Boronic Acids in Molecular Self-Assembly

Norifumi Fujita, Seiji Shinkai, and Tony D. James
Chem. Asian J. ***2008***, 3, 1076 – 1091

Yong Guan
Aug 15, 2008

Introduction

- **Self-assembly** is a term used to describe processes in which a disordered system of pre-existing components forms an organized structure or pattern as a consequence of specific, local interactions among the components themselves, without external direction.

http://en.wikipedia.org/wiki/Self-assembly

Introduction

- 1860--Frankland documented the preparation of ethylboronic acid, with the first synthetic publication on organoboronchemistry.

- 1880--Michaelis and Becker

$$BCl_3 + HgPh_2 \longrightarrow PhBCl_2 \xrightarrow{H_2O} PhB(OH)_2$$

- 1909

  the classical synthesis of boronic acids from Grignard reagents and trialkyl borates.

E. Frankland, B. F. Duppa, *Justus Liebigs Ann. Chem.* **1860**, *115*, 319.
A. Michaelis, P. Becker, *Ber. Dtsch. Chem. Ges.* **1880**, *13*, 58.
A. Michaelis, P. Becker, *Ber. Dtsch. Chem. Ges.* **1882**, *15*, 180.
E. Khotinsky, M. Melamed, *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 3090.

Importance

- Why is the boronic acid-diol interaction an important force in molecular assembly?

- (a) The boronic acid–diol interaction is reversible.

- (b) The boronic acid–diol interaction is a covalent binding interaction and unlike non-covalent interactions, the interaction is directional.

- (c) The diol unit used for the assembly is ubiquitous in nature in the form of saccharides.

Boronic Acid–Diol Complexation

- The first quantitative investigation into the interactions between boronic acids and polyols in 1959.

  Lorand and Edwards added a range of polyols to solutions of phenylboronic acid.

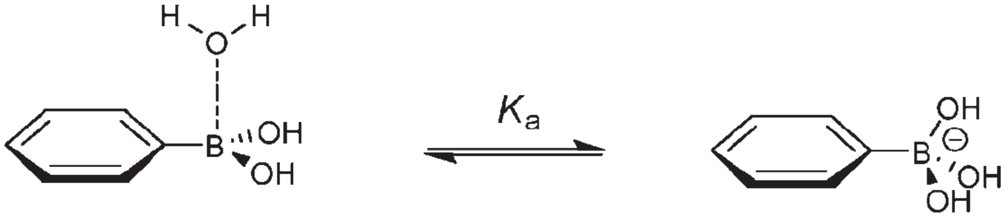
  The pH of the solutions was adjusted such that there was an equal speciation of phenylboronic acid in its neutral and anionic forms; the pH matching the pK_a.

  As diol was added, the pH of the systems decreased, allowing binding constants to be determined through the technique of pH depression.

J. P. Lorand, J. O. Edwards, *J. Org. Chem.* **1959**, *24*, 769.

Boronic Acid–Diol Complexation

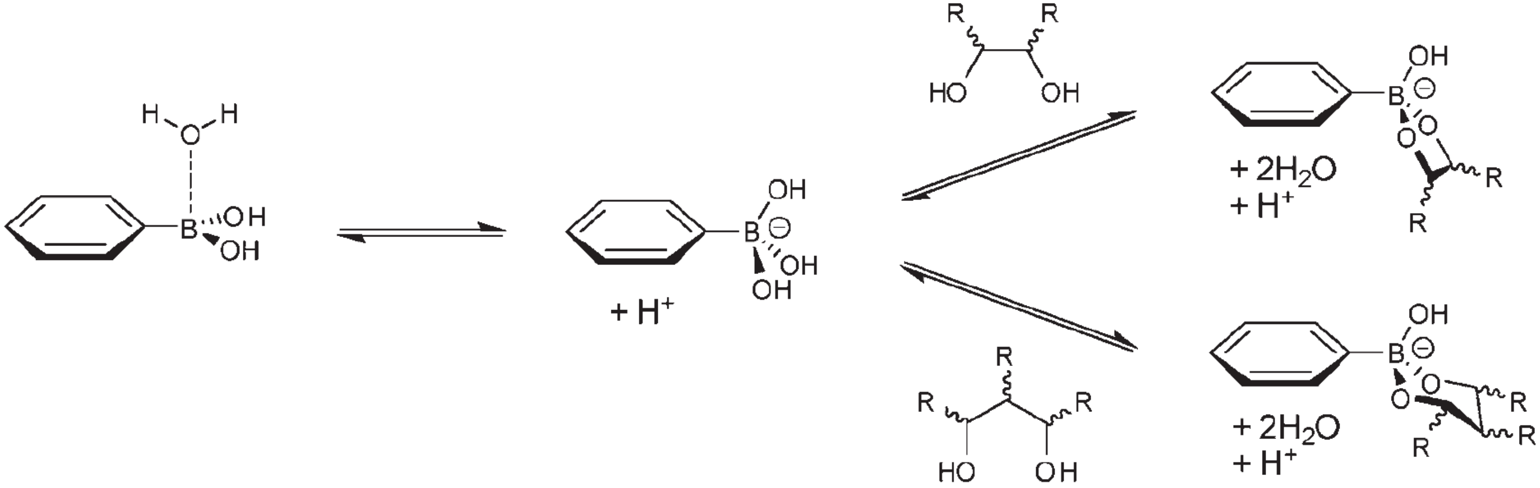
- Conclusions



As the phenylboronic acid and water react a solvated hydrogen ion is liberated, thereby defining the acidity constant K_a, where pK_a=8.70 in water at 25 ℃

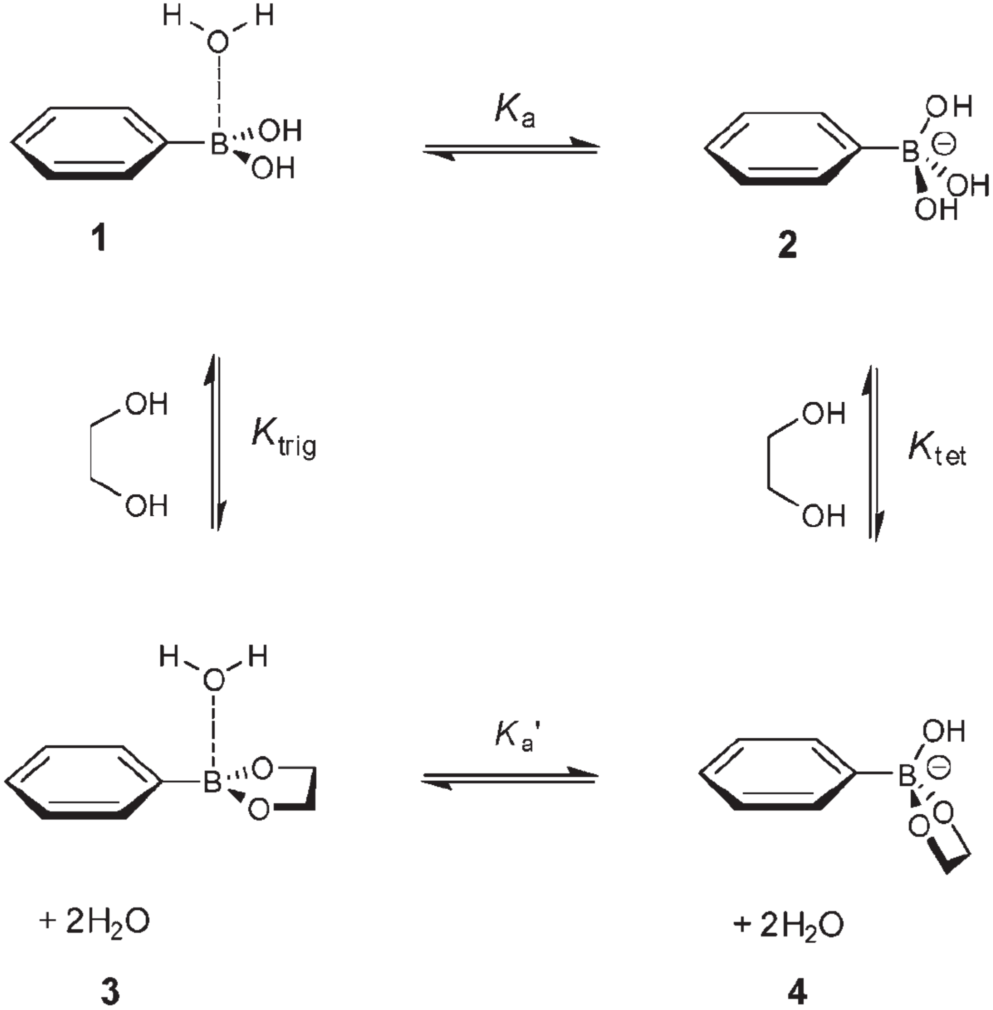
L. I. Bosch, T. M. Fyles, T. D. James, *Tetrahedron* **2004**, *60*, 11175.

Boronic Acid–Diol Complexation



Until recently it was believed that the kinetics of this interconversion was fastest in aqueous basic media where the boron is present in its tetrahedral anionic form

Boronic Acid–Diol Complexation



Fructose	$\log K_{tet}$	3.8
	$\log K_{trig}$	< -1.4
Glucose	$\log K_{tet}$	2.3
	$\log K_{trig}$	-0.3
Mannitol	$\log K_{tet}$	3.4
	$\log K_{trig}$	0.3
Sorbitol	$\log K_{tet}$	3.9
	$\log K_{trig}$	0.8

$K_{tet} > K_{trig}$

phenylboronic acid binding fructose in 0.5m NaCl water log K_{tet}=3.8, log K_{trig}<-1.4.

L. I. Bosch, T. M. Fyles, T. D. James, *Tetrahedron* **2004**, *60*, 11175.

Boronic Acid–Diol Complexation

- The neutral boronic acid becomes more acidic upon diol complexation.

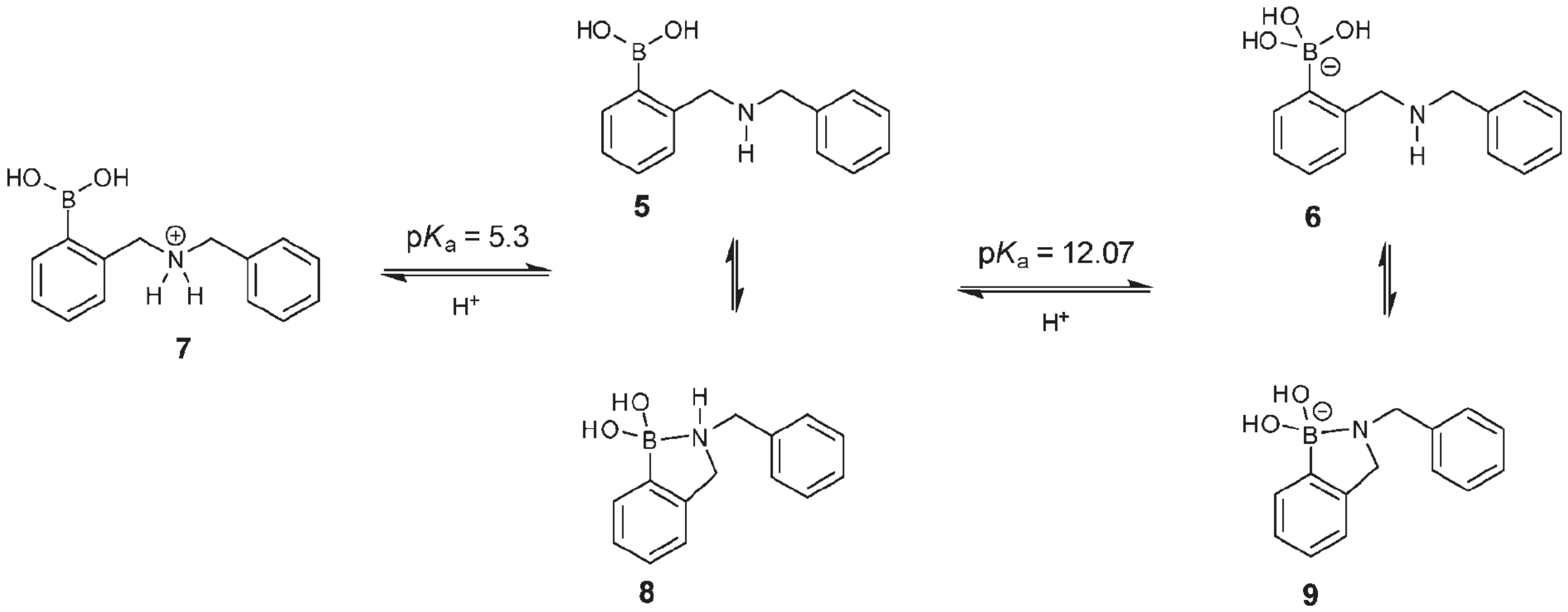
- The acidity constant of the bound complex is defined by K_a'

- $pK_a > pK_a'$.

- The pK_a of phenylboronic acid=9.0 in 0.1m NaCl 1:2 (v/v) methanol/water; the pK_a' of phenylboronic acid bound to fructose=5.2;

L. I. Bosch, T. M. Fyles, T. D. James, *Tetrahedron* **2004**, *60*, 11175.

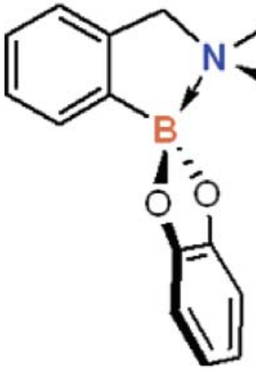
Amine–Boron (N–B) Interactions



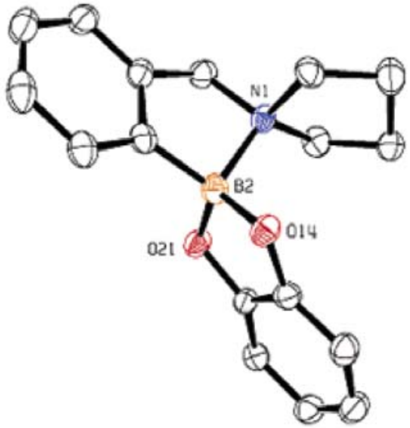
N–B interaction to be 13 kJ mol^{-1} or less in the absence of solvent
the same as that of a hydrogen bond

L. I. Bosch, T. M. Fyles, T. D. James, *Tetrahedron* **2004**, *60*, 11175.

Amine–Boron (N–B) Interactions



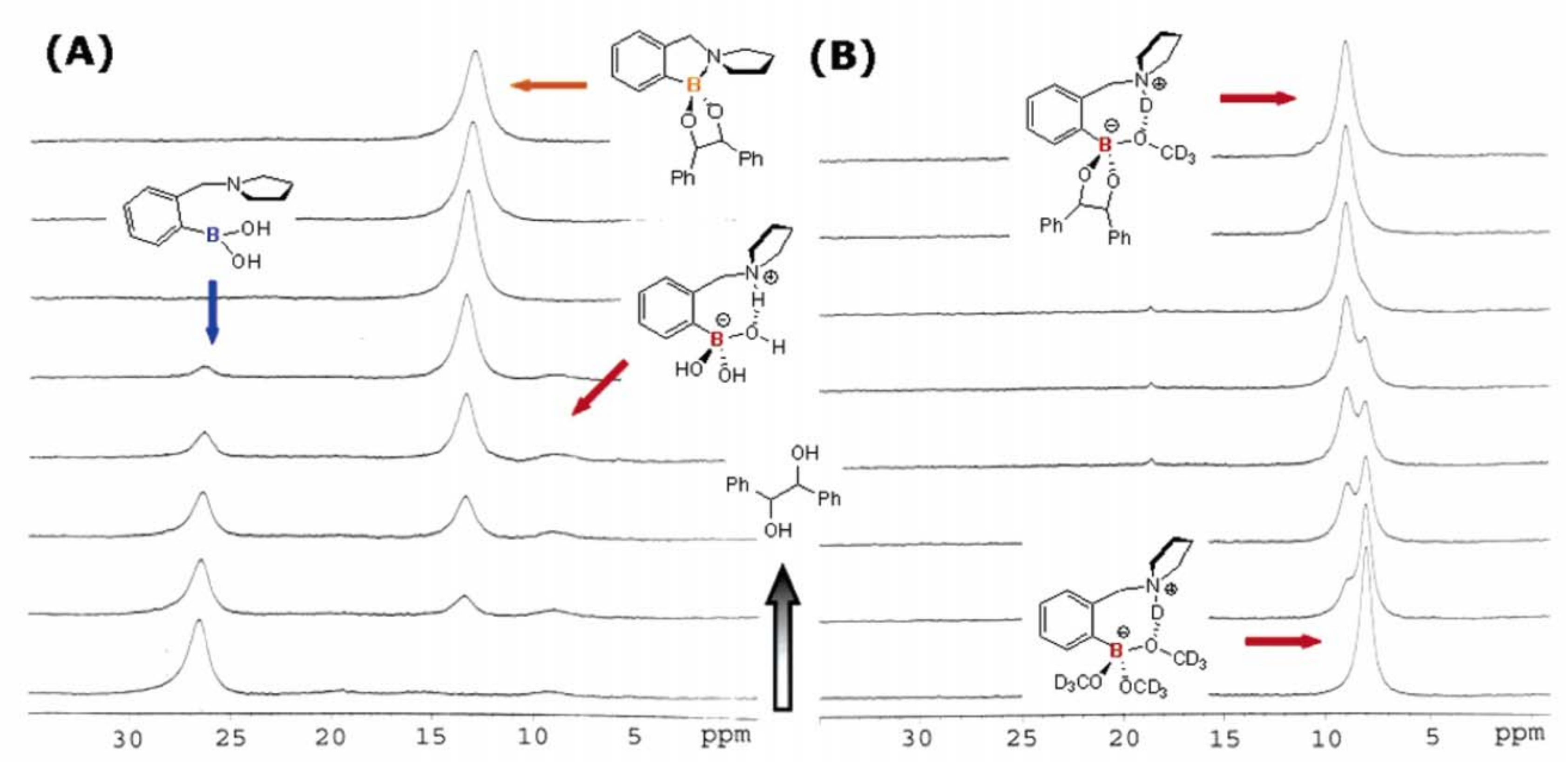
7



The N-B bond length is 1.683 Å

L. Zhu, S. H. Shabbir, M. Gray, V. M. Lynch, S. Sorey, E. V. Anslyn, *J. Am. Chem. Soc.* **2006**, *128*, 1222.

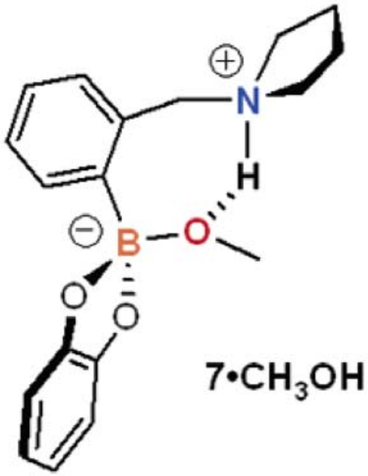
Amine–Boron (N–B) Interactions



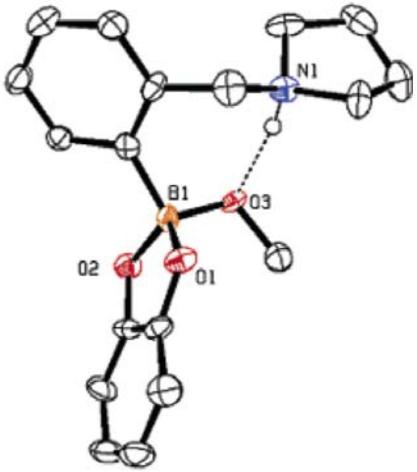
^{11}B NMR spectra of compound **4** (10 mM) in the presence of 0-80 mM catechol to create complex **7** in $CDCl_3$ (A) and CD_3OD (B), respectively.

L. Zhu, S. H. Shabbir, M. Gray, V. M. Lynch, S. Sorey, E. V. Anslyn, *J. Am. Chem. Soc.* **2006**, *128*, 1222.

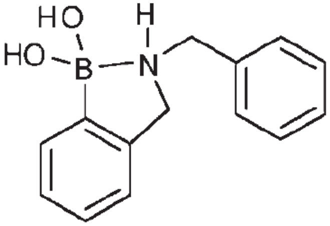
Amine–Boron (N–B) Interactions



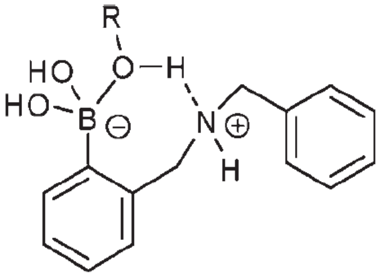
7•CH_3OH

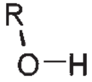


The average B-O bond length is 1.50 Å, and the O-B-O bond angle of the cyclic catechol boronate is 102.43°



Not correct





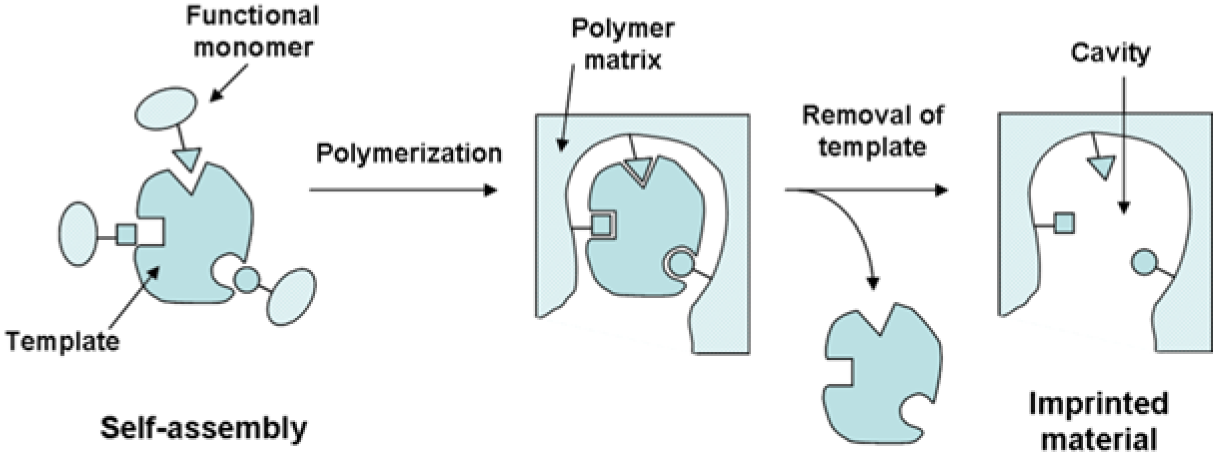
protic solvent

R = H (water),
R = CH_3 (methanol),
R = CH_3CH_2 (ethanol) etc

L. Zhu, S. H. Shabbir, M. Gray, V. M. Lynch, S. Sorey, E. V. Anslyn, *J. Am. Chem. Soc.* **2006**, *128*, 1222.

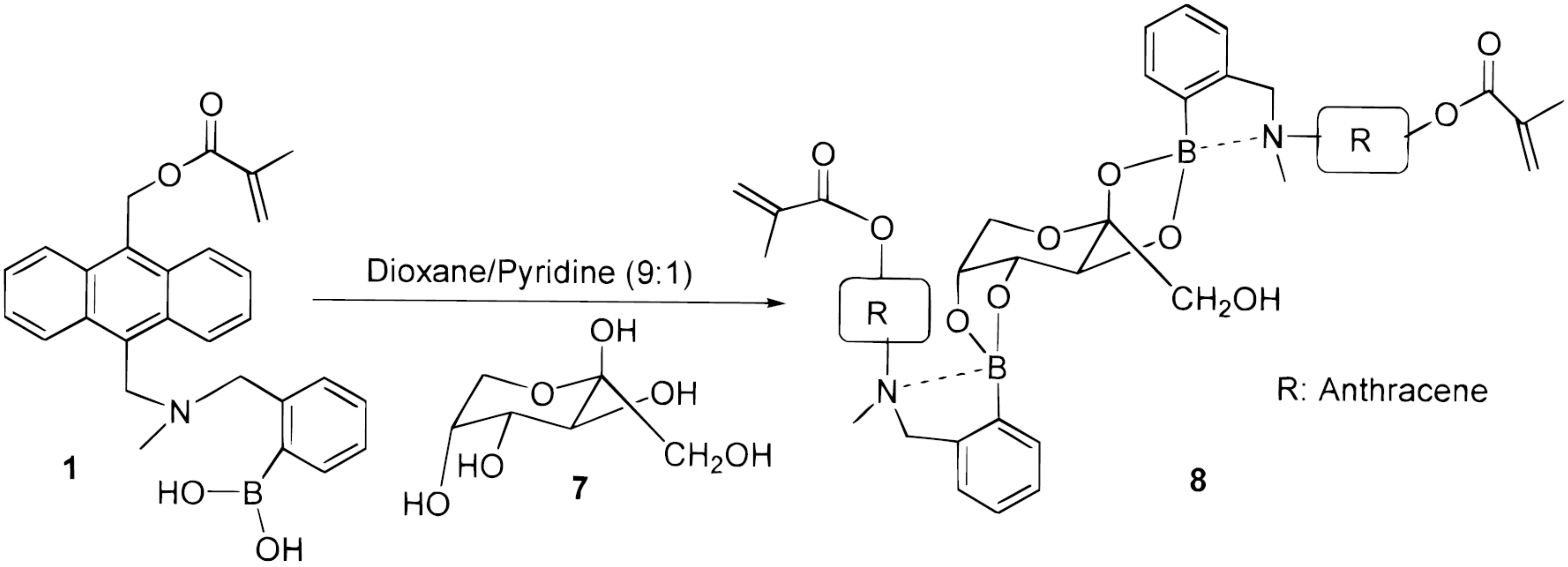
Molecular Imprinting

- In chemistry, **molecular imprinting** is a technique to create template-shaped cavities in polymer matrices with memory of the template molecules.

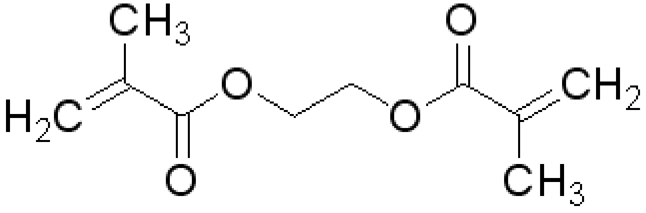


http://en.wikipedia.org/wiki/Molecular_imprinting

Molecular Imprinting



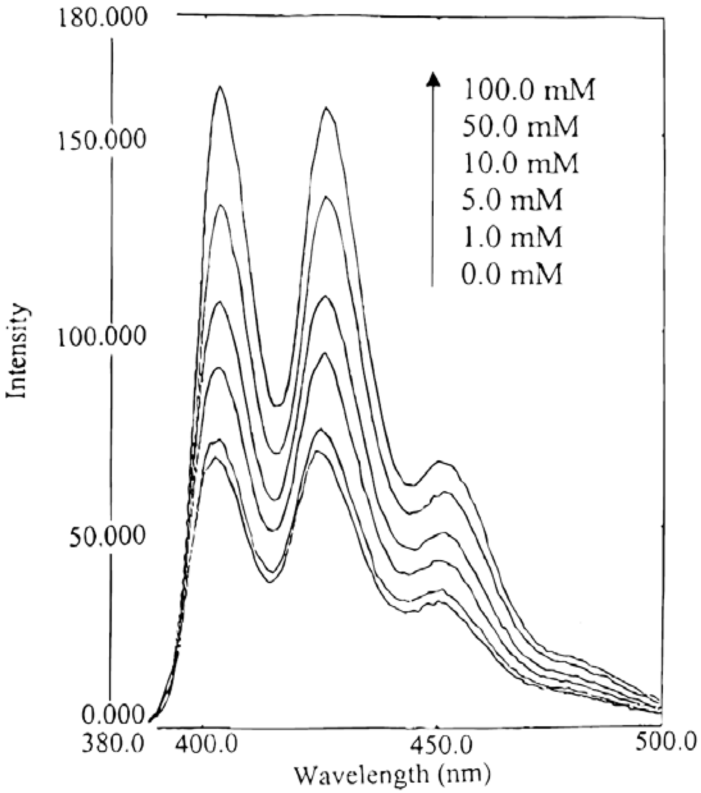
The templated unit was then used in the preparation of a poylmer using 2-hydroxyethyl methacrylate as a comonomer and EGDM (ethylene glycol dimethacrylate) as cross-linker.



EGDM

W. Wang, S. Gao, B. Wang, *Org. Lett.* **1999**, *1*, 1209.
S. Gao, W. Wang, B. Wang, *Bioorg. Chem.* **2001**, *29*, 308.

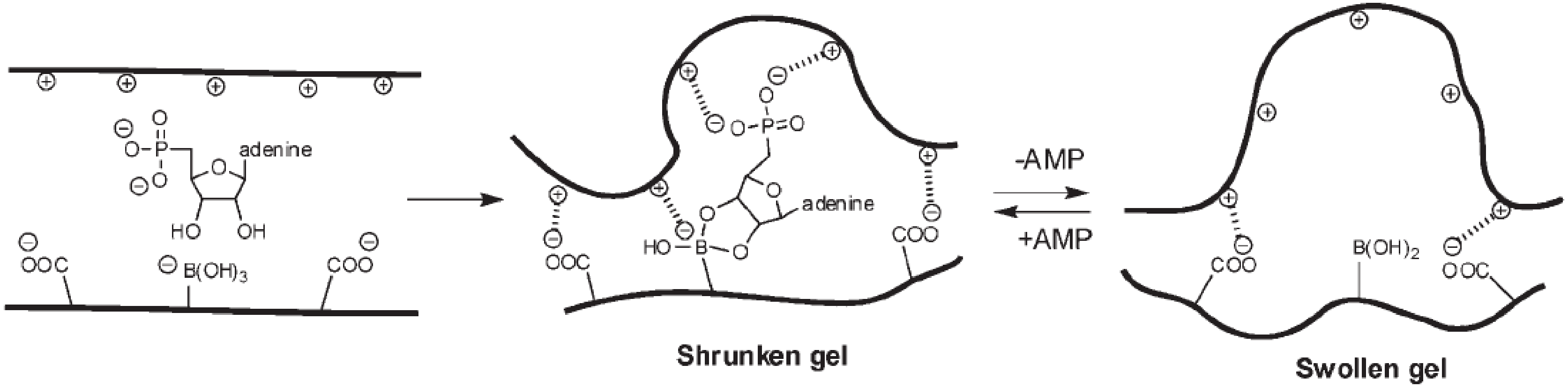
Molecular Imprinting



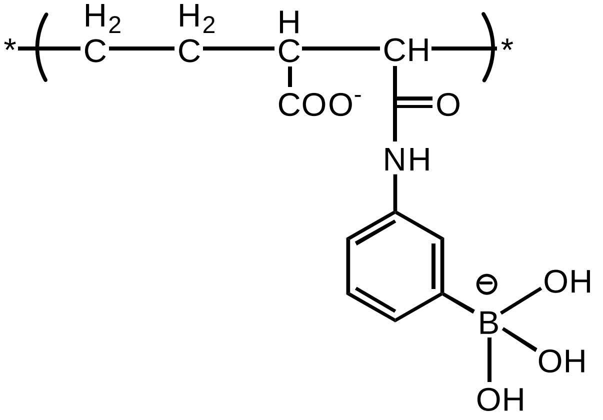
A typical set of fluorescence spectra of D-fructose-imprinted polymer at different concentrations of D-fructose (λ_{ex}, 370 nm; λ_{em}, 426 nm).

W. Wang, S. Gao, B. Wang, *Org. Lett.* **1999**, *1*, 1209.
S. Gao, W. Wang, B. Wang, *Bioorg. Chem.* **2001**, *29*, 308.

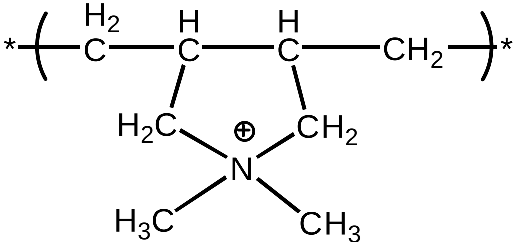
Molecular Imprinting



AMP-imprinted polyion complex



polyanion



polycation

Y. Kanekiyo, Y. Ono, K. Inoue, M. Sano, S. Shinkai, *J. Chem. Soc. Perkin Trans. 2* **1999**, 557.

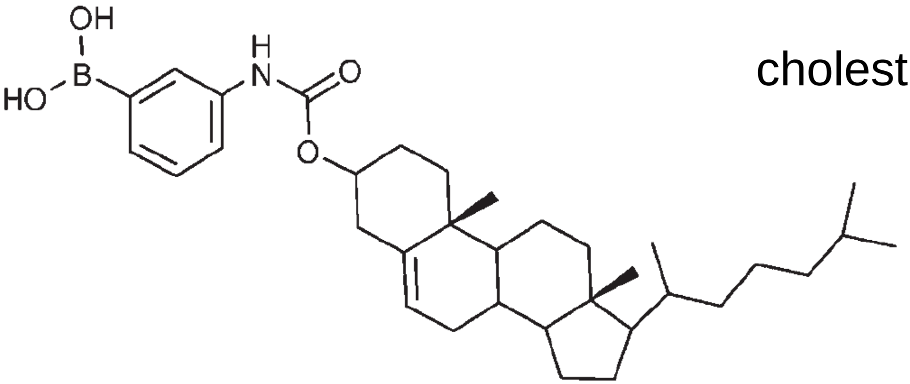
Air–Water Interface

- The self-assembled Langmuir films developed at the air–water interface allow accurate placing of boronic acid receptors for saccharide recognition.

- The position of the receptors can be randomly dispersed or templated by guests in the subphase. Once formed, the Langmuir monolayers can then be transferred to a solid support using Langmuir–Blodgett (LB) techniques.

- This attribute makes the monolayer environment one of the best for producing durable solid supported sensors.

Air–Water Interface



cholesterylboronic acid derivative

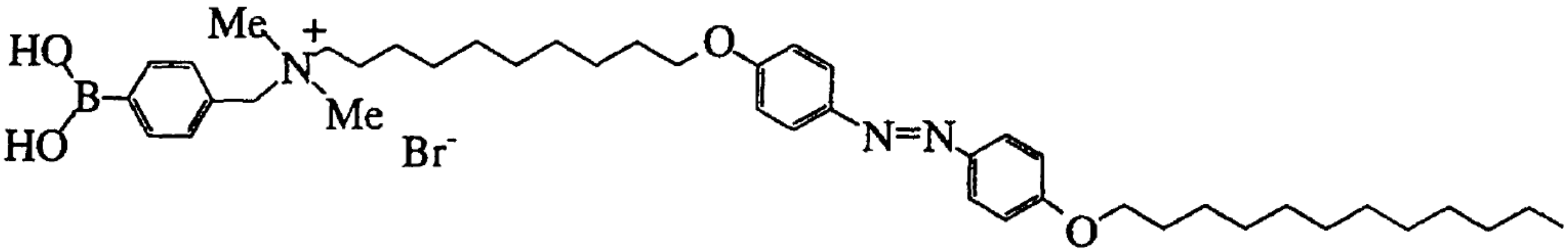
-Selectively recognize enantiomers of fructose

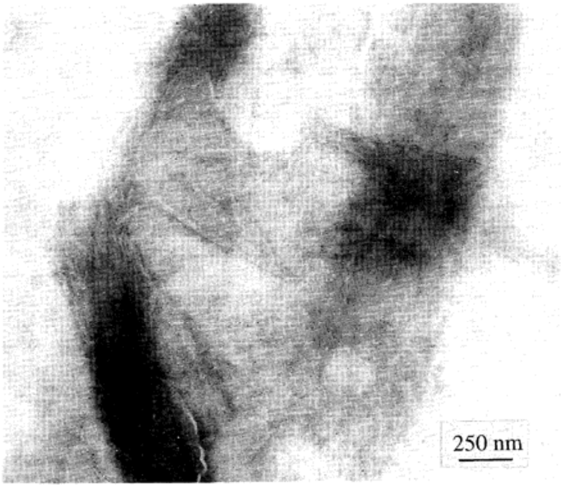
-Quaternized amines added into the subphase facilitate the saccharide detection by the monolayer at neutral pH.

-Assistance of closely located ammonium cations in the formation of a boronate anion is believed to be the source of enhancement.

R. Ludwig, T. Harada, K. Ueda, T. D. James, S. Shinkai, *J. Chem. Soc. Perkin Trans. 2* **1994**, 697.

Heterogenous and Polymeric Systems





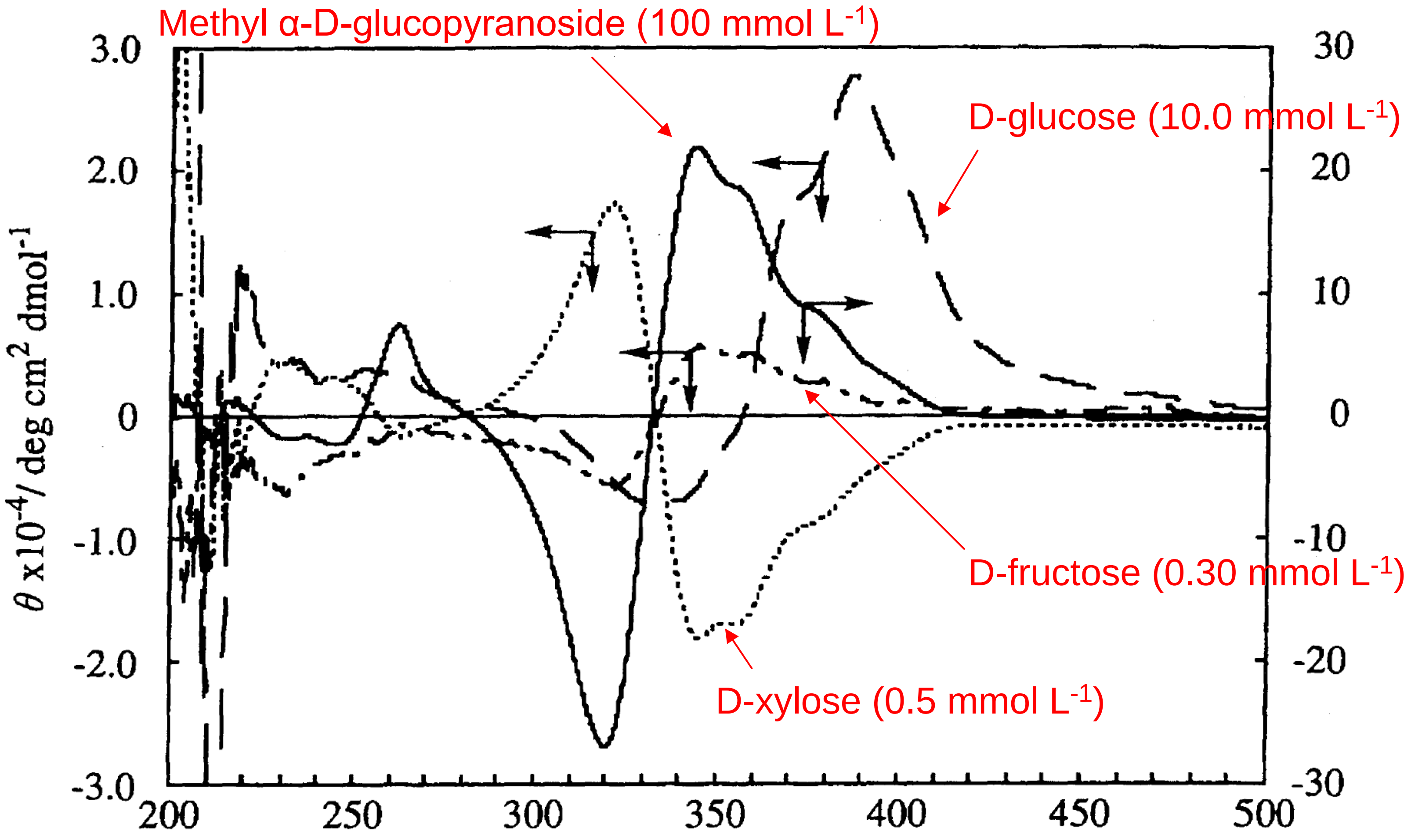
Compound bearing a boronic acid group and a chromophoric azobenzene group forms a micelle-like, orderless aggregate in aqueous solution.

When saccharides are added, a stable membrane is formed.

TEM: In the presence of D-fructose

T. Kimura, M. Takeuchi, S. Shinkai, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2197.

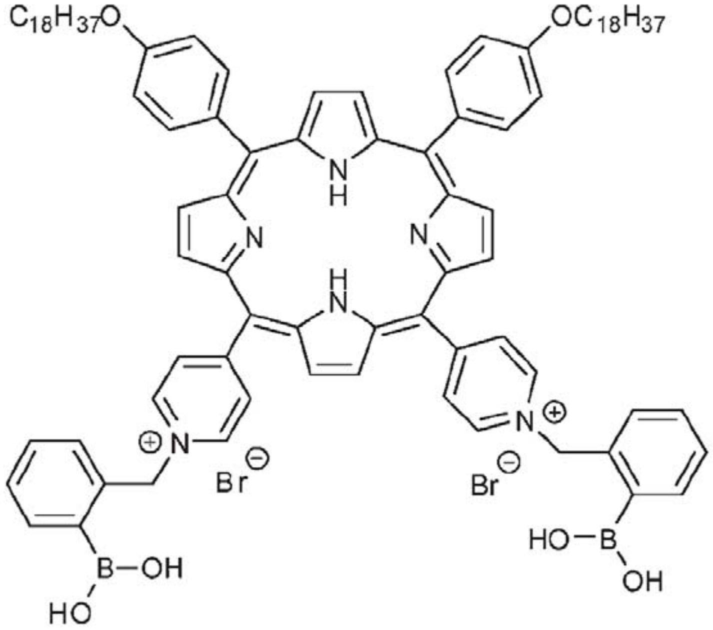
Heterogenous and Polymeric Systems

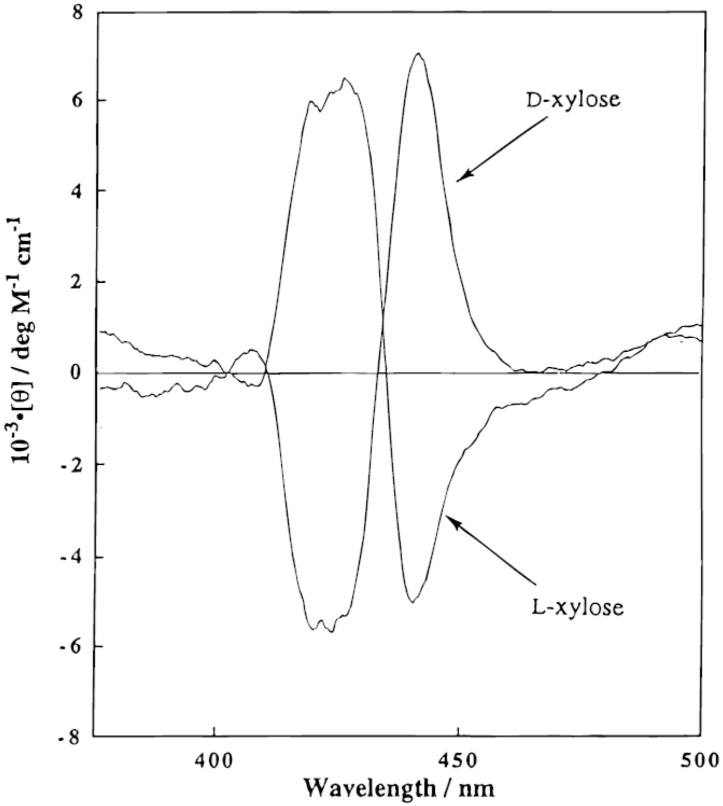


CD spectra of compound (5.00×10^{-5} mol L^{-1})in the presence of saccharides

T. Kimura, M. Takeuchi, S. Shinkai, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2197.

Heterogenous and Polymeric Systems

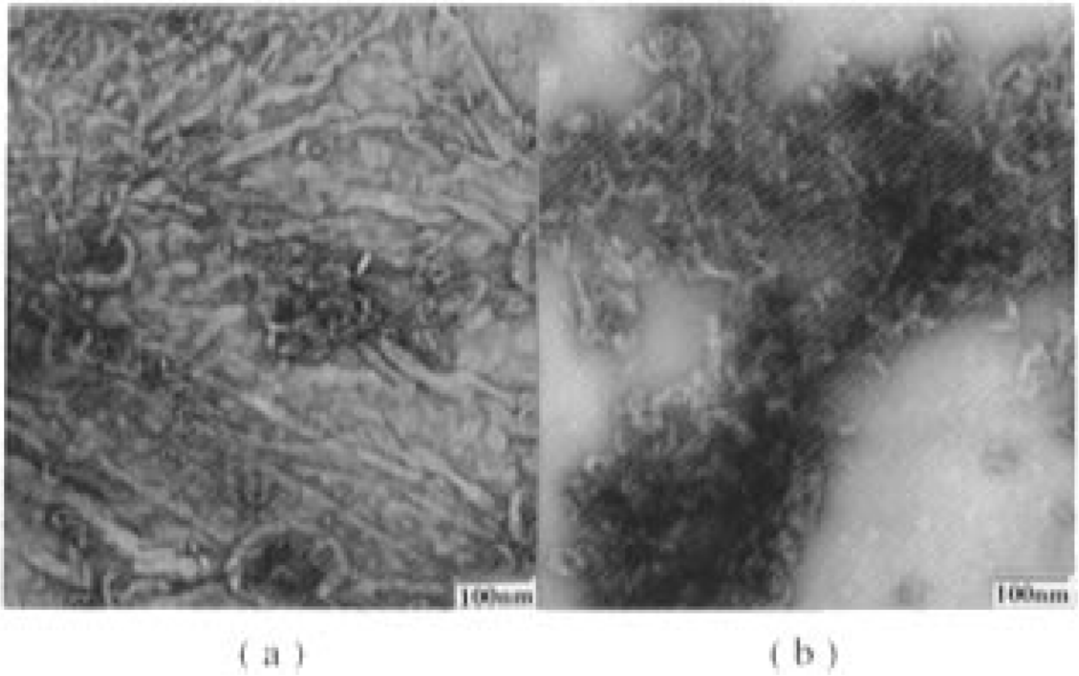




CD spectra of **2** (2.00×10^{-5} M) in the presence of D- or L-xylose (1.00×10^{-2} M): 25 ℃, 0.3 vol % methanol, pH 10.0 with 0.10 M carbonate buffer.

S. Arimori, M. Takeuchi, S. Shinkai, *J. Am. Chem. Soc.* **1996**, *118*, 245.

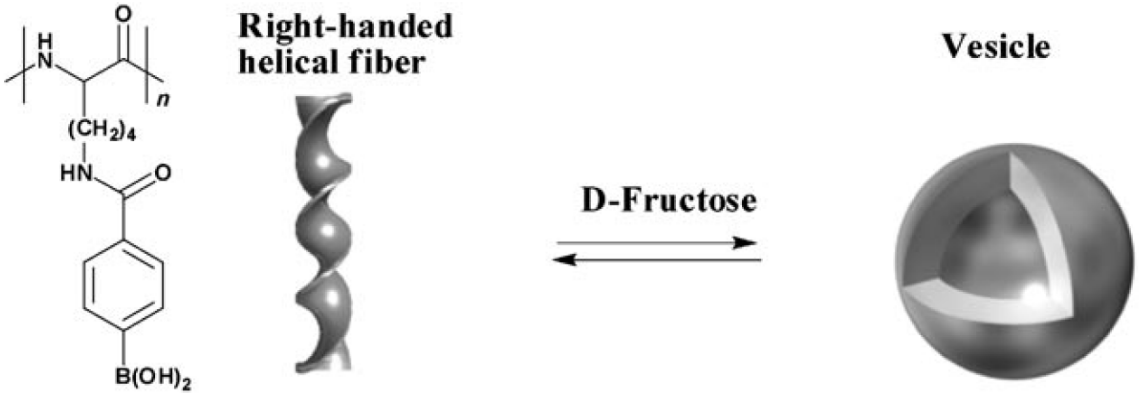
Heterogenous and Polymeric Systems



TEM’s of **2** in the presence of (a) D-fructose and (b) D-ribose. **2** gave a picture similar to (a) in the presence of D-glucose and similar to (b) in the presence of D-fucose.
2 gave well-developed fibrous (or tubular) aggregates in the presence of D-fructose or D-glucose. On the other hand, **2** gave less-developed coagulated fibrous aggregates in the presence of D-ribose or D-fucose

S. Arimori, M. Takeuchi, S. Shinkai, *J. Am. Chem. Soc.* **1996**, *118*, 245.

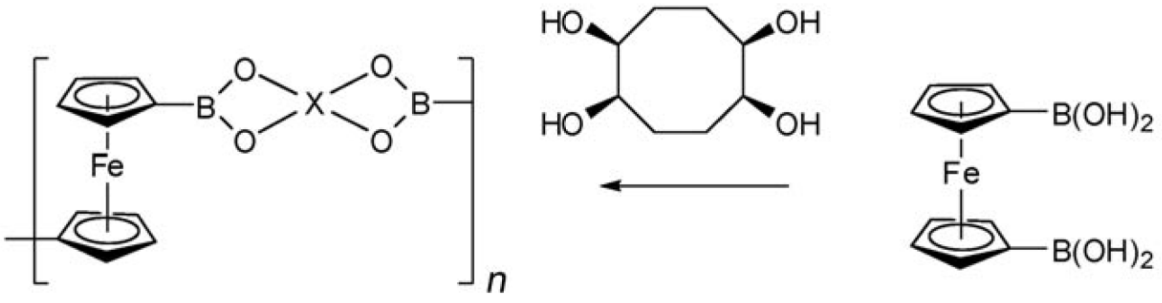
Heterogenous and Polymeric Systems

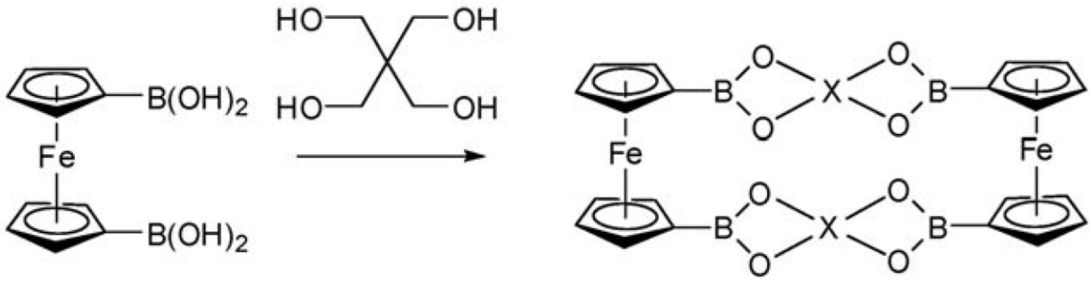


When D-fructose which shows high affinity with the boronic acid group was added, the sol phase and the vesicular aggregate were changed back to the gel phase and the fibrous aggregate, respectively

H. Kobayashi, K. Koumoto, J. H. Jung, S. Shinkai, *J. Chem. Soc. Perkin Trans. 2* **2002**, 1930.

Heterogenous and Polymeric Systems

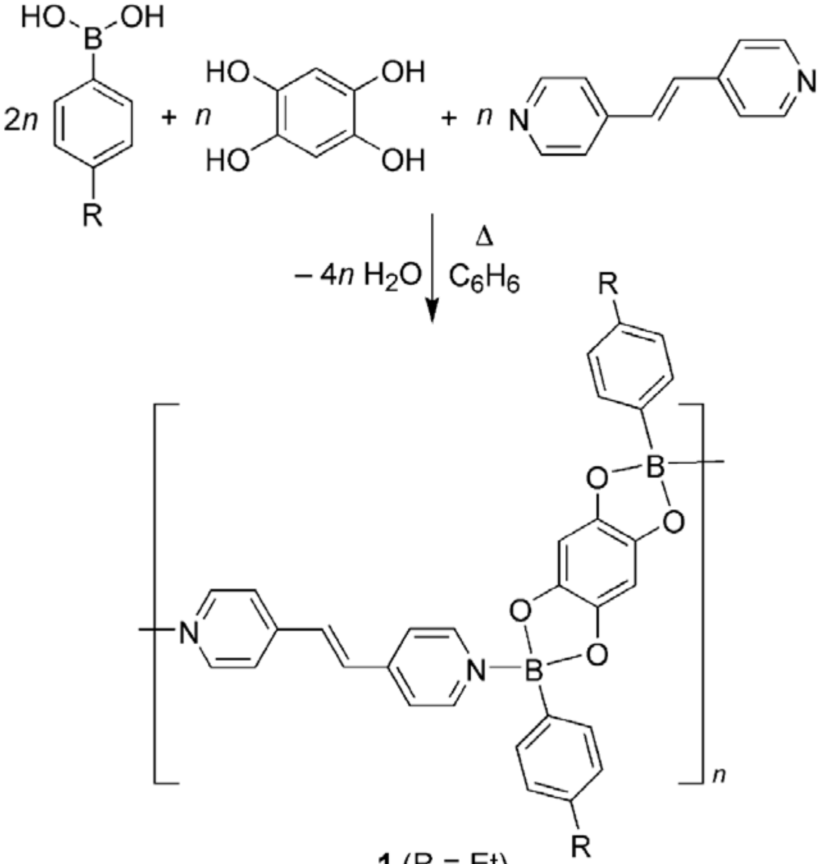




When pentaerythritol is condensed with 1,1’-ferrocenediboronic acid, a macrocycle is formed, but when (1*R*,2*S*,5*R*,6*S*)-tetrahydroxycyclooctane is used, a polymeric material is produced.

J. K. Day, C. Bresner, I. A. Fallis, L. L. Ooi, D. J. Watkin, S. J. Coles, L. Male, M. B. Hursthouse, S. Aldridge, *Dalton Trans.* **2007**, 3486.

Heterogenous and Polymeric Systems



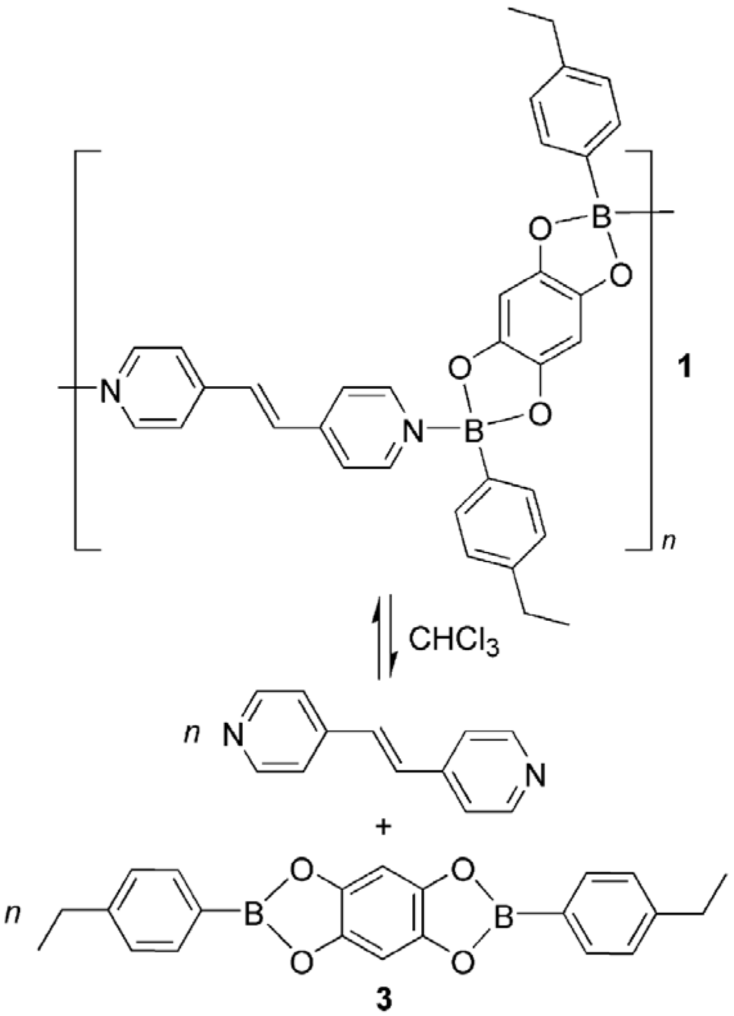
1 (R = Et)
2 (R = *t*Bu)

self-assembled polymeric system using monoarylboronic acids, 1,2,4,5-tetrahydroxybenzene and 1,2-bis(4-pyridyl)ethylene

the strong color of the polymers is due to efficient intrastrand charge-transfer excitations from the tetraoxobenzene to the dipyridyl linker.

N. Christinat, E. Croisier, R. Scopelliti, M. Cascella, U. Röhlisberger, K. Severin, *Eur. J. Inorg. Chem.* **2007**, 5177.

Heterogenous and Polymeric Systems

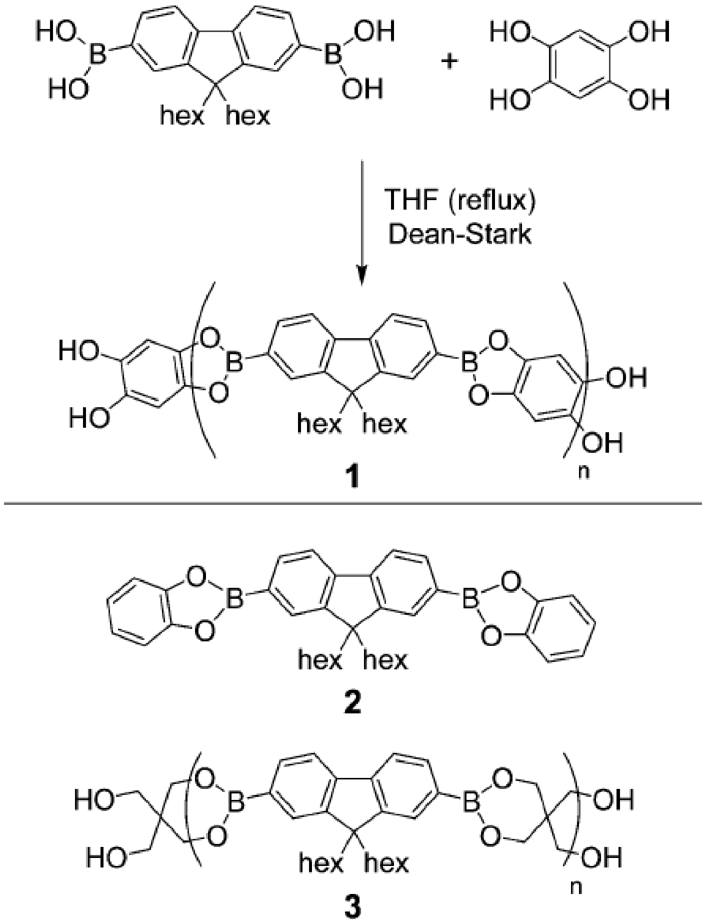


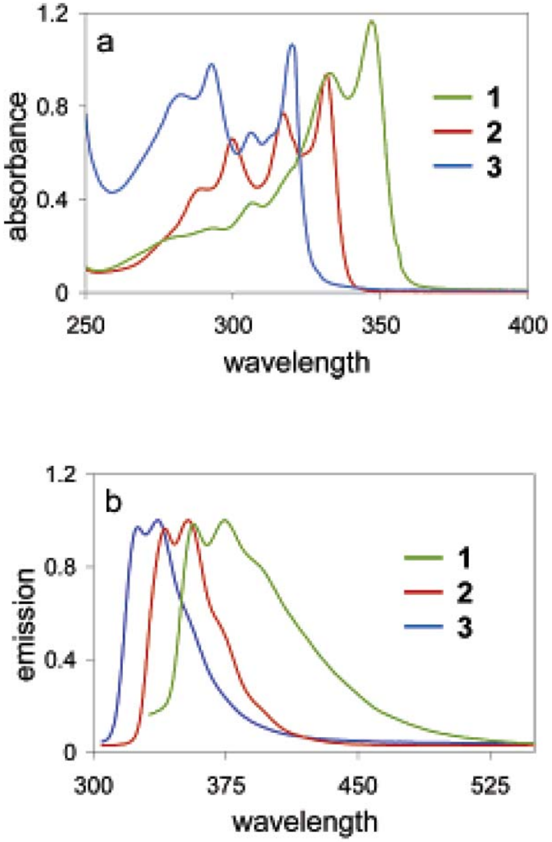
When dissolved in $CHCl_3$, polymer **1** splits into 1,2-bis(4-pyridyl)ethylene and bis(dioxaborole) **3**.

At RT, **1** has low solubility in common organic solvents.
Upon heating, however, it was possible to dissolve them in chloroform.
A strong change in color: the dark-purple solids gave rise to weakly yellow solutions.
When the hot chloroform solutions were cooled to RT, the purple polymers started to precipitate after a few minutes.

N. Christinat, E. Croisier, R. Scopelliti, M. Cascella, U. Röhlisberger, K. Severin, *Eur. J. Inorg. Chem.* **2007**, 5177.

Self-Assembled Blue-Emissive Materials

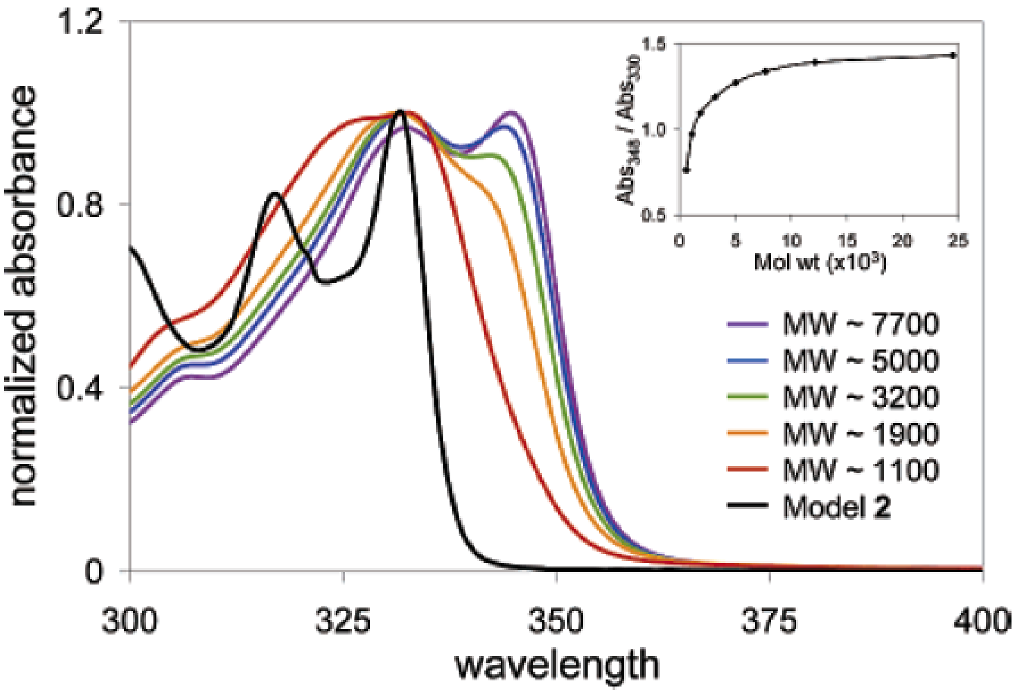




9,9-dihexylfluorene-2,7-diboronic acid and 1,2,4,5-tetrahydroxybenzene

W. Niu, M. D. Smith, J. J. Lavigne, *J. Am. Chem. Soc.* **2006**, *128*, 16466.

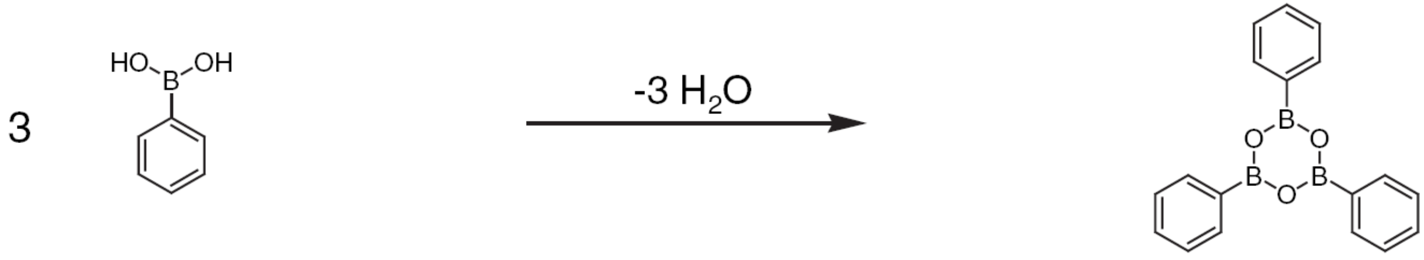
Self-Assembled Blue-Emissive Materials



Normalized absorption spectra for **2** and poly(dioxaborole)s (**1**) of varying length. Inset: Change in the polymer absorption compared to oligomer **2** as a function of molecular weight.

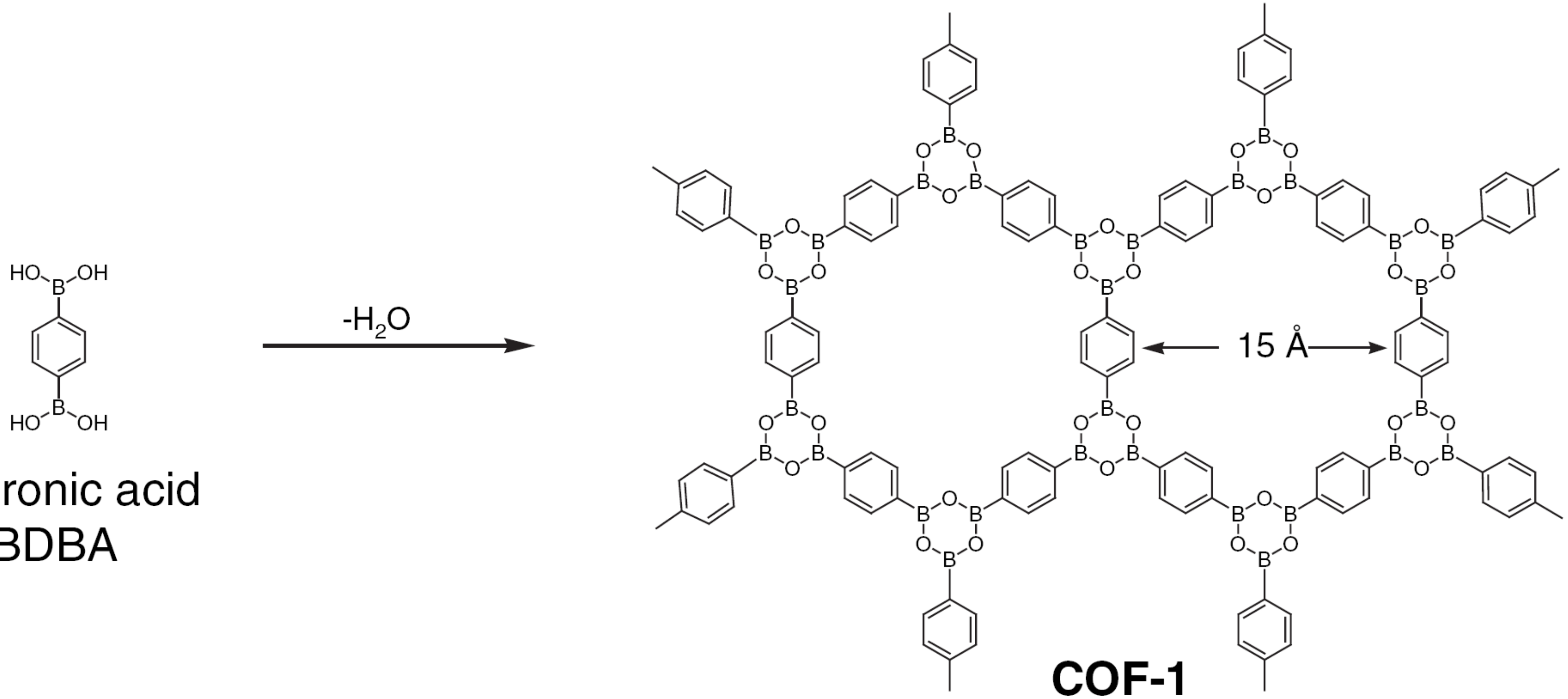
W. Niu, M. D. Smith, J. J. Lavigne, *J. Am. Chem. Soc.* **2006**, *128*, 16466.

Covalent Organic Frameworks (COFs)



boronic acid

boroxine anhydride

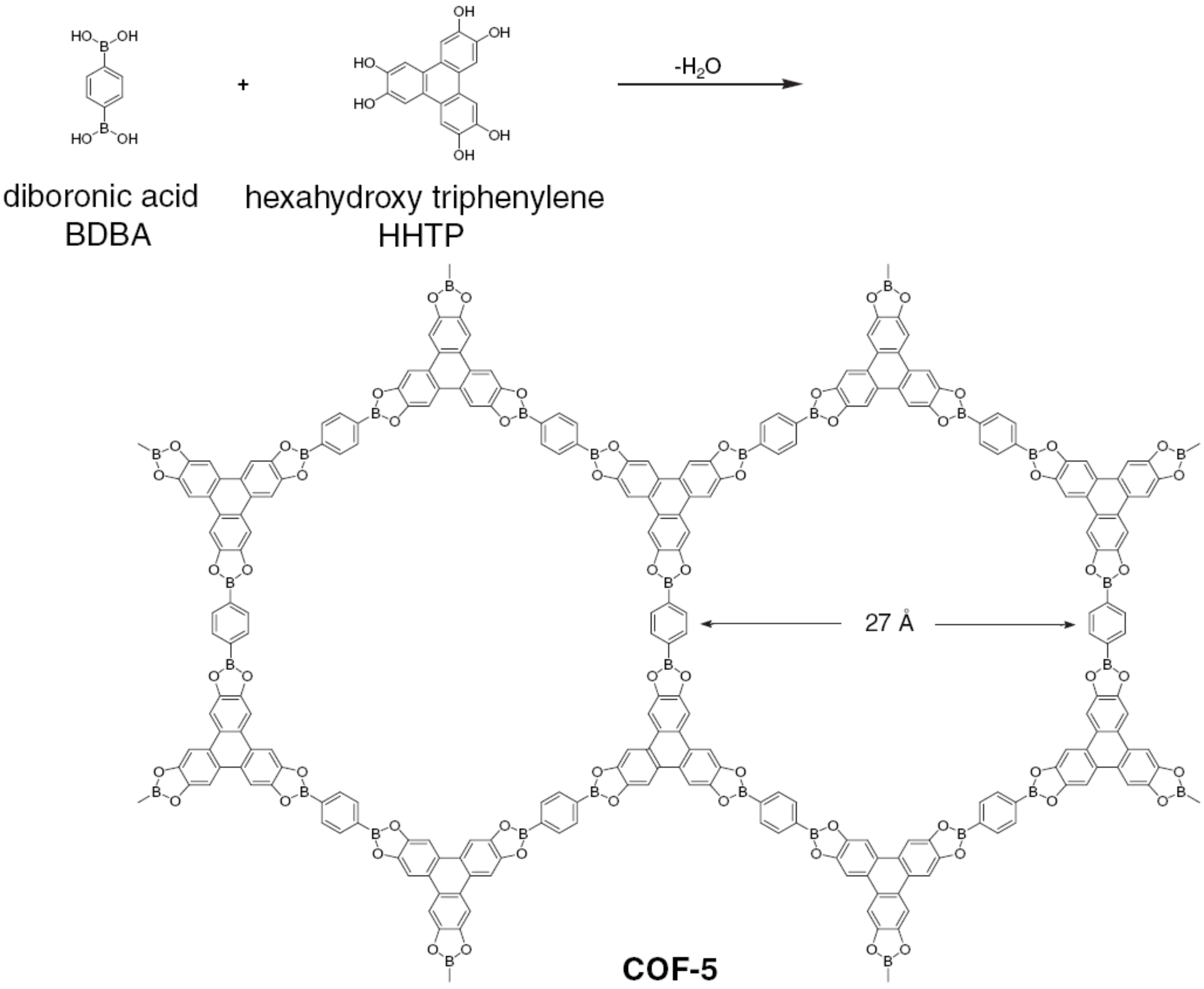


diboronic acid
BDBA

COF-1

A. P. Cote, A. I. Benin, N. W. Ockwig, M. OPKeeffe, A. J. Matzger, O. M. Yaghi, *Science* **2005**, *310*, 1166.

Covalent Organic Frameworks (COFs)



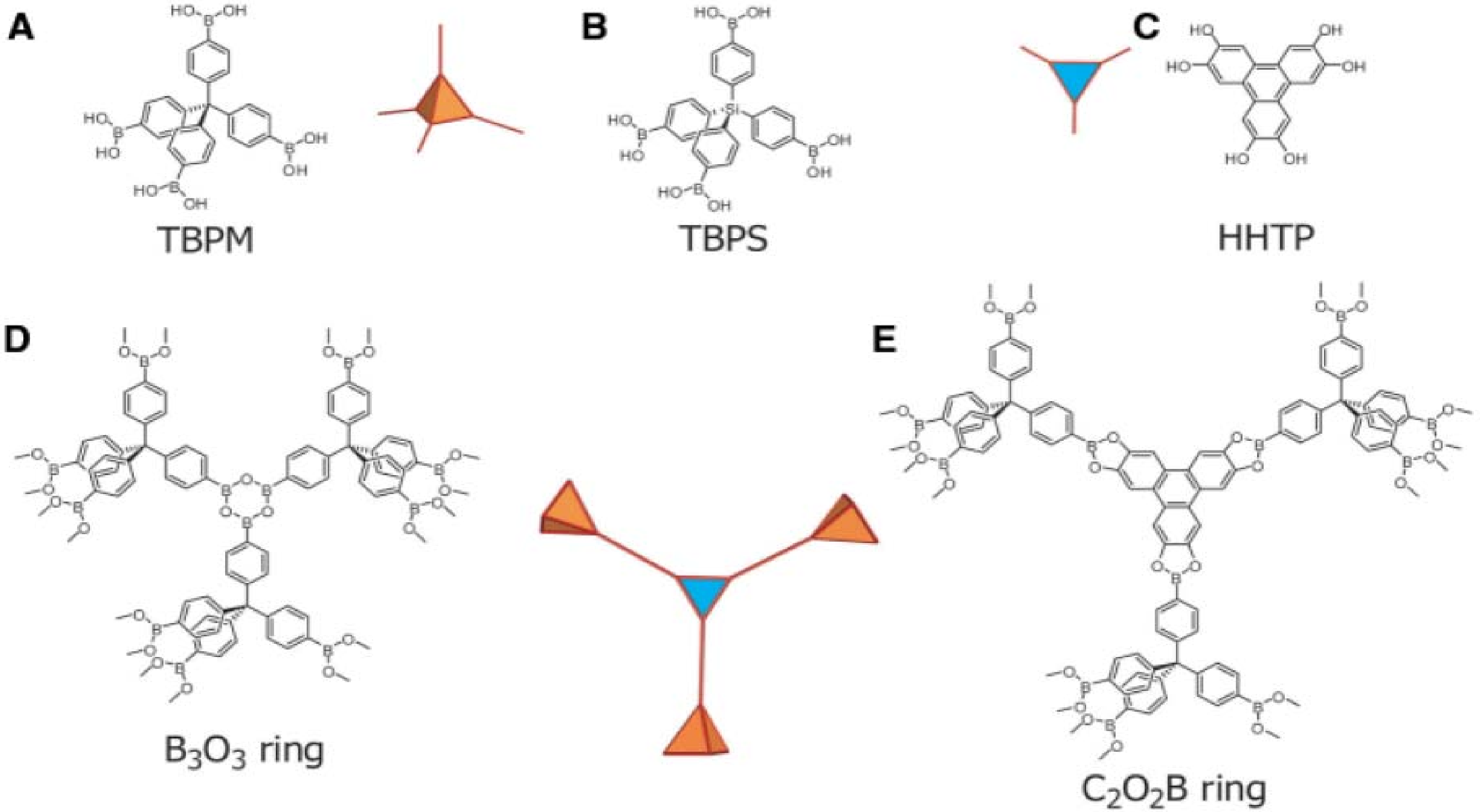
diboronic acid
BDBA

hexahydroxy triphenylene
HHTP

COF-5

A. P. Cote, A. I. Benin, N. W. Ockwig, M. OPKeeffe, A. J. Matzger, O. M. Yaghi, *Science* **2005**, *310*, 1166.

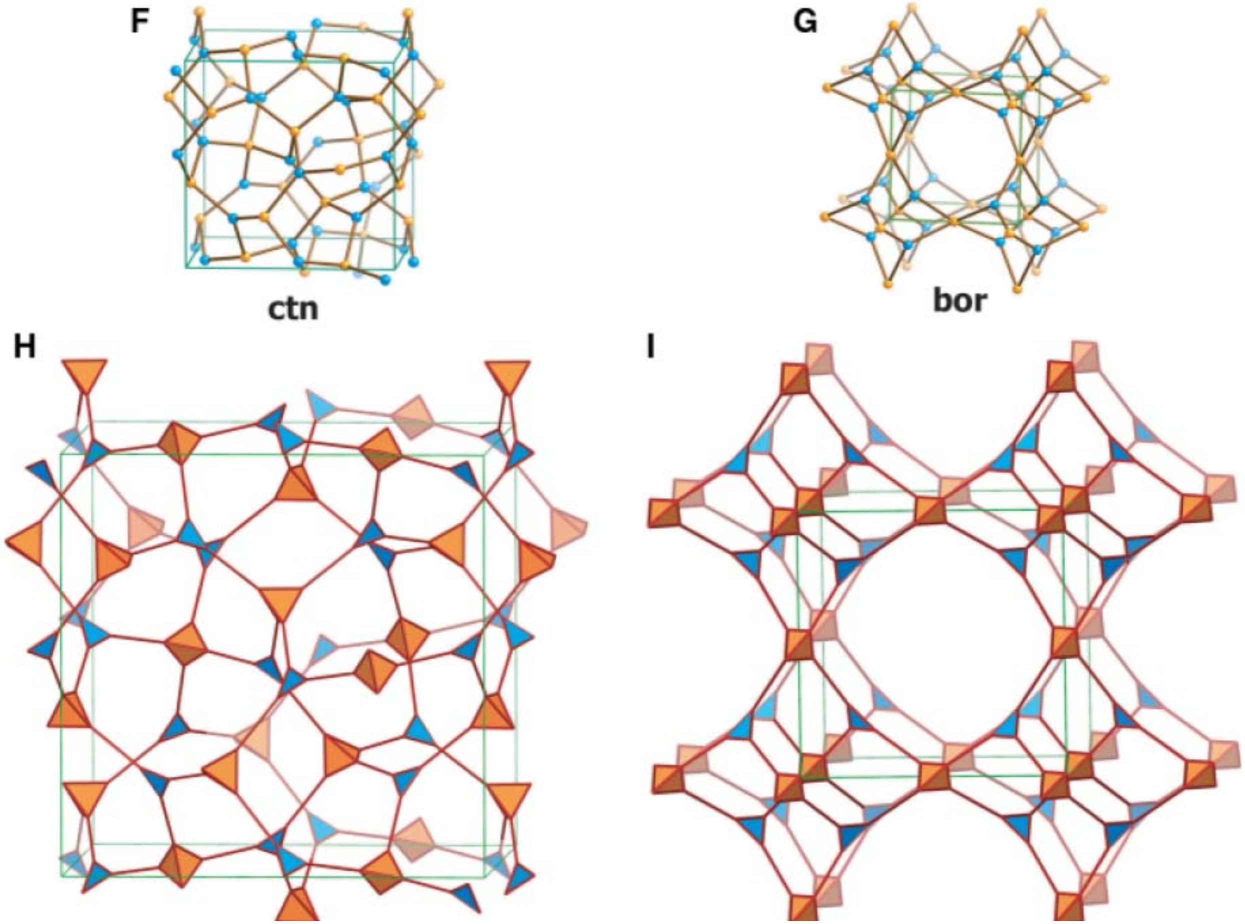
Covalent Organic Frameworks (COFs)



tetrahedral tetra(4-dihydroxyborylphenyl)methane (TBPM), and its silane analog (TBPS), and triangular hexahydroxytriphenylene (HHTP)

H. M. El-Kaderi, J. R. Hunt, J. L. Mendoza-Cortes, A. P. Cote, R. E. Taylor, M. OPKeeffe, O. M. Yaghi, *Science* **2007**, *316*, 268.

Covalent Organic Frameworks (COFs)



H. M. El-Kaderi, J. R. Hunt, J. L. Mendoza-Cortes, A. P. Cote, R. E. Taylor, M. OPKeeffe, O. M. Yaghi, *Science* **2007**, *316*, 268.

Covalent Organic Frameworks (COFs)

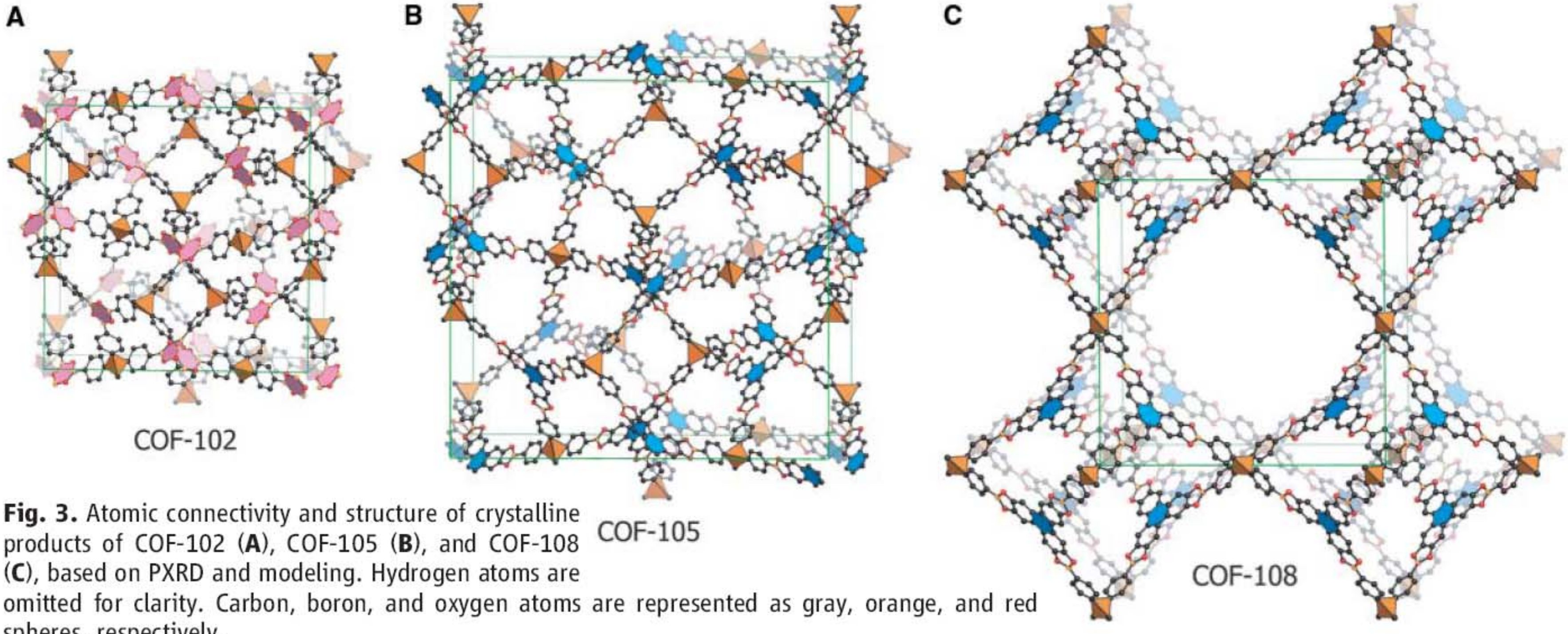
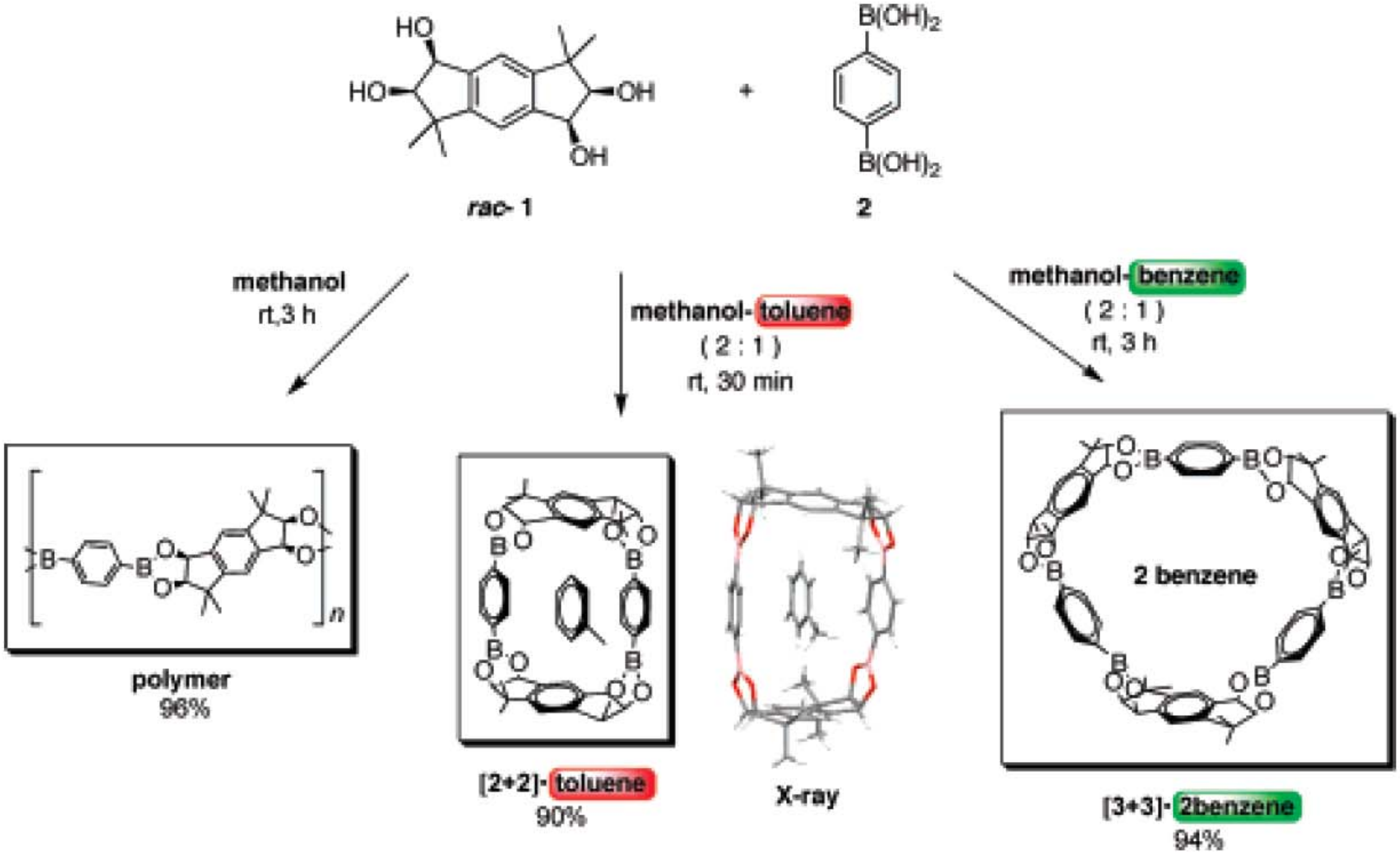


Fig. 3. Atomic connectivity and structure of crystalline products of COF-102 (**A**), COF-105 (**B**), and COF-108 (**C**), based on PXRD and modeling. Hydrogen atoms are omitted for clarity. Carbon, boron, and oxygen atoms are represented as gray, orange, and red spheres, respectively.

H. M. El-Kaderi, J. R. Hunt, J. L. Mendoza-Cortes, A. P. Cote, R. E. Taylor, M. OPKeeffe, O. M. Yaghi, *Science* **2007**, *316*, 268.

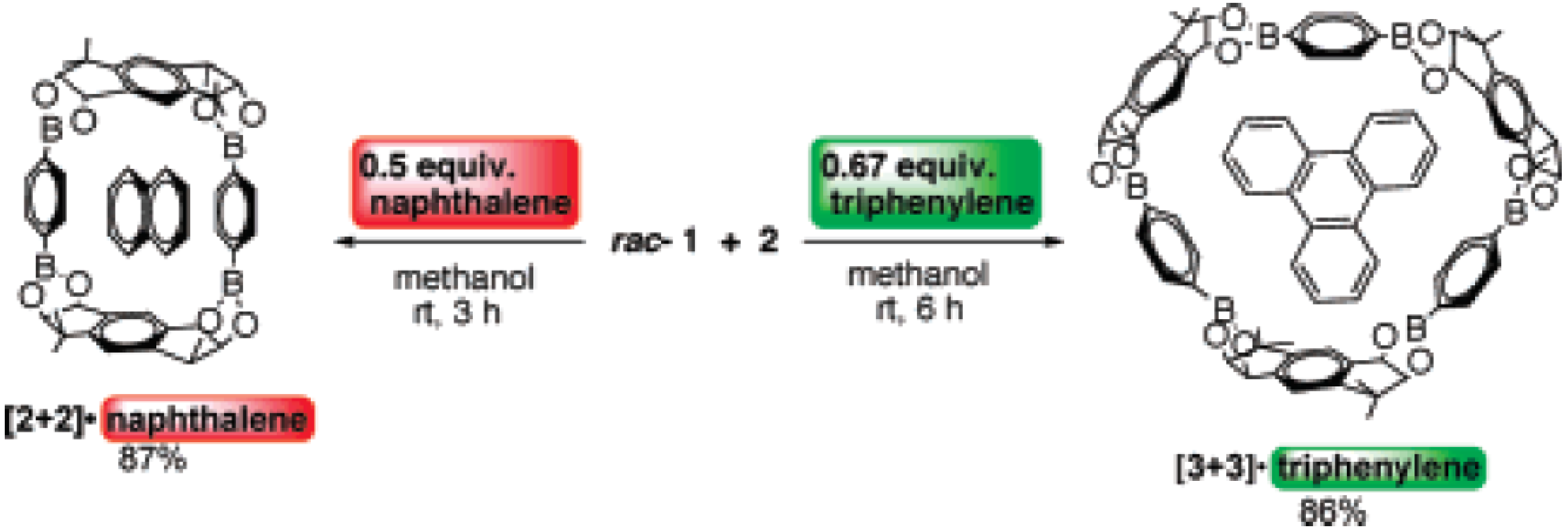
Macrocycles and Cages



The reaction of racemic tetrol **1** and 1,4-benzenedi(boronic acid) **2** in methanol (left), in methanol/toluene (2:1) (middle), and methanol/benzene (2:1) (right), and the X-ray structure of [2 + 2]·toluene (white, hydrogen; pink, boron; gray, carbon; red, oxygen).

N. Iwasawa, H. Takahagi, *J. Am. Chem. Soc.* **2007**, *129*, 7754.

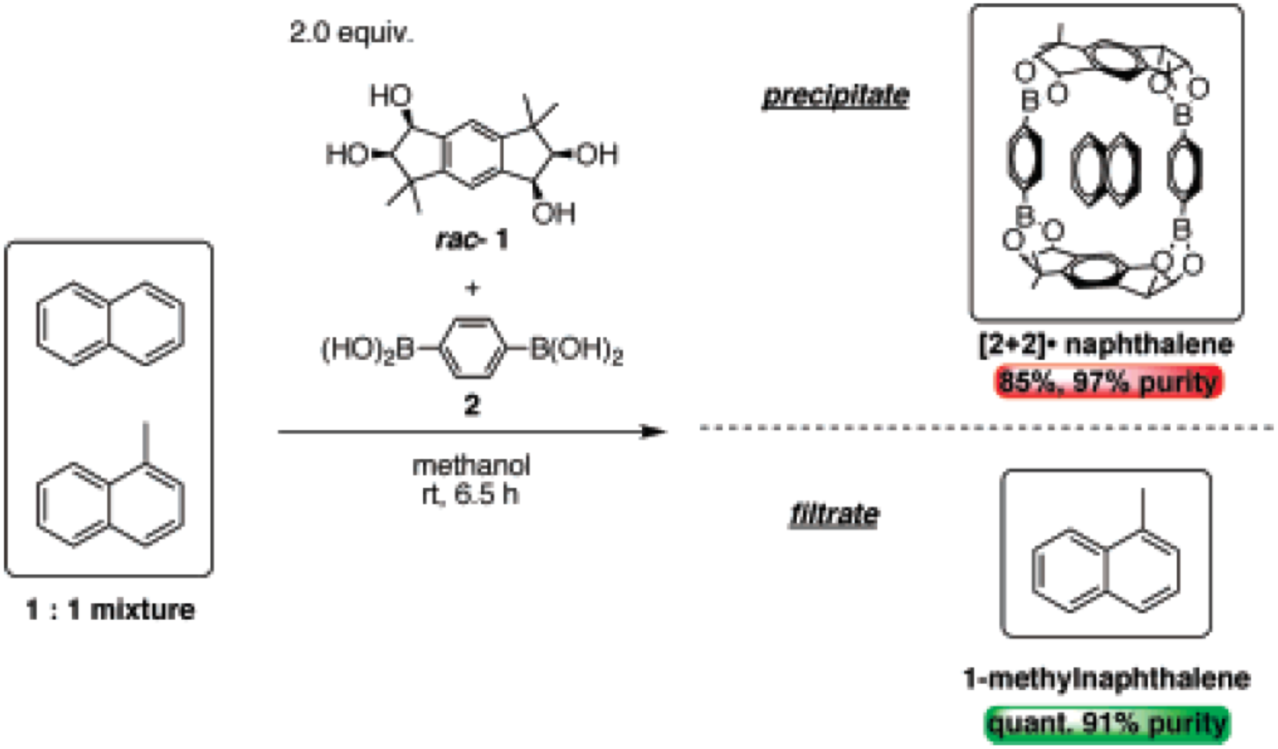
Macrocycles and Cages



Naphthalene-induced self-assembly of [2 + 2]·naphthalene and triphenylene-induced self-assembly of [3 + 3]·triphenylene

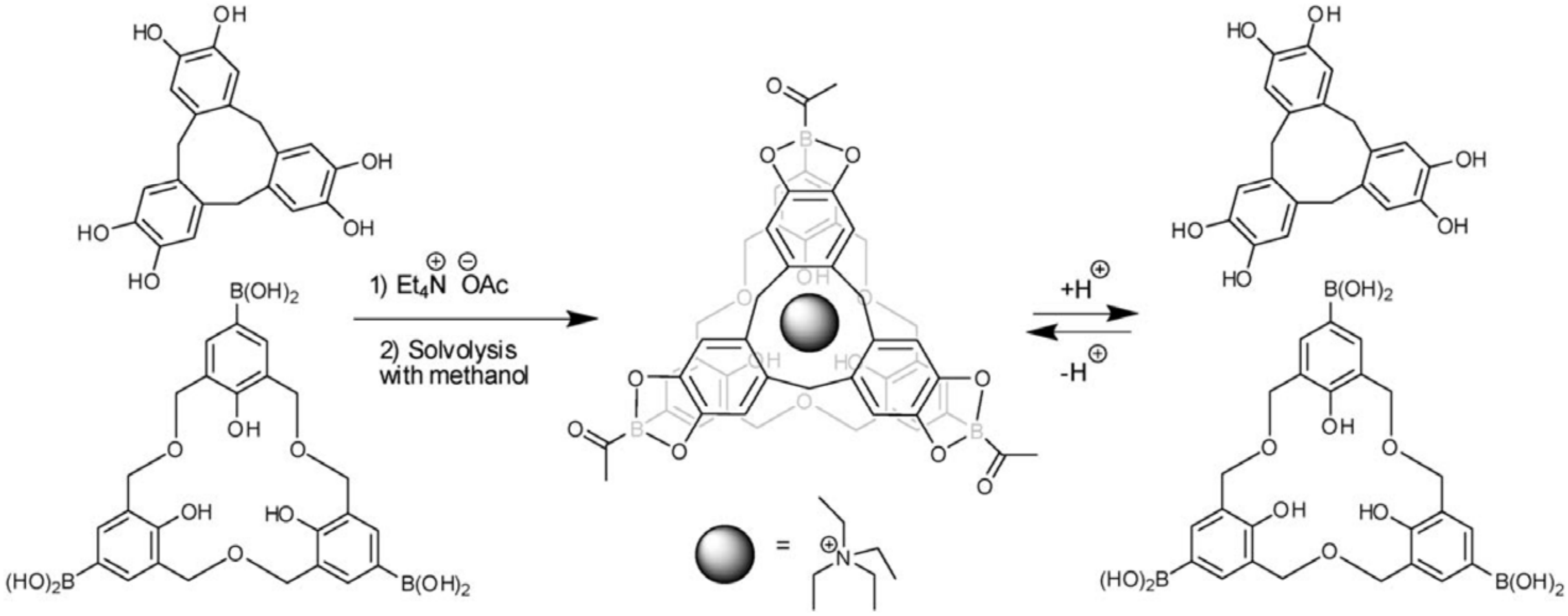
N. Iwasawa, H. Takahagi, *J. Am. Chem. Soc.* **2007**, *129*, 7754.

Macrocycles and Cages



N. Iwasawa, H. Takahagi, *J. Am. Chem. Soc.* **2007**, *129*, 7754.

Macrocycles and Cages



Et$_4$N$^+$ > Me$_4$N$^+$ > K$^+$ with AcO$^-$ salts and AcO$^-$ > F$^-$ > I$^-$ with Et$_4$N$^+$ salts, respectively.
The capsulation is dictated mainly by size of the cation and basicity of the anion.
In the former case, C-H π interactions seem to play a significant role for the event.

K. Kataoka, T. D. James, Y. Kubo, J. Am. Chem. Soc. **2007**, *129*, 15126.

Conclusions and Future Prospects

Many of these systems take advantage of the fact that:

- (a) The boronic acid–diol interaction is reversible.
- (b) The boronic acid–diol interaction is directional.
- (c) The boronic acid–diol interaction can take advantage of a cheap and diverse chiral pool of diols.

There is growing interest in the development of porous molecular frameworks and molecular capsules and cages derived from the facile boronic acid–diol interaction.

The frameworks will lead to the development of new materials with applications in gas storage, catalysis, and separation.

The capsules will be employed in receptor and sensor development, extraction, or for drug delivery.

Thank You