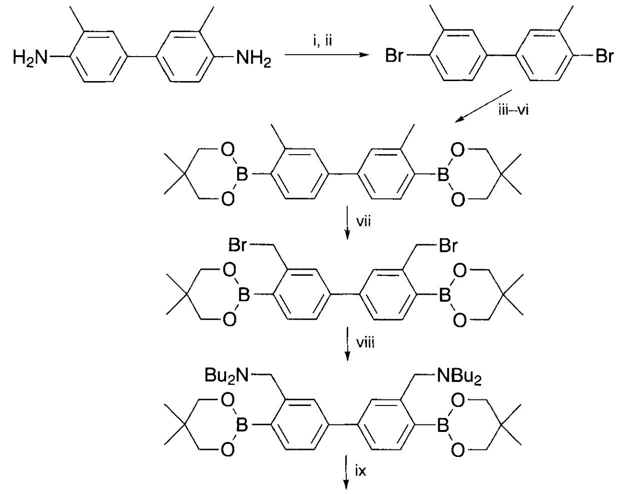
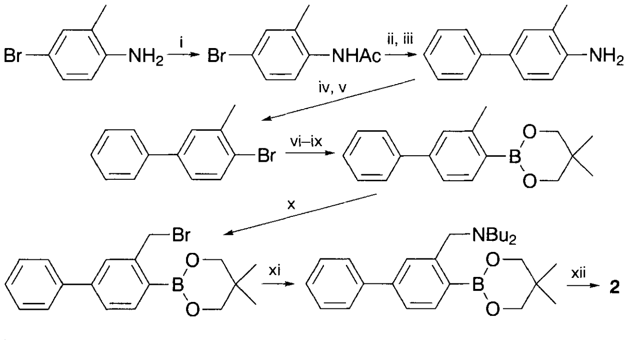


Scheme 1 *Reagents and conditions (yields)*: i, NaNO$_2$, 50% H$_2$SO$_4$; ii, CuBr, 47% HBr (30%); iii, butyllithium, THF, −78 °C; iv, B(OMe)$_3$, THF, −78 °C; v, 2 mol dm^{-3} HCl, room temp.; vi, 2,2-dimethyl-1,3-propanediol, toluene, reflux (35%); vii, NBS, CCl$_4$ (76%); viii, Bu$_2$NH, K$_2$CO$_3$, MeCN, room temp. (93%); ix, dil. HCl, CHCl$_3$, room temp. (41%)



Scheme 2 *Reagents and conditions (yields)*: i, AcCl, Et$_3$N, CH$_2$Cl$_2$, 0 °C (95%); ii, Pd(PPh$_3$)$_4$, PhB(OH)$_2$, Na$_2$CO$_3$, 80 °C (87%); iii, 2 mol dm^{-3} HCl, reflux (97%); iv, NaNO$_2$, 50% H$_2$SO$_4$; v, CuBr, 47% HBr (35%); vi, butyllithium, THF, −78 °C; vii, B(OMe)$_3$, THF, −78 °C; viii, 2 mol dm^{-3} HCl, room temp.; ix, 2,2-dimethylpropane-1,3-diol, toluene, reflux (82%); x, NBS, CCl$_4$ (87%); xi, Bu$_2$NH, K$_2$CO$_3$, MeCN, room temp. (72%); xii, Na$_2$CO$_3$ aq., Et$_2$O, room temp.

When D-fucose was used instead of L-fucose, a symmetrical CD spectrum with one negative minimum and two positive maxima was observed (Fig. 1). When D-glucose was used, the exciton-coupling band disappeared and one positive maximum (*ca.* 280 nm) and one negative minimum (234 nm) appeared (Fig. 2). The molecular mass (determined by a light-scattering method) increased with the reaction time: the highest molecular masses achieved for L-fucose and D-glucose were 1.06 × 10^5 and 4.00 × 10^4, respectively.†

To obtain further insights into the CD activity we prepared a 1:2 complex **3** from **1** and methyl α-L-fucopyranoside and a 2:1 complex **4** from **2** and L-fucose. Interestingly, **3** was almost CD-silent whereas **4** gave an exciton-coupling band similar to those observed for the polymeric **1**·fucose complexes but did not possess the 230 nm band (Fig. 1). The results suggest that the exciton-coupling band stems from the interaction of two dipole moments in biphenyl units flanking a fucose unit and the 230 nm band stems from the polymeric repeat structure. The 2:1 complex **5** prepared from **2** and D-glucose also gave the CD spectrum similar to that of the corresponding polymer although the λ_{max} slightly shifts to shorter wavelength (Fig. 2).

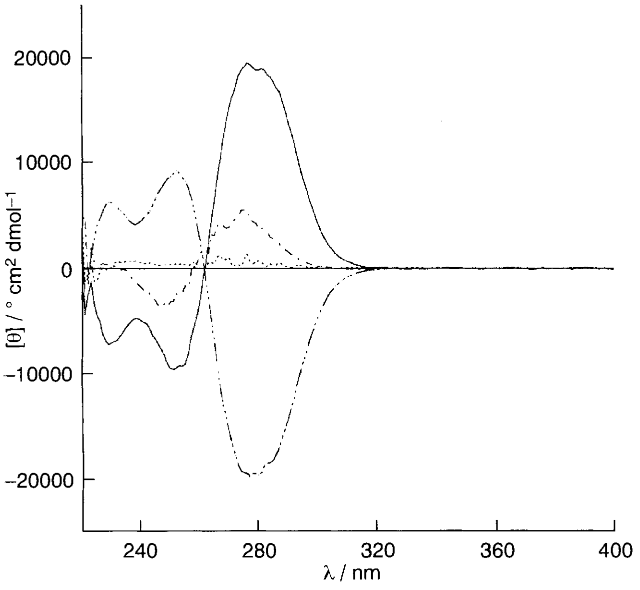


Fig. 1 CD spectra of polymers prepared from an equimolar mixture of **1** and fucose [L-fucose (—, 1.16 mmol dm^{-3}), D-fucose (— ---, 1.20 mmol dm^{-3})], **3** (---, 1.10 mmol dm^{-3}) and **4** (– – – –, 1.04 mmol dm^{-3}): 25 °C, dichloromethane

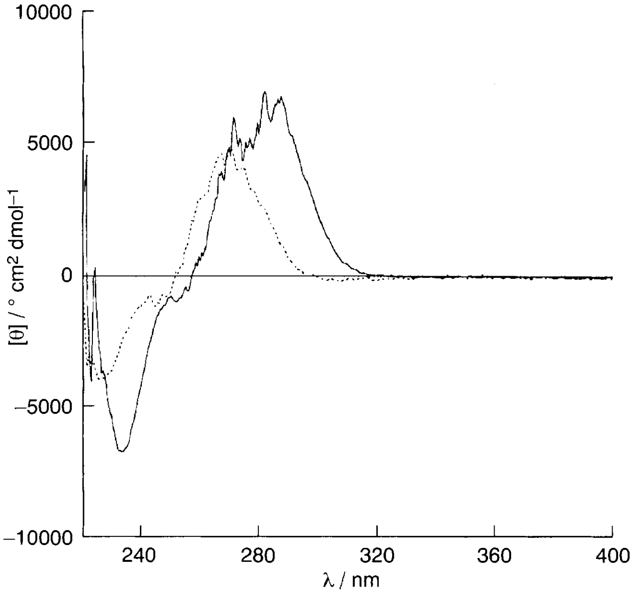


Fig. 2 CD spectra of a polymer prepared from an equimolar mixture of **1** and D-glucose (—, 1.48 mmol dm^{-3}) and **5** (---, 0.92 mmol dm^{-3}): 25 °C, dichloromethane

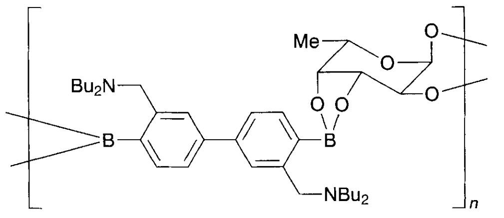


Fig. 3 Polymer structure resulting from **1** and L-fucose: the pyranose form is adopted here but the involvement of the furanose form is not ruled out

We believe that this is the first example for self-condensation of saccharides giving polymers containing saccharides in the main chain. However, a very important problem still remains unresolved: a saccharide is an unsymmetrical molecule having a 'head' (1,2-diol) and a 'tail' (3,4- or 4,6-diol). At present it is not clear whether the saccharide units are incorporated into the polymer in a head-to-tail manner or in a random manner. We believe that if all saccharide units are fixed in a head-to-tail orientation, the polymer should be twisted into a helical structure as observed for DNA. The effort to arrange saccharide units in a head-to-tail orientation is currently continued in this laboratory.

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Footnote

† The polymer obtained from **1** and L-fucose gave satisfactory elemental analysis ν_{max}(KBr)/cm^{-1} 1383 (B–O). The polymer obtained from **1** and D-glucose was also satisfactory although the polymers are hygroscopic and several water molecules may be included.

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