EFFECT OF BORON TRIFLUORIDE ON THE TRANSESTERIFICATION OF BORONATE

ESTERS

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A Thesis

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In Partial Fulfillment

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Master of Science

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by

Dulamini I. Ekanayake

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DEDICATION

To my parents, husband, sister, and brother

ABSTRACT

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Boronate ester-based materials have received interest and found utility in many applications. The preeminent goal of this research is to advance the field of boron-oxygen based porous materials. The formation of these materials has been predominantly facilitated by boron-oxygen dynamic covalent character. In an effort to understand and improve this process, we are investigating the effect of boron trifluoride, a well-known Lewis acid catalyst, on synthesis and exchange of dioxaboroles. From our previous studies, we have observed an increase in reaction rate as well as beneficial side reactions, which have driven the reaction equilibrium to unexpected products from the transesterification of phenyl pinacol boronate ester (PPB) in the presence of boron trifluoride.

Initially, we studied the effect of boron trifluoride on the transesterification of different boronate esters (dioxaboroles) with catechol. Then, we synthesized bis boronate ester materials by combining the knowledge learned in the above-described work. Finally, we investigated the Lewis acid-catalyzed (boron trifluoride and para-toluene sulfonic acid) pinacol rearrangement of different diols (pinacol, hydrobenzoin, and benzpinacol).

In the presence of boron trifluoride all transesterification reactions of boronate esters with catechol showed an improvement. Additionally, we were able to find a method to isolate catechol boronate ester on the gram scale.

KEY WORDS: Boronate esters, transesterification, boron trifluoride, pinacol rearrangement

ACKNOWLEDGEMENTS

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CHAPTER I

INTRODUCTION

Organic synthesis is an important field not only in chemistry but also to the public. Many of the materials we use on a daily basis are the results of the efforts of synthetic organic chemists. Conventionally, organic reactions are run under kinetically controlled conditions, where the bond formation is irreversible, and the experimental conditions should be chosen carefully to obtain a good yield of the desired product. Recently, dynamic covalent chemistry (DCC) has become an area of interest because it involves reactions that proceed under dynamic conditions, where the bond formation is reversible. This reversible nature allows for error checking or proof-reading phenomena during the reaction to achieve the most thermodynamically stable products.[1]

Previously, supramolecular chemistry has been used to build up 2D and 3D materials. Self-assembly is a process that forms ordered aggregates spontaneously. Usually, self-assembly is reversible and involves non-covalent interactions such as hydrogen bonds and van der Waals forces.[2] The reversible nature allows these reactions to proceed through several kinetic intermediates before reaching a final thermodynamic product.

Self-assembly has been used to synthesize molecules or components, which have different sizes, structures, or functions. However, self-assembly involves weak interactions, and the assembly can be broken with a little energy. In contrast, DCC involves covalent bonds rather than noncovalent interactions, and the material, once formed, is typically more stable.

1.1 Dynamic Covalent Chemistry (DCC)

DCC has been used to develop two-dimensional (2-D) macrocycles, and three-dimensional (3-D) macromolecular cages which have many potential applications.[3] 2-D shape-persistent macrocycles have found utility in developing conducting molecular wires, sensors, and liquid crystals.[4] 3-D organic molecular cages have been studied for catalysis, gas adsorption, and small-molecule separation.[4]

There are several types of dynamic covalent reactions (DCR), such as imine exchange, olefin metathesis, alkyne metathesis, disulfide exchange, and boronic acid condensation.[5]

The imine exchange reaction involves the exchange of alkyl groups on the nitrogen (Figure 1).[6] Imine exchange is widely used in the synthesis of covalent organic polyhedrons (COPs).[5] The reversibility of imine base systems was first studied by Stoddart and co-workers.[7]
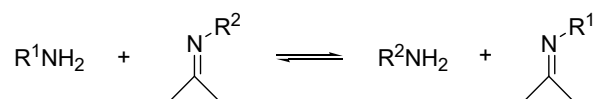
Figure 1. Imine exchange reaction.

Metathesis reactions involve the exchange of substituents on atoms that are connected through single, double, or triple bonds. Olefin cross metathesis involves the interchange of carbon atoms between two double bonds (Figure 2).[1] These reactions require special catalysts. There are several olefin metathesis-based oligomeric materials and shape-persistent macrocycles that have been reported.[5,8,9]
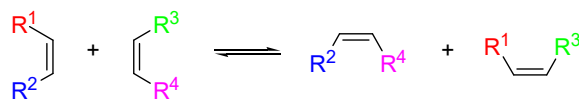
Figure 2. Olefin cross metathesis reaction.

Alkyne metathesis deals with the breaking and forming of C–C triple bonds (Figure 3). Alkyne metathesis has been successfully used to develop shape-persistent molecular cages and macrocycles.[5,10,11]
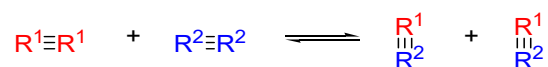
Figure 3. Alkyne metathesis reaction.

Disulfide exchange (Figure 4) is another DCR which has been used to develop polymers and macrocycles.[5]
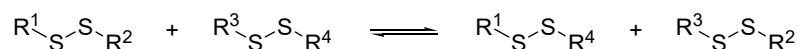
Figure 4. Disulfide exchange reaction.

Boronic acids can easily and reversibly undergo self-condensation at room temperature to form boroxine (Figure 5).

1.1   **1.2**
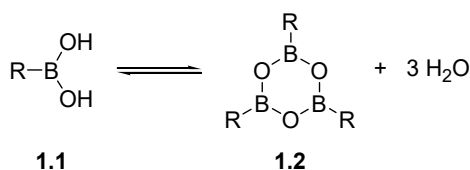
Figure 5. Boronic acid-boroxine equilibrium.

In addition, boronic acids react with simple alcohols, diols, diamines, etc., to form esters or boraza compounds (Figure 6).
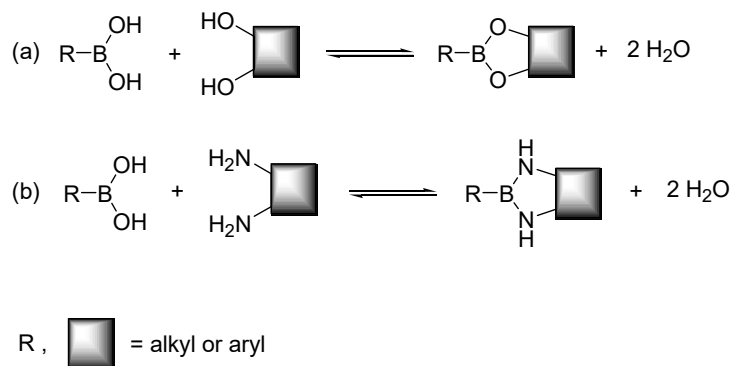
Figure 6. (a) Boronic acid-diol equilibrium and (b) boronic acid-diamine equilibrium.

Recently, B-O and B-N based dynamic covalent bonds have gained interest in the field of shape-persistent molecular architectures. In this regard, our research focuses on developing macrocycles using B-O and B-N compounds, i.e., boronic acid, boronate ester (dioxaborole), diazaborole, and oxazaborole based macrocycles.

1.2 Boronic acids

Boronic acids are organic acids, which have reactivity analogous to carboxylic acids. Unlike carboxylic acids, boronic acids do not exist in nature. They are synthesized from primary boron sources such as boric acid (Figure 7). However, like carboxylic acids, boronic acids can undergo esterification and transesterification. The boron atom in a boronic acid has a vacant P orbital. Therefore, boronic acids can also act as Lewis acids.[12] Boron atoms can interact with variety of atoms and molecular motifs such as oxygen, nitrogen, hydrogen, simple alcohols, anions, etc.[13] Boronic acid and diol interactions are important because the boron-diol interaction is covalent and reversible. This reversible nature allows the formation of the most thermodynamically stable products.[14]

R'' R−B R'	OH R−B R'	OH R−B OH	OH HO−B OH
borane	borinic acid	boronic acid	boric acid

dioxaborolane	dioxaborole	dioxaborinane	dioxaborepin	dioxazaborocine

R, R', R" = Alkyl or Aryl group
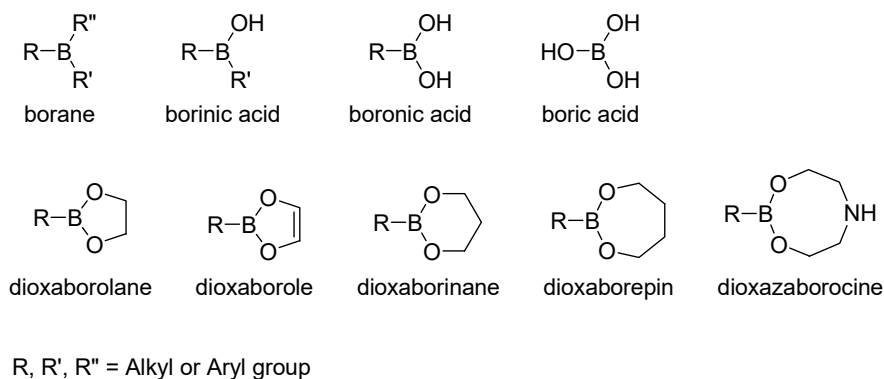
Figure 7. Oxygenated boron compounds and boronate esters.

1.3 Boronate esters

The first cyclic boronate ester was reported by Kuivila and co-workers in 1954.[15] They found a new cyclic boronate ester by reacting phenylboronic acid (PBA) and a saturated solution of mannitol. In 1959, the first quantitative investigation of boronate ester synthesis from boronic acid and polyols was investigated by Lorand and Edward.[16] From their studies, they were also able to find that the conjugate base of phenylboronic acid has a tetrahedral structure rather than trigonal structure.

Boronic acids can also interact with dicarboxylic acids, α-hydroxy carboxylic acids, and diols such as 1,2- and 1,3-diols. The latter two form five (dioxaborolanes) and six (dioxaborinanes) membered cyclic boronate esters, respectively. It has also been shown that dioxaborinanes are more stable than dioxaborolanes.[14]

The formation of cyclic boronic esters has led to their applications in a number of areas due to the reversibility of this condensation reaction.[12] Boronate esters (dioxaborole) have been explored for applications in organic and medicinal chemistry[17] and they have been used as protecting groups in carbohydrate chemistry,[18] general

substrates in the Suzuki coupling,[19] chiral derivatizing agents,[17] and glucose-selective fluorescence sensors.[20]

The reversible nature of the condensation reaction between boronic acids and diols opens the way towards the synthesis of bulky and complex compounds like boronate ester based macrocycles. To date, a considerable number of studies have been carried out to synthesize new classes of dioxaboroles, poly(dioxaborole)s, dioxaborole based macrocycles, and dioxaborole based COFs.

In 1961, Smolinsky synthesized four different derivatives of 1,3,2-dioxaborole (**1.3**) (Figure 8).[21] It was observed that the phenyl substituent on the boron atom increased the stability toward air oxidation, the order of stability being **1.3a** > **1.3c** > **1.3b** > **1.3d**.

$$a\ R, R_1 = C_6H_5$$
$$b\ R = C_6H_5; R_1 = CH(CH_3)_2$$
$$c\ R = CH_3; R_1 = C_6H_5$$
$$d\ R = CH_3; R_1 = CH(CH_3)_2$$

1.3
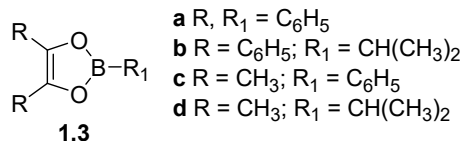
Figure 8. Different derivatives of 1,3,2-dioxaborole compounds.

1.4 Oligoboronate esters

Lavigne and coworkers synthesized and characterized bis(dioxaborole)s **1.4** and **1.5** based on 1,4- benzenediboronic acid and 1,2,4,5-tetrahydroxybenzene (THB), respectively (Figure 9).[22] From this study, they found that the structural properties in the small molecule analogues could be used to identify the properties of the larger oligomeric systems. They also studied the substituent effects on the structure and supramolecular assembly of bis(dioxaborole)s derived from THB (Figure 10).[23] The same group has synthesized fluorene-based bis(dioxaborole)s by the condensation reaction between fluorenyl diboronic acid and a 1,2-diol or THB (Figure 11).[24] They also found that dioxaborole formation is reversible and cross-reactive.

1.4   **1.5**
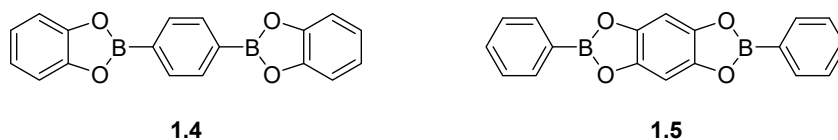
Figure 9. Bis(dioxaborole)s **1.4** and **1.5**.

1.6a-c

a R_1, R_2 = H
b R_1 = H, R_2 = OCH(CH$_3$)$_2$
c R_1= OCH(CH$_3$)$_2$, R_2 = H

1.7a-b

a R_3 = H
b R_3 = C$_6$H$_{13}$
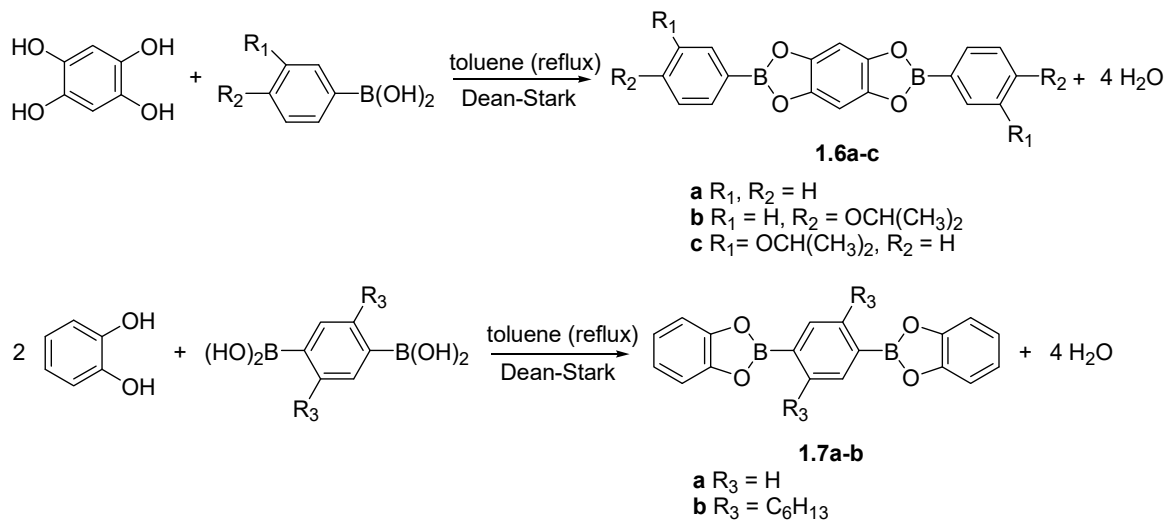
Figure 10. Synthesis of different aromatic bis(dioxaborole)s through dehydration.

1.8a-c

a R = (H)
b R = (OCH$_3$)
c R = (NO$_2$)

1.9
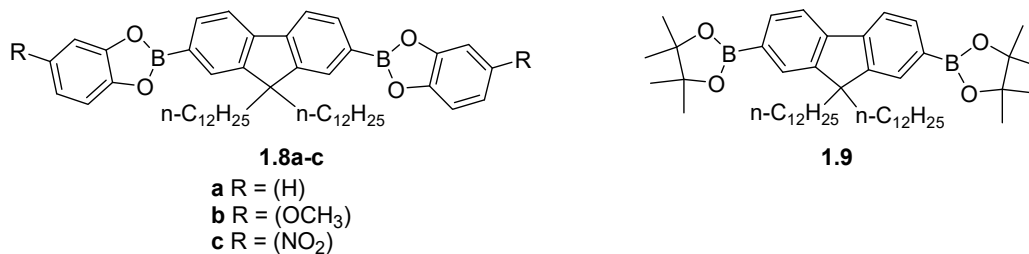
Figure 11. Fluorene-based bis(dioxaborole)s.

In 2006, Lavigne and coworkers reported several novel poly(dioxaborole)s. The self-assembly of a conjugated poly(boronate ester)s (**1.10**) was facilitated by the condensation reaction between 9,9-dihexylfluorene-2,7-diboronic acid (**1.11**) and THB (Figure 12).[25]
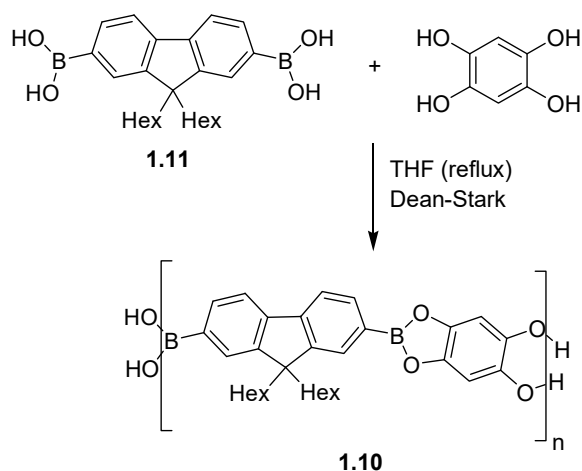
Figure 12. Synthesis of conjugated poly(boronate ester) **1.10**.

They also prepared polymer (**1.12**) by the condensation reaction of benzene-1,4-diboronic acid with THB in toluene and methanol (Figure 13).[22] They confirmed poly(dioxaborole) formation using FTIR and NMR spectroscopy.
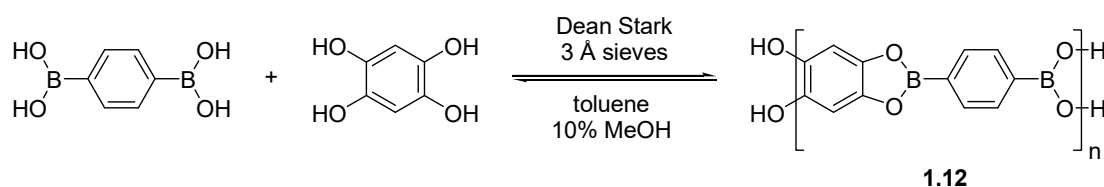
Figure 13. Synthesis of poly(boronate ester) **1.12**.

1.5 Boronate ester-based macrocycles

To date, the syntheses of several boronate ester based macrocycles have been reported. In 2004, the synthesis of dioxaborole based macrocycle (**1.13**) was reported by Severin and coworkers from a multi-component condensation reaction of 3-formylphenyl boronic acid, pentaerythritol, and 1,4-diaminobenzene.[26] This multi-component reaction allows the synthesis of nanometer-sized macrocycles and cages from very simple starting materials. They confirmed the formation of macrocycle by X-ray crystallographic analysis. Macrocycle synthesis via [4+2+2] assembly is shown in Figure 14. The same

group has synthesized macrocycles using three and four component systems.[27] In this study, the macrocycle was synthesized by Lewis acidic benzodioxaboroles, both in solution and in the solid-state.
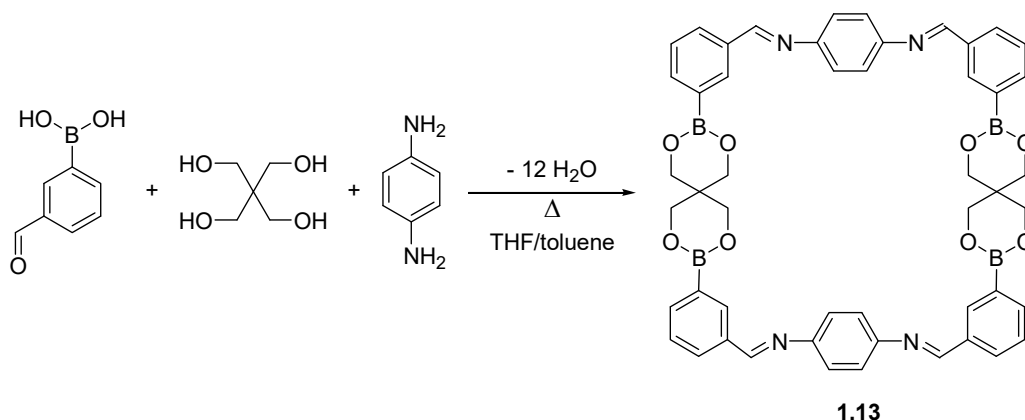
Figure 14. Synthesis of a boronate ester based macrocycle **1.13** from a [4+2+2] condensation.

In 2007, Iwasawa and coworkers were able to obtain chiral macrocycles (**1.14**) from the condensation of 1,4-benzenediboronic acid and a chiral tetraol (**1.15**, Figure 15).[28] They used aromatic solvents such as toluene and benzene for this macrocycle synthesis, in order to understand whether π-π interactions between the component molecules would facilitate the formation of a supramolecular structure, and they found that there is an influence of these solvents on the size of the macrocycle. In 2009, the same group synthesized two diastereomeric cage compounds from racemic tetraol and 1,3,5-benzenetri(boronic acid).[29]
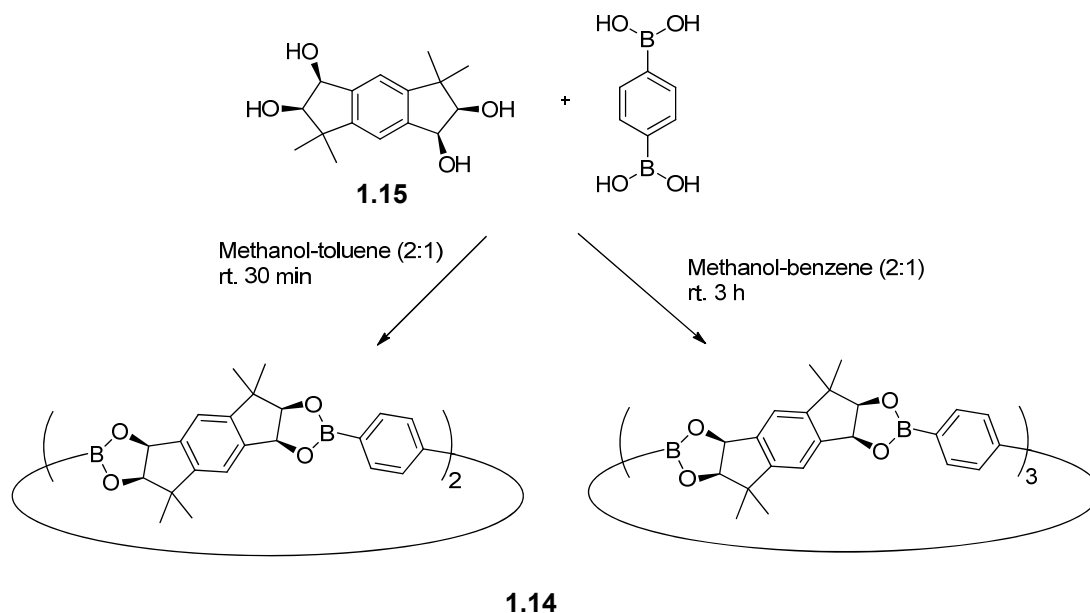
Figure 15. Synthesis of boronate ester-based macrocycle **1.14**.

Lüning and coworkers found that 2,6-bis(alkenyloxy) substituted arylboronic acids can be cyclotrimerized with the help of a tetrol as a template (Figure 16).[30] They reported the first synthesis of trimacrocycle **1.16** from a suitable template. This macrocycle consists of three boronic acids in the endo-positions. They stated that the endo-positions are good receptors for polyols and therefore suitable for testing in sensing devices.
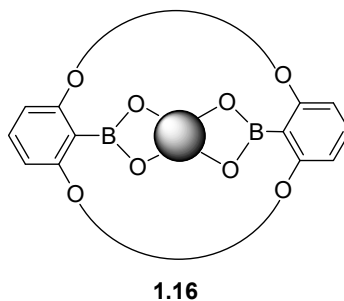
Figure 16. First reported trimacrocycle **1.16**.

In 2014, four different macrocycles were synthesized by Barba and coworkers from the multicomponent reaction of (3-aminophenyl)boronic acid, pentaerythritol, and

four different aldehyde derivatives.[31] These macrocycles consist of both Lewis acids

(boron) and bases (nitrogen and oxygen) and can be used for the identification of diprotic

molecules. Macrocycle (**1.17**) synthesis via [2+1+1] multicomponent reaction is shown in

Figure 17.
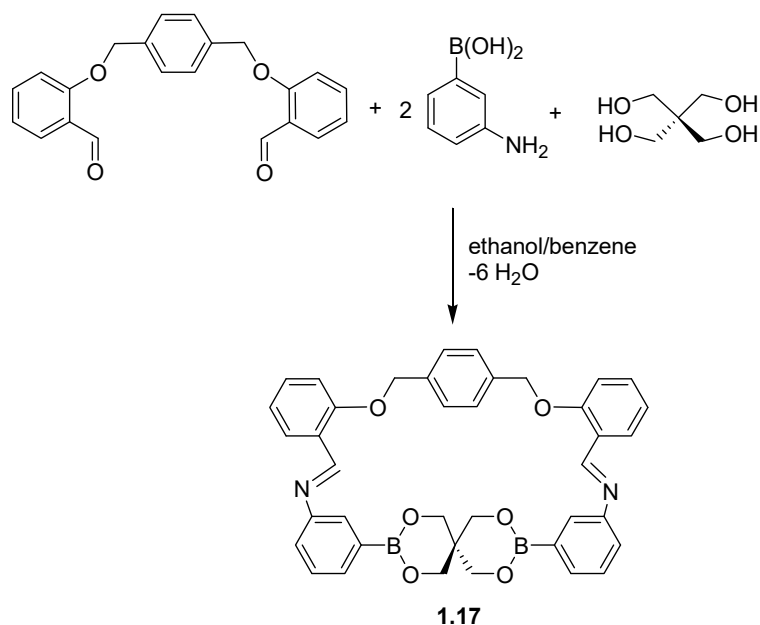
Figure 17. Synthesis of macrocycle **1.17** by a [2+1+1] multicomponent reaction.

More recently, Northrop and coworkers have reported several boronate ester

based macrocycles. They have synthesized boronate ester based rectangles (**1.18**) from

linear bis-catechols and 1,4-benzene diboronic acid (Figure 18).[32] From the spectroscopic

and computational analysis, they found that these macrocycles have extended π-

conjugation on the rectangles.
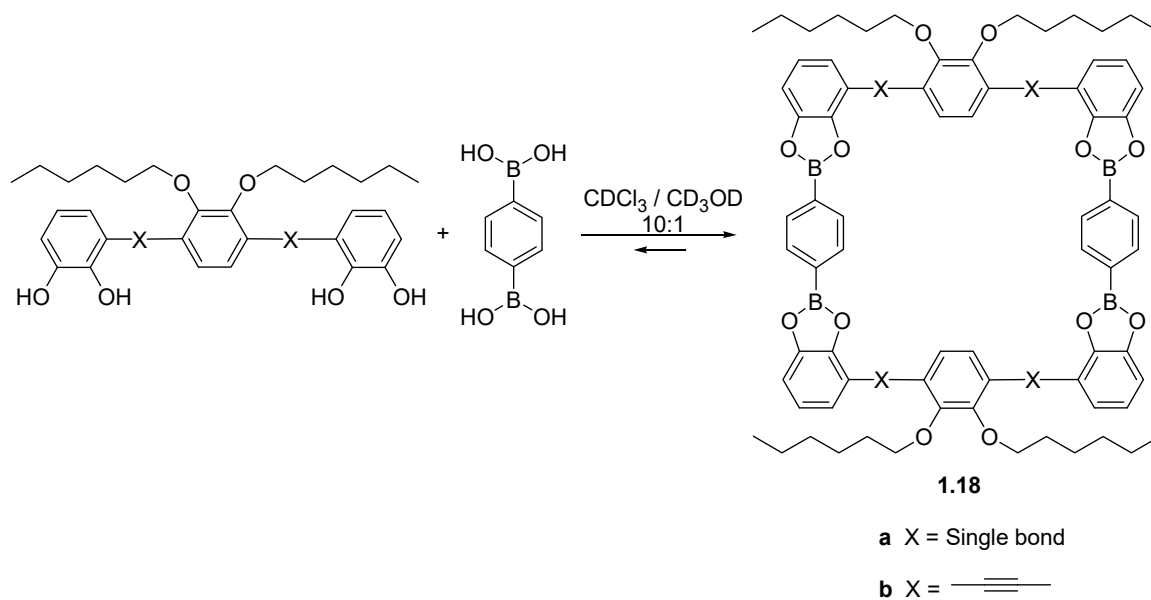
Figure 18. Formation of boronate ester rectangles **1.18**.

The same group developed a macrocycle (not shown) by [2+2] condensation reactions between 1,4-benzene diboronic acid and newly synthesized phenanthrene-based bis(catechol) derivatives (**1.19-1.21**) (Figure 19).[33]
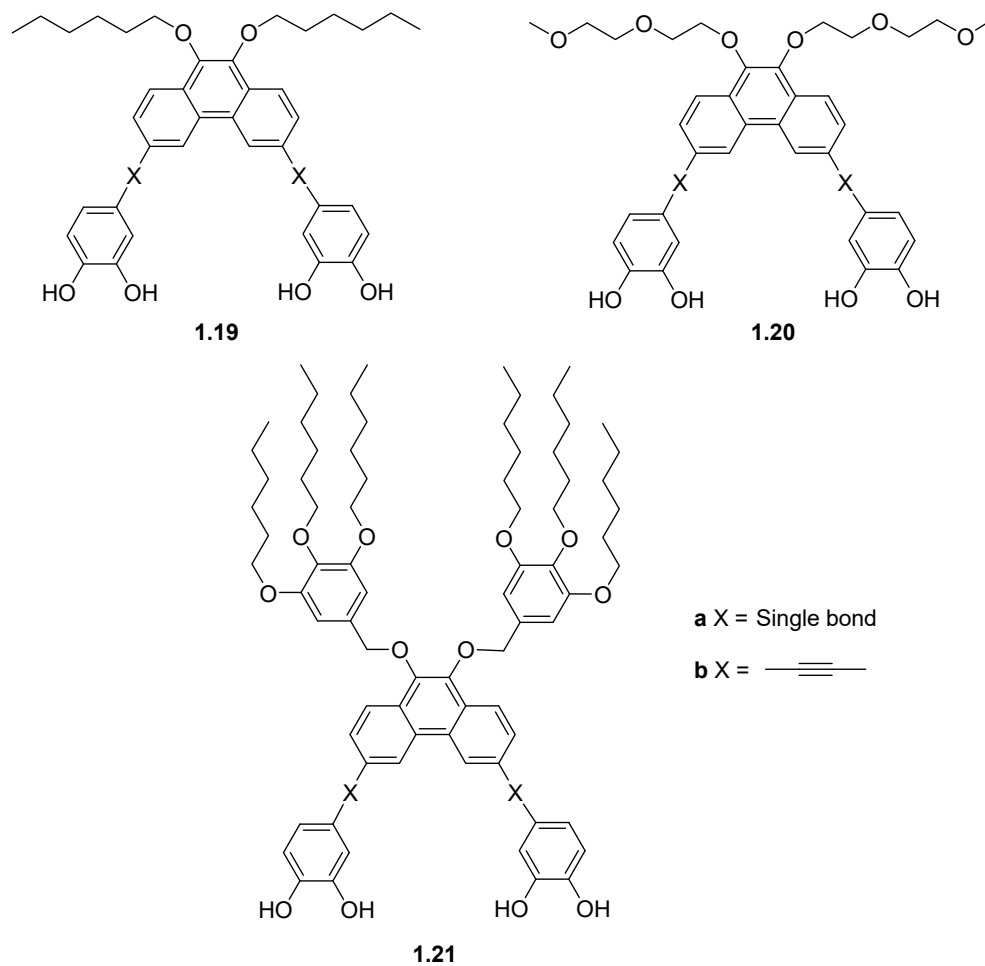
Figure 19. Phenanthrene-based bis(catechol) derivatives.

In 2016, Northrop and coworkers synthesized additional boronate ester-based macrocycles, which are analogues of 2D COFs (**1.22a-1.22d**) (Figure 20 and Figure 21).[34] Due to the hydrophobicity of these alkyl substituted macrocycles, they are hydrolytically more stable than the corresponding 2D COFs.
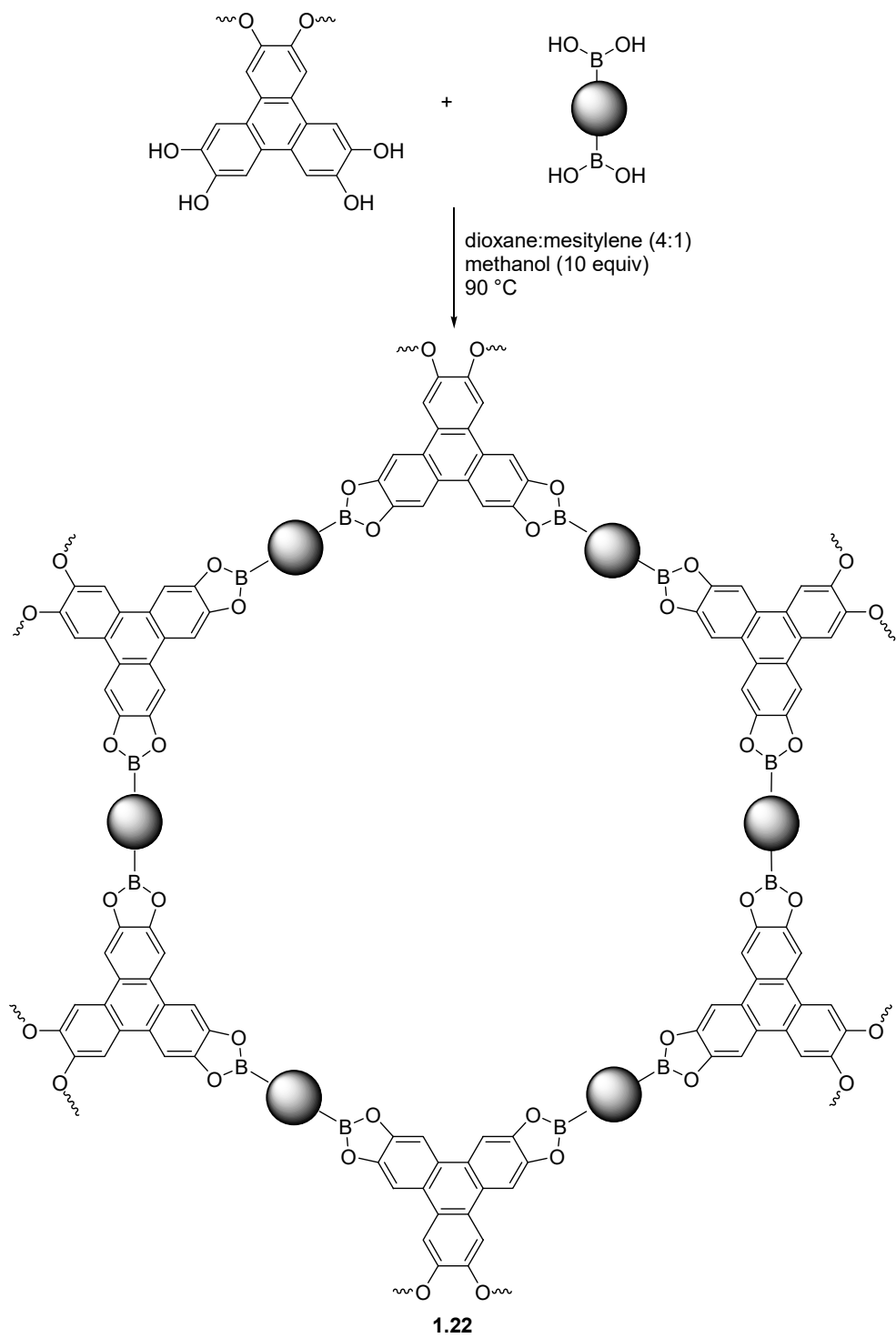
Figure 20. Synthesis of boronate ester based macrocycle **1.22**.
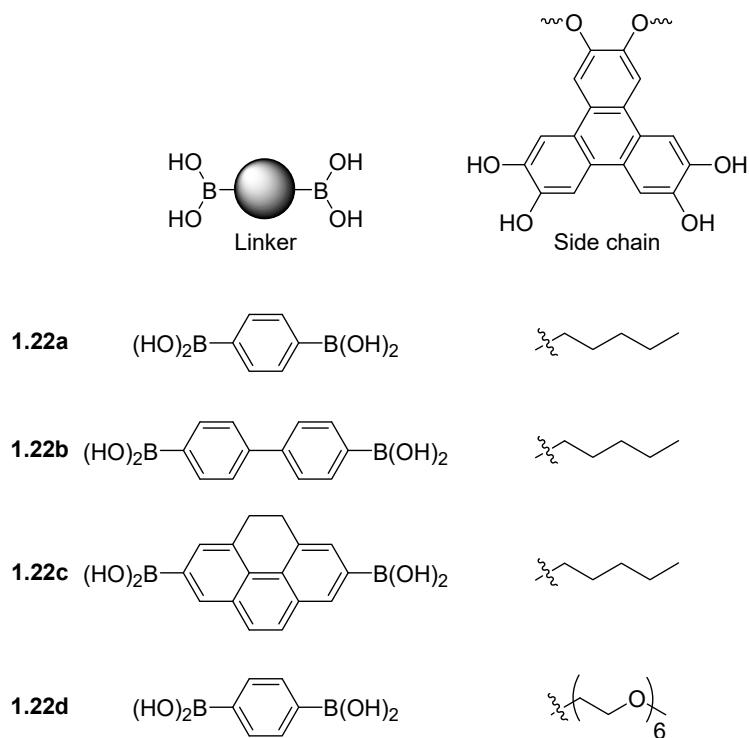
Figure 21. Boronate ester macrocycles **1.22a-1.22d**.

1.6 Boronate ester-based covalent organic frameworks

Oligoboronate esters have been extended to 3D materials by the incorporation of trifunctional monomers. The more ordered of these materials are known as covalent organic frameworks (COFs). Recently, porous materials have achieved great interest due to their outstanding performance and wide applications in areas such as gas storage, gas separation, super hydrophobic interfaces, catalysis, energy conversion, energy storage, and optoelectronics.[35] Therefore, new classes of porous materials are continuously being developed. Among these porous materials, COFs have been the focus of a growing amount of research recently. COFs are thermally remendable porous polymers which are made by reversible dynamic covalent linkages like B-O, C-N, B-N, and B-O-Si, which provides a self-healing capability for the material formation.[36] Since COFs consist of light elements, they have low mass densities. They also possess high thermal stabilities

and provide permanent porosity due to rigid building blocks. Because of these novel properties, COFs have found utility in the areas noted above. According to the building block dimensionality, COFs can be divided into two groups, two-dimensional (2D) and three-dimensional (3D) COFs.[35]

To date, several B-O based COFs have been reported. The first COFs were reported by Yaghi and co-workers in 2005.[37] They synthesized COF-1 by the self-condensation of boronic acids to produce boroxine anhydride-based linkages in the form of B_3O_3 rings (Figure 22). COF-1 was prepared as a crystalline material by the self-condensation of 1,4-benzenediboronic acid. The same group synthesized boronate ester based COF-5 by the condensation reaction of 1,4-benzenediboronic acid and hexahydroxytriphenylene (HHTP) (Figure 23).
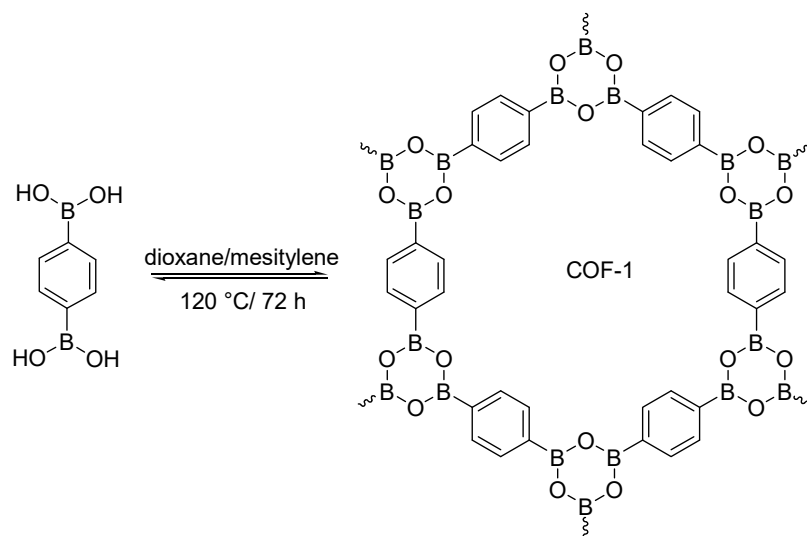
Figure 22. Synthesis of COF-1.
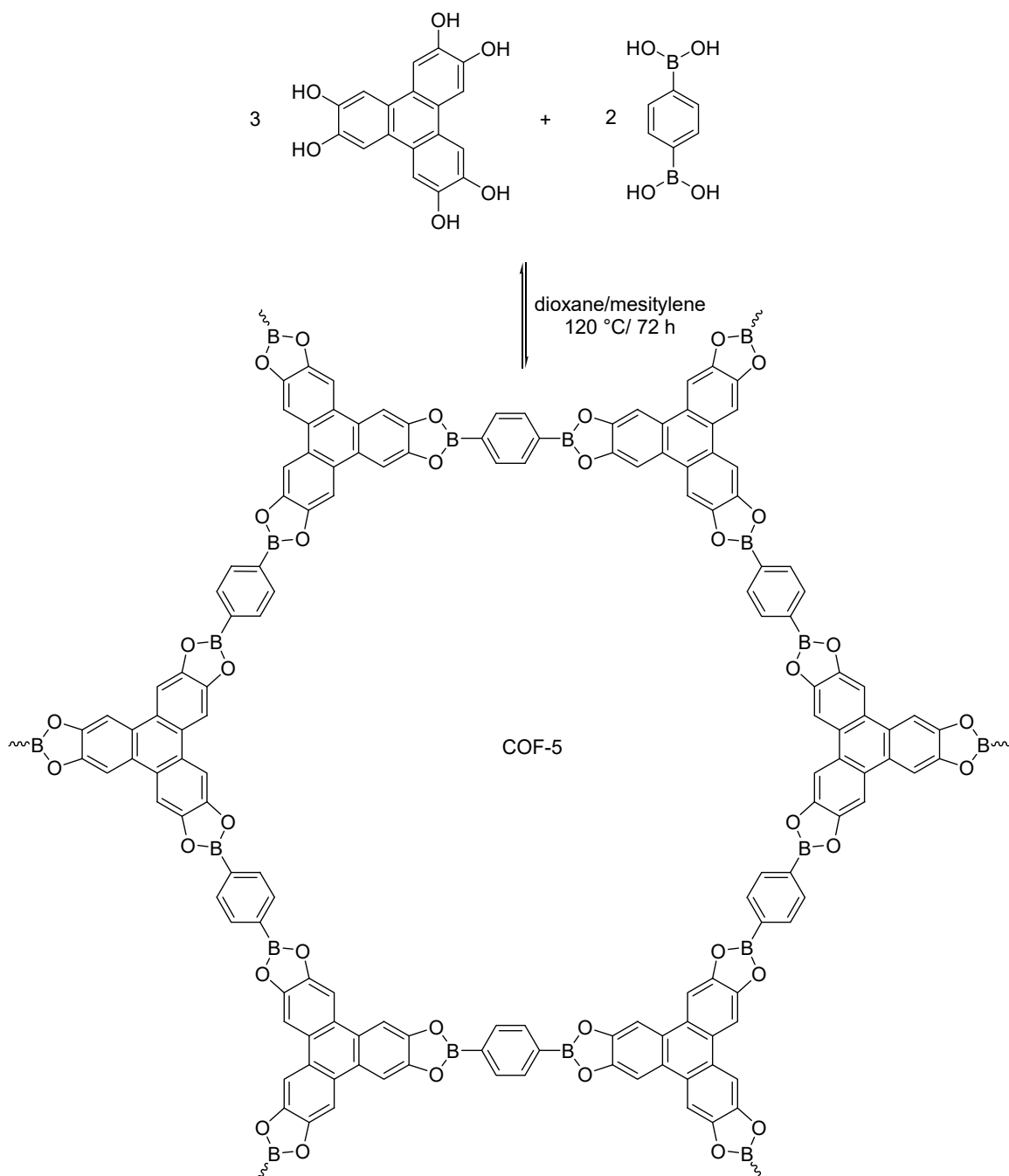
Figure 23. Synthesis of COF-5.

In 2006, Lavigne and coworkers were able to synthesize COF-18Å from a trifunctional boronic acid and benzene tetraol (Figure 24).[38] COF-18Å refers to the covalent organic framework which has 18 Å diameter pores.
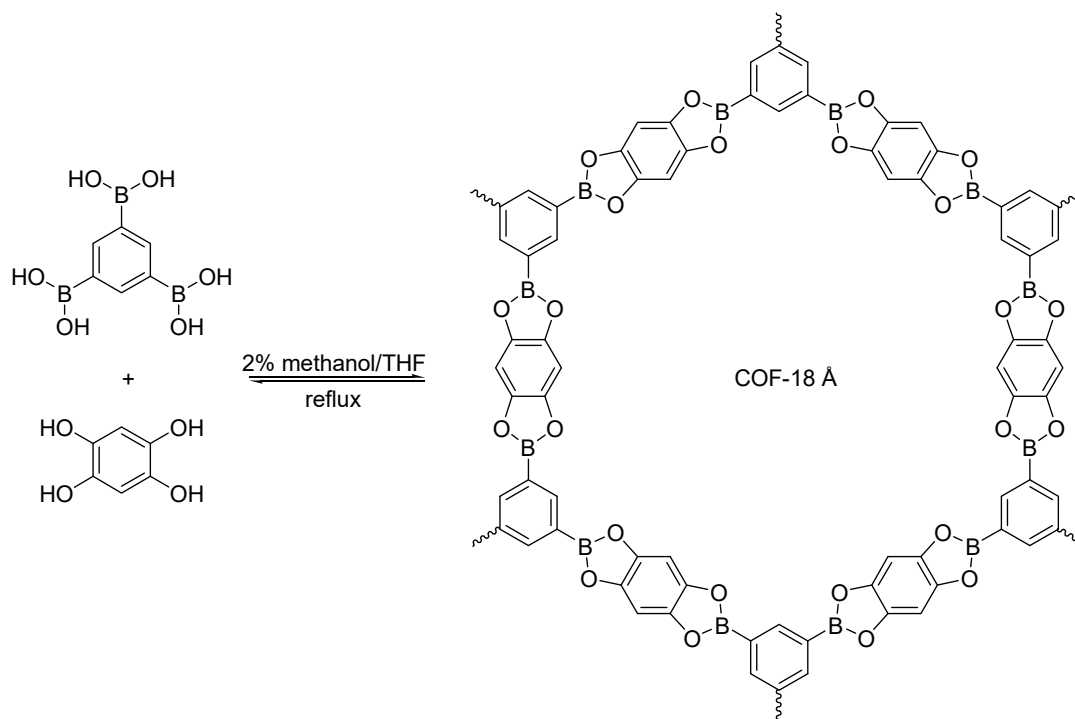
Figure 24. Synthesis of COF-18Å.

Recently, Dichtel and coworkers synthesized COF-5 and COF-10 by using polyfunctional boronic acids and acetonide-protected HHTP in the presence of a Lewis acid catalyst $BF_3 \cdot OEt_2$ (Figure 25).[39] The method they proposed was more convenient than conventional COF synthesis and it helped to overcome previous solubility issues. Through mechanistic studies, they found that boronic acid-BF_3 complexes influence the rate of the boronate ester formation. The powder XRD, IR, and N_2 adsorption isotherms studies confirmed these COFs have similar surface areas as previously reported COFs.
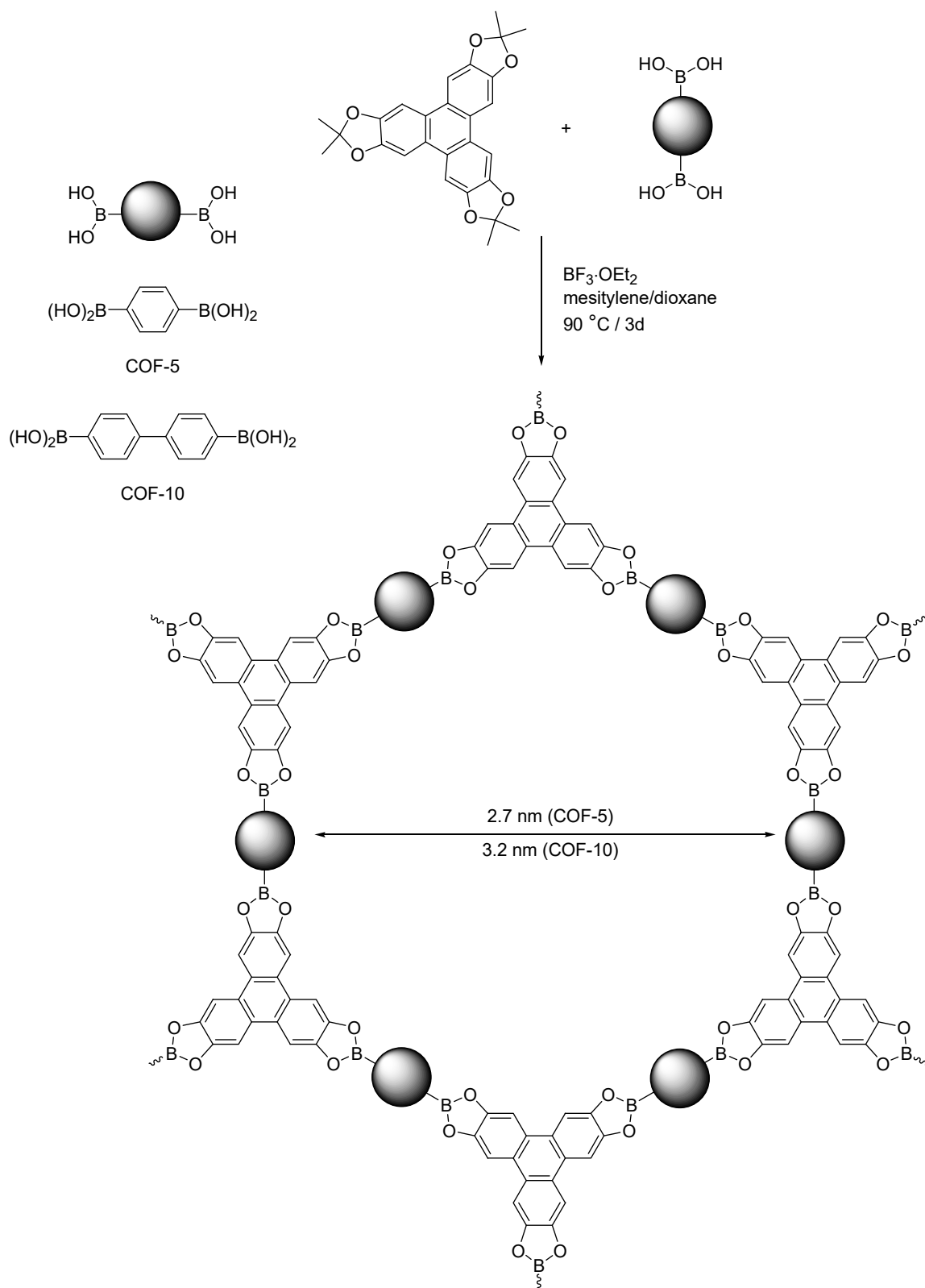
Figure 25. BF₃·OEt₂ catalyzed synthesis of COF-5 and COF-10.

1.7 Aims of this work

Previously, COFs have been synthesized from the reaction of boronic acids with diols. We are interested in using boronate esters because they are less polar, more stable, easier to isolate, and typically more soluble in organic solvents than boronic acids. Additionally, transesterification is one of the simplest and most convenient methods to synthesize boronate esters. One of the main goals of our research is to synthesize di/trifunctional monomers, which have the capability to self-assemble into larger materials, similar to the latter examples in the previous section, i.e., COFs.

In our current work, we investigated the effect of boron trifluoride on the transesterification of boronate esters with catechol (chapter III). Catechol boronate esters are of interest due to the π-conjugation and have been used frequently in COF synthesis. The synthesis of stable boronate ester based monomers may allow for the straightforward synthesis of shape-persistent macrocyclic and COF materials. Then, we used this methodology to synthesize bis/oligomeric boronate ester materials and more complex dioxaboroles by combining the knowledge learned in the above-described work (chapter III). Separately, we studied the effect of Lewis acids on the dehydration/rearrangement of pinacol and other 1,2-diols (chapter IV).

CHAPTER II

MATERIALS AND METHODS

2.1 General Experimental

The starting materials and reagents were purchased from commercial sources unless otherwise mentioned. The syntheses of the boronate ester starting materials used in chapter III are described below in sections 2.2 and 2.3. Some of the boronate esters were synthesized *in situ* (see section 2.2) and others were synthesized on a preparative (gram) scale using vacuum distillation or mixing in chloroform (see section 2.3). These esters were used without further purification for the experiments described in chapter III.

Analytical thin-layer chromatography (TLC) was performed on Agela MF254 pre-coated silica plates. Visualization was carried out with UV light (254 nm).

^{1}H-NMR spectra were taken on JEOL Eclipse 300$^+$ spectrometer. Chemical shifts are reported in δ (ppm) relative to residual solvent protons (CDCl$_3$: 7.26). Splitting patterns are designated as s (singlet); d (doublet); t (triplet); m (multiplet). The progress of the small-scale reactions was monitored by ^{1}H-NMR spectroscopy. The equivalents of BF$_3$·OEt$_2$, extent of esterification, and extent of transesterification were determined based on the ^{1}H-NMR integrations of the relevant proton signals.

2.2 *In situ* synthesis of boronate esters

Boronic acid can readily react with diols to give cyclic boronate esters. Commercially available phenylboronic acid (**2.1**) was reacted with different diols **2.2**-**2.9** (Figure 26). All diols except **2.5**, **2.8**, and **2.9**, were commercially available and used as received. The esterification reactions were carried out in NMR tubes using CDCl$_3$ as the

solvent. An equimolar mixture of boronic acid **2.1** and diol (0.082 mmol each) was added to an NMR tube along with CDCl$_3$ (0.7 mL). The reaction progress was monitored using ^{1}H-NMR spectroscopy. The extent of esterification was determined based on the ^{1}H-NMR integrations of the relevant proton signals (Figure 26 and Table 1). Most reactions were completed within minutes (before spectra could be recorded) and 100% esterification was observed (Figure 27). However, diol **2.4** took about 3 h to reach completion. This is likely due to the steric hindrance from the four methyl groups present in this diol.
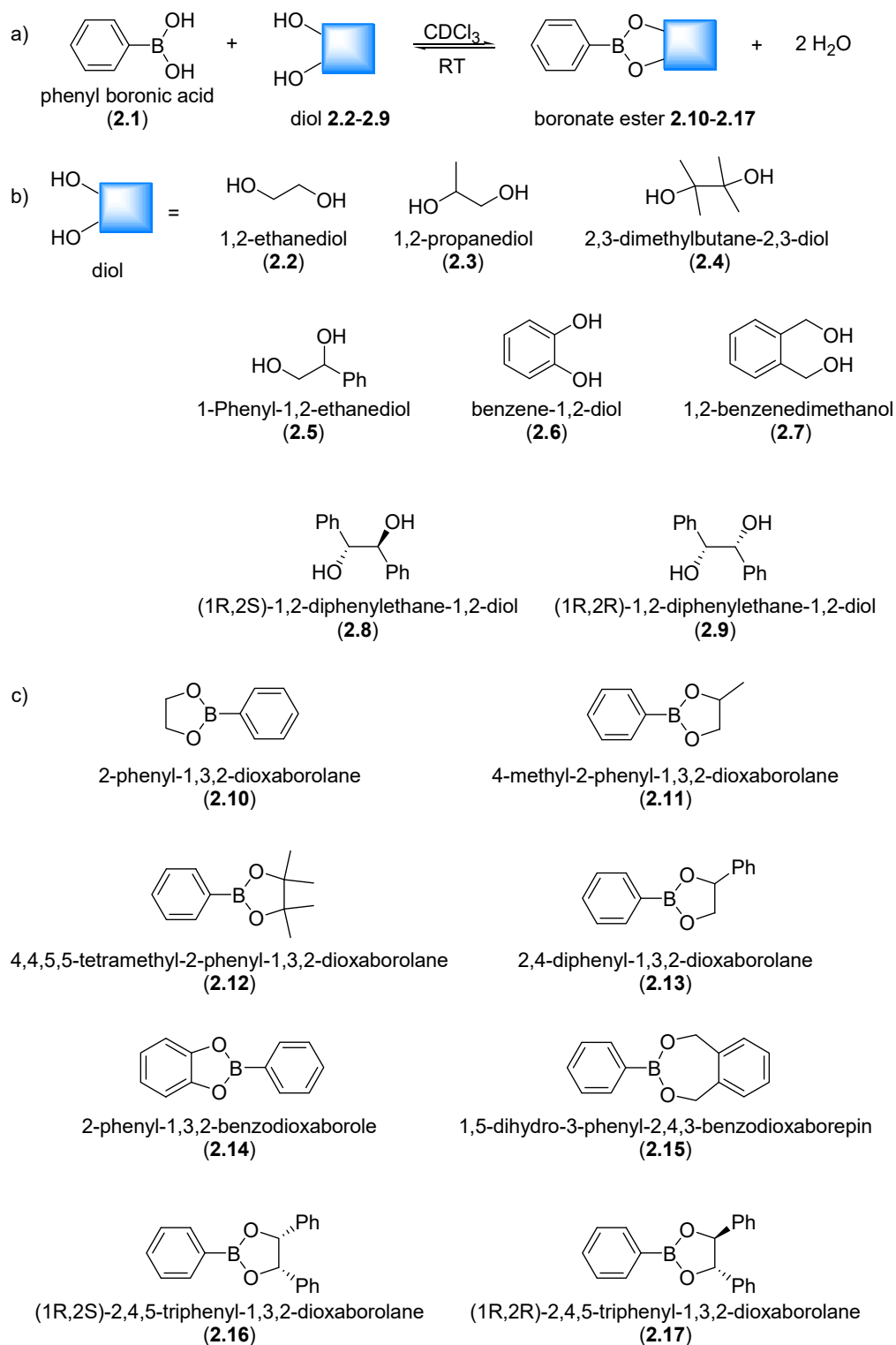
Figure 26. a) Schematic representation of boronic acid-diol esterification, b) different

diols studied **2.2**-**2.9**, and c) boronate esters **2.10**-**2.17**.

Table 1

¹H-NMR signals used to determine the percent esterification

Reaction	starting material	product
2.1 + **2.2**	δ 7.70 ppm (**2.1**)	δ 7.80 ppm (**2.10**)
2.1 + **2.3**	δ 7.70 ppm (**2.1**)	δ 7.80 ppm (**2.11**)
2.1 + **2.4**	δ 1.23 ppm (**2.4**)	δ 1.34 ppm (**2.12**)
2.1 + **2.5**	δ 7.70 ppm (**2.1**)	δ 7.89 ppm (**2.13**)
2.1 + **2.6**	δ 7.70 ppm (**2.1**)	δ 8.10 ppm (**2.14**)
2.1 + **2.7**	δ 7.70 ppm (**2.1**)	δ 7.80 ppm (**2.15**)
2.1 + **2.8**	δ 7.70 ppm (**2.1**)	δ 8.07 ppm (**2.16**)
2.1 + **2.9**	δ 7.70 ppm (**2.1**)	δ 7.98 ppm (**2.17**)

Figure 27. The reaction progress of phenyl boronic acid (**2.1**) with diols **2.2-2.9**.

2.3 Preparative scale synthesis of boronate esters

2.3.1 Preparation by vacuum distillation

Boronate esters **2.10** and **2.12** were synthesized from diols **2.2** and **2.4**, respectively, via vacuum distillation (Figure 28).
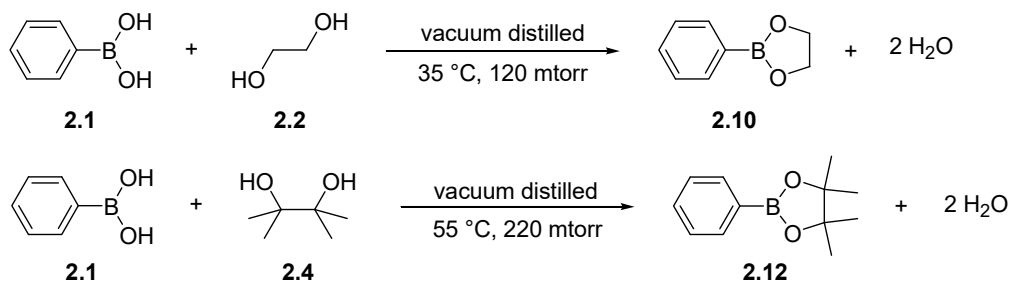
Figure 28. Synthesis of boronate esters **2.10** and **2.12**.

2-Phenyl-1,3,2-dioxaborolane (2.10). Phenylboronic acid **2.1** (0.61 g, 5 mmol, 1 equiv) and 1,2-ethanediol **2.2** (0.31 g, 5 mmol, 1 equiv) were heated and distilled under reduced pressure (35 ˚C, 120 mtorr, 25% power). A yellow oil (0.54 g, 73%) was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.80 (d, 2H), 7.40-7.35 (m, 3H), 4.37 (s, 4H).

4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaborolane (2.12). Phenylboronic acid **2.1** (1.22 g, 10 mmol, 1 equiv) and pinacol **2.4** (1.18 g, 10 mmol, 1 equiv) were distilled under reduced pressure (55 ˚C, 220 mtorr, 34% power). White crystals (1.87 g, 92%) were obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.80 (d, 2H), 7.45-7.35 (m, 3H), 1.34 (s, 12H).

2.3.2 Preparation of dioxaborolanes in chloroform

An equimolar amount of phenylboronic acid **2.1** and diol (**2.3**, **2.5**, **2.8**, or **2.9**) were dissolved in CHCl$_3$ (Figure 29). Simple evaporation of the solvent resulted in the isolation of esters **2.11**, **2.13**, **2.16**, and **2.17**, respectively.
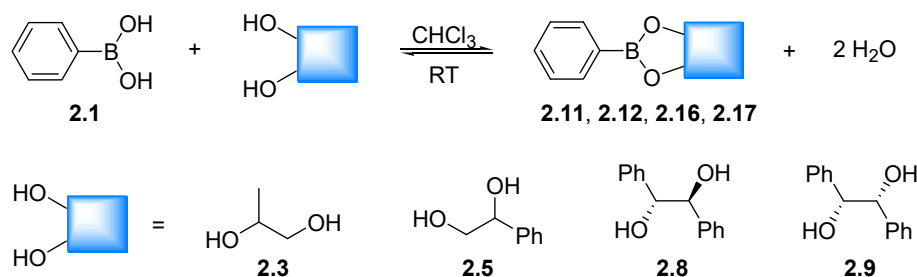
Figure 29. Synthesis of different boronate esters.

4-Methyl-2-phenyl-1,3,2-dioxaborolane (2.11). Phenylboronic acid **2.1** (1.60 g, 13 mmol, 1 equiv) and 1,2-propanediol **2.3** (1.00 g, 13 mmol, 1 equiv) were mixed in CHCl$_3$ (5 mL) in a vial. The reaction mixture was stirred for 1 h at room temperature. Then, the solvent was removed under reduced pressure. A clear oil (1.63 g, 78%) was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.80 (d, 2H), 7.49-7.35 (m, 3H), 4.71-4.66 (m, 1H), 4.47 (t, 1H), 3.89 (t, 1H), 1.42 (d, 3H).

2,4-Diphenyl-1,3,2-dioxaborolane (2.13). Phenylboronic acid **2.1** (0.100 g, 0.82 mmol, 1 equiv) and 1-phenyl-1,2-ethanediol **2.5** (0.113 g, 0.82 mmol, 1 equiv) were mixed in CHCl$_3$ (5 mL) in a vial. The reaction mixture was stirred for 1 h at room temperature. Then, the solvent was removed under reduced pressure. A white solid (0.180 g, 99%) was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.93 (d, 2H), 7.54-7.33 (m, 8H), 5.60 (t, 1H), 4.74 (t, 1H), 4.20 (t, 1H).

(1R,2S)-2,4,5-Triphenyl-1,3,2-dioxaborolane (2.16). Phenylboronic acid **2.1** (7.0 mg, 0.058 mmol, 1 equiv) and meso-hydrobenzoin **2.8** (12.4 mg, 0.058 mmol, 1 equiv) were mixed in CHCl$_3$ (5 mL) in a vial. The reaction mixture was stirred for 1 h at room temperature. Then, the solvent was removed under reduced pressure. A white solid (16.0 mg, 92%) was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 8.04 (d, 2H), 7.61-7.46 (m, 3H), 7.09-6.95 (m, 10H), 5.93 (s, 2H).

*(1R,2R)-2,4,5-Triphenyl-1,3,2-dioxaborolane (**2.17**)*. Phenylboronic acid **2.1** (2.8 mg, 0.023 mmol, 1 equiv) and d-hydrobenzoin **2.9** (5.0 mg, 0.023 mmol, 1 equiv) were mixed in CHCl$_3$ (5 mL) in a vial. The reaction mixture was stirred for 1 h at room temperature. Then, the solvent was removed under reduced pressure. A white solid (6.6 mg, 96%) was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 8.00 (d, 2H), 7.57-7.34 (m, 13H), 5.33 (s, 2H).

2.3.3 Preparation of phenyl pinacol boronate esters

2-(4-Bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2.20**) and 2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2.21**) were synthesized using similar conditions as above for 4-bromophenylboronic acid (**2.18**) and 4-methoxyphenylboronic acid (**2.19**) with pinacol **2.4** (Figure 30).
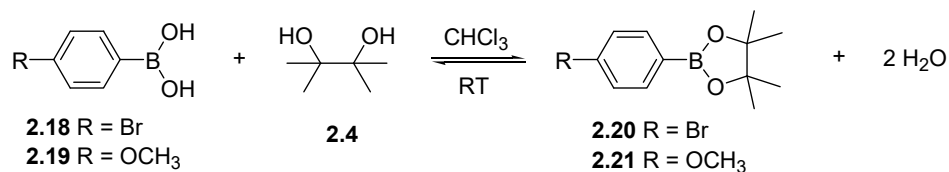
Figure 30. Synthesis of phenyl substituted pinacol boronate esters **2.20** and **2.21**.

*2-(4-Bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2.20**)*. Commercially available 4-bromophenylboronic acid (**2.18**) (15.0 mg, 0.075 mmol, 1 equiv) and pinacol (**2.4**) (8.9 mg, 0.075 mmol, 1 equiv) were mixed in CHCl$_3$ (3 mL) in a vial. The reaction mixture was stirred for 1 h at room temperature. Then, the solvent was removed under reduced pressure. A white solid (14.3 mg, 68%) was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.64 (d, 2H), 7.49 (d, 2H), 1.33 (s, 12H).

*2-(4-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2.21**)*. Commercially available 4-methoxyphenylboronic acid (**2.19**) (11.4 mg, 0.075 mmol, 1

equiv) and **2.4** (8.9 mg, 0.075 mmol, 1 equiv) were mixed in CHCl$_3$ (3 mL) in a vial. The reaction mixture was stirred for 1 h at room temperature. Then, the solvent was removed under reduced pressure. A white solid (13.2 mg, 75%) was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.74 (d, 2H), 6.88 (d, 2H), 3.82 (s, 3H), 1.33 (s, 12H).

2.3.4 Preparation of bis-pinacol boronate esters in chloroform

2,2'-(1,4-Phenylene)bis[4,4,5,5-tetramethyl-1,3,2-dioxaborolane] (**2.23**) and 2,2'-[1,1'-biphenyl]-4,4'-diylbis[4,4,5,5-tetramethyl-1,3,2-dioxaborolane] (**2.25**) were synthesized by the condensation of 1,4-benzenediboronic acid (**2.22**) and biphenyl-4,4'-diboronic acid (**2.24**) with pinacol **2.4** (2 equiv) in CHCl$_3$ (Figure 31).

Initially, bisboronic acids **2.22** and **2.24** did not dissolve in CHCl$_3$. Eventually, after adding pinacol (**2.4**) and heating the reaction mixture all starting materials dissolved and were converted to the corresponding esters **2.23** and **2.25**, respectively.
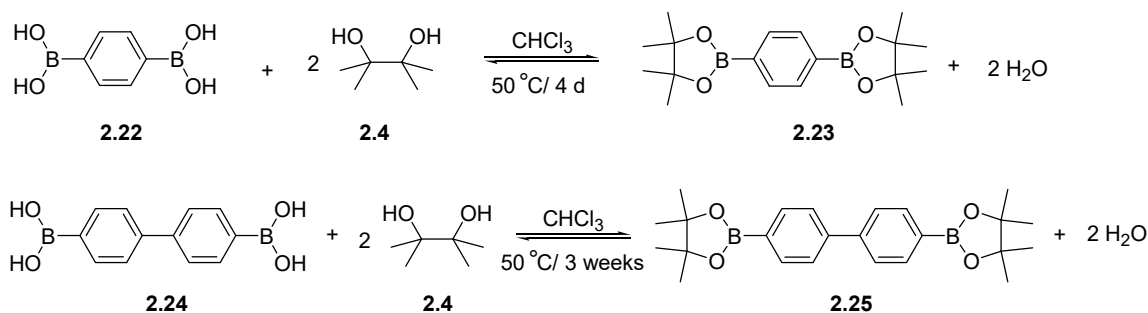
Figure 31. Synthesis of bisboronate esters **2.23** and **2.25**.

*2,2'-(1,4-Phenylene)bis[4,4,5,5-tetramethyl]-1,3,2-dioxaborolane (**2.23**).*
Commercially available **2.22** (12.4 mg, 0.075 mmol, 1 equiv) and **2.4** (17.7 mg, 0.15 mmol, 2 equiv) were mixed in a vial in CHCl$_3$ (10 mL). The reaction mixture was stirred and heated at 50 ˚C for 4 days to dissolve all the starting materials. After 4 days, the CHCl$_3$ was removed under reduced pressure at room temperature. The resulting

compound was a white solid (22.3 mg, 93%). ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.79 (s, 4H), 1.34 (s, 24H).

     *2,2'-[1,1'-Biphenyl]-4,4'-diylbis[4,4,5,5-tetramethyl]-1,3,2-dioxaborolane (**2.25**)*. Commercially available **2.24** (18.0 mg, 0.074 mmol, 1 equiv) and **2.4** (17.7 mg, 0.15 mmol, 2 equiv) were mixed in a vial in CHCl$_3$ (10 mL). The reaction mixture was stirred and heated at 50 ˚C for 3 weeks to dissolve all the starting materials. After 3 weeks, the CHCl$_3$ was removed under reduced pressure at room temperature. The resulting compound was a white solid (27.5 mg, 90%). ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.85 (d, 4H), 7.62 (d, 4H), 1.34 (s, 24H).

CHAPTER III

THE EFFECT OF BORON TRIFLUORIDE ON THE TRANSESTERIFICATION

OF BORONATE ESTERS

3.1 Background

Transesterification may be a useful alternative esterification (of boronic acids and diols) for synthesis of boronate ester materials (Figure 32). In some cases, when boronate esters are not available in boronic acid form, transesterification would be more convenient than esterification. It is also known that boronate esters are less polar and easier to handle than boronic acids.
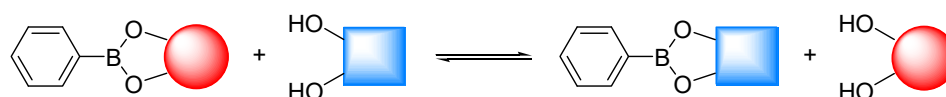
Figure 32. Transesterification of boronate esters.

Brown and coworkers studied the relative rates of transesterification of phenyl ethylene glycol boronate ester (PEB) with various diols to understand the factors affecting the relative stability of boronate esters.[40] Of the diols studied, they found that boronate esters consisting of saturated bicyclic hydrocarbons (pinanediol boronic esters) are most stable and diisopropyl tartrate boronate esters are thermodynamically least stable (Figure 33). They also found that six-membered borinanes are relatively more stable than their corresponding five-membered borolanes.
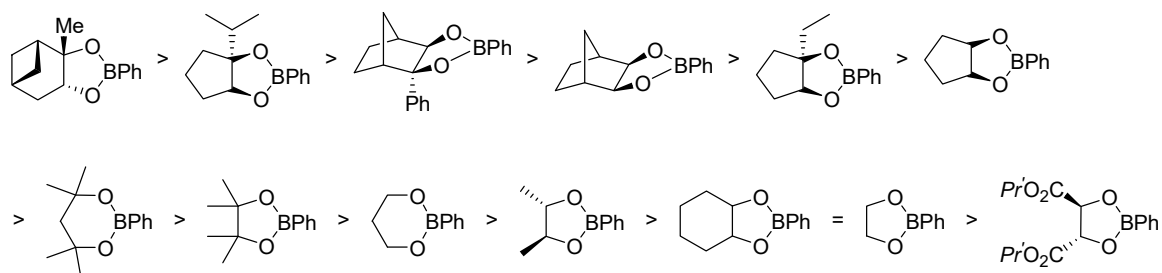
Figure 33. Decreasing order of stability of various boronate esters.

Our group has explored the transesterification of phenyl pinacol boronate ester **3.1** with different diols using BF$_3$·OEt$_2$ as a catalyst.[41] From our previous studies, we observed 100% transesterification of ester **3.1** and catechol (**3.2**) to dioxaborole **3.3** and pinacol (**3.4**). Subsequent pinacol rearrangement resulted in the formation of pinacolone (**3.5**) (Figure 34). Boron triflouride not only changed the rate of the transesterification reaction but also affected the equilibrium by removing pinacol via the pinacol rearrangement.
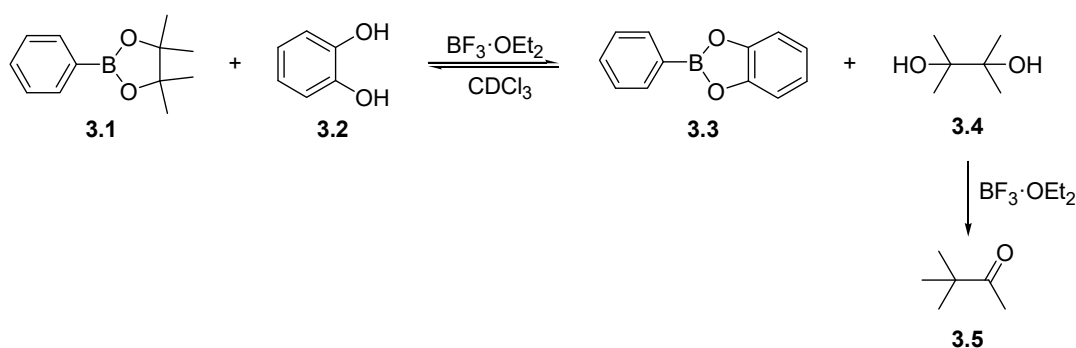
Figure 34. BF$_3$·OEt$_2$ promoted transesterification between boronate ester **3.1** with diol **3.2**.

Similar results were obtained with neopentyl glycol (**3.6**) in the presence of BF$_3$·OEt$_2$ (Figure 35). However, the transesterification of ester **3.1** with ethylene glycol (**3.8**) in the presence of BF$_3$·OEt$_2$ did not result in high conversion; only 10% of ester **3.9**

was observed. It was hypothesized that transesterification of diol **3.8** may be low due to the coordination of BF₃ with this diol instead of facilitating transesterification.[41]
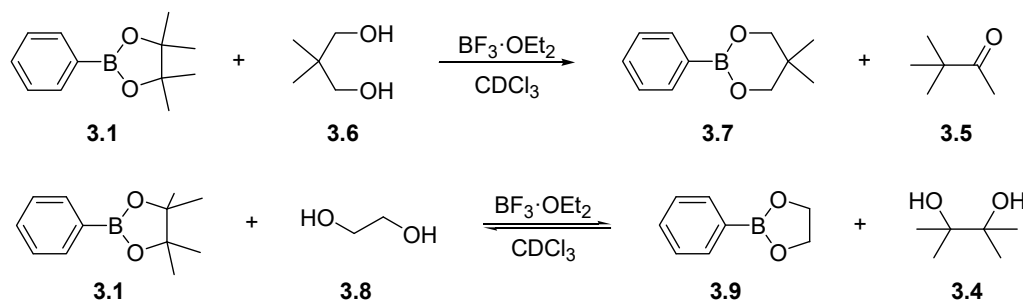
Figure 35. BF₃·OEt₂ promoted transesterification between boronate ester **3.1** and diols **3.6** and **3.8**.

3.2 Objectives

First, we carried out further studies on the transesterification of boronate ester **3.1** with diol **3.8** in the presence of BF₃·OEt₂, in order to find the exact reason for the inefficient transesterification.

Then, we investigated the effect of BF₃·OEt₂ on the transesterification of various simple boronate esters and substituted pinacol boronate esters with catechol. Since we were able to find an efficient method to transesterify ester **3.1** into ester **3.3** in the presence of BF₃·OEt₂, our next goal was to investigate a method to isolate ester **3.3**. Catechol boronate ester (**3.3**) is an important monomer in synthesizing macrocycles and COF. Due to the π-conjugation of these boronate esters, it will likely have desirable properties (electric and electronic) when developing large molecular architectures.

Finally, we focused on the effect of BF₃·OEt₂ on synthesizing of bis/oligo-boronate ester materials. Bis(dioxaborole)s are formed from the condensation reaction between diboronic acids with aromatic 1,2-diols or mono boronic acids with tetraols.

3.3 Results and Discussion

3.3.1 Boron trifluoride-ethylene glycol interaction

To begin, we wanted to better understand the nature of the interaction between ethylene glycol (**3.8**) and BF$_3$·OEt$_2$. Therefore, diol **3.8** was mixed with BF$_3$·OEt$_2$ in CDCl$_3$ (Figure 36). A shift of the diol **3.8** peak was observed in the ^{1}H-NMR spectrum (Figure 37).
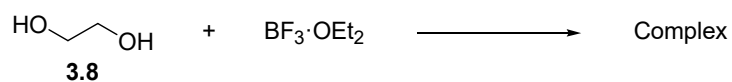
Figure 36. The reaction of diol **3.8** with BF$_3$·OEt$_2$.
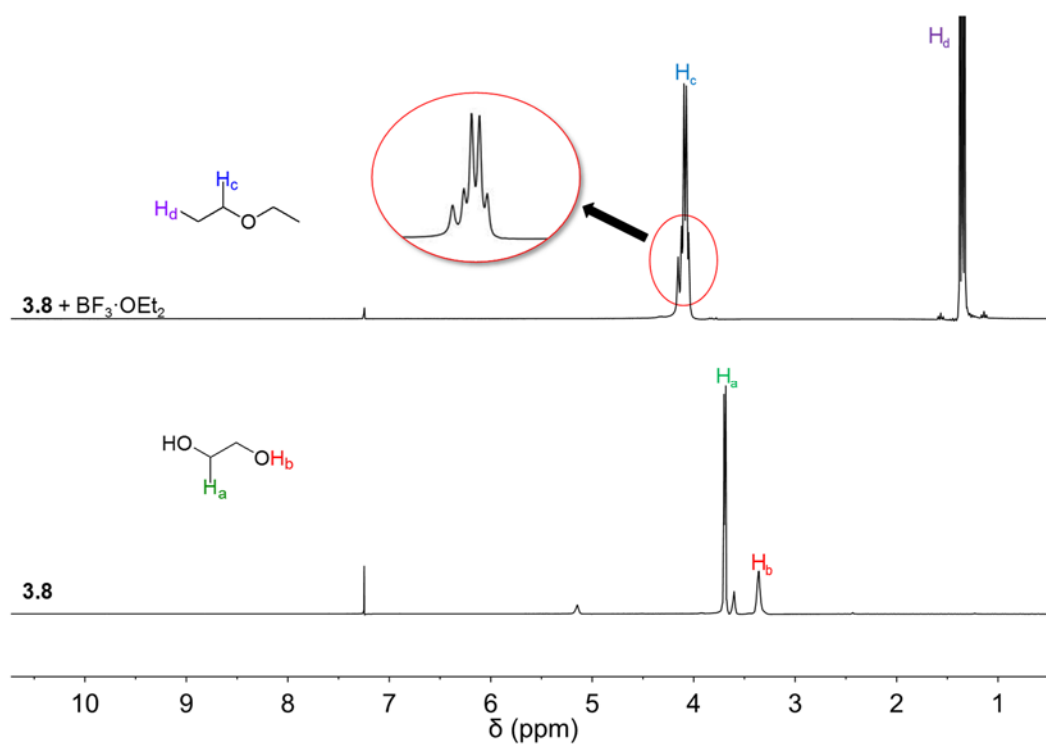
Figure 37. ^{1}H-NMR spectra of diol **3.8** with and without BF$_3$·OEt$_2$.

3.3.2 Transesterification of dioxaborolanes in an NMR tube

Next, we thought we could see if this complexation could be used to our advantage in the transesterification of ester **3.9** with catechol. Therefore, ester **3.9** was mixed with catechol (**3.2**) in CDCl$_3$, and BF$_3$·OEt$_2$ was added (Figure 38).

3.9   **3.2**   **3.3**   **3.8**
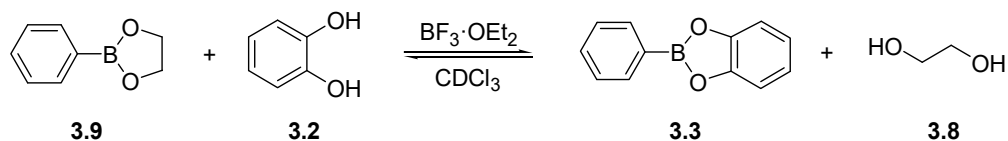
Figure 38. The reaction between boronate ester **3.9** and diol **3.2** with BF$_3$·OEt$_2$ in CDCl$_3$.

In the absence of BF$_3$·OEt$_2$ there is only 27% transesterification of ester **3.9** to ester **3.3**. However, after adding 10 equiv of BF$_3$·OEt$_2$, 98% conversion of ester **3.9** to ester **3.3** was observed. Then, in a separate experiment 10 equiv of BF$_3$·OEt$_2$ was added after ester **3.9** and catechol **3.2** were allowed to reach equilibrium. It showed 97% transesterification by the time NMR was obtained (<10 min). In Figure 39, the circles show the results of the first study and triangles show the results of the second study.
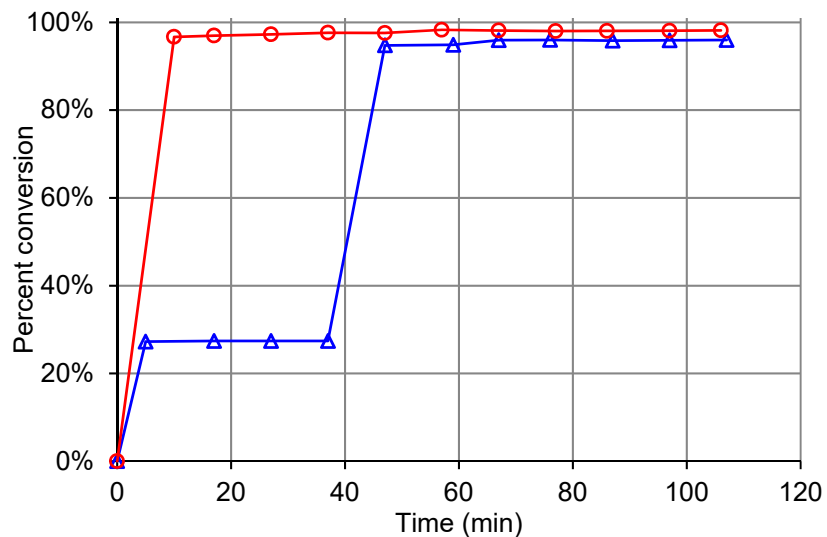
Figure 39. Transesterification of boronate ester **3.9** with diol **3.2** in the presence of

BF$_3$·OEt$_2$.

Then, the same transesterification was carried out with the different equivalents of

BF$_3$·OEt$_2$ to investigate the relationship between the percent transesterification and the

amount of BF$_3$·OEt$_2$. Figure 40 shows the results of the transesterification of ester **3.9**

with catechol **3.2** in the presence of the different equivalents of BF$_3$·OEt$_2$. The percent

transesterification increased with an increasing amount of BF$_3$·OEt$_2$. There was no

significant difference in the transesterification with greater than 3.5 equivalents.
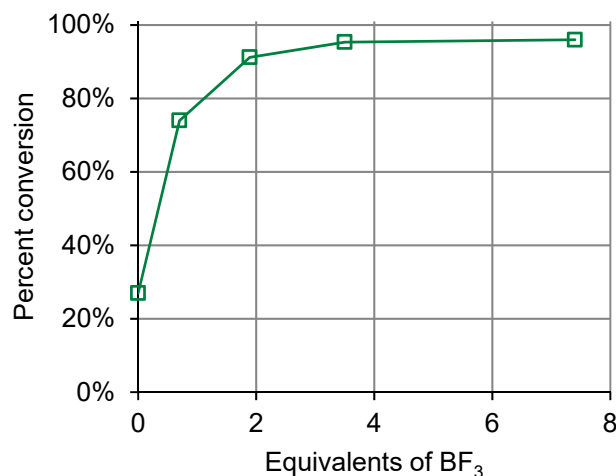
Figure 40. Transesterification of ester **3.9** with catechol **3.2** in the presence of five

different equivalents of BF$_3$·OEt$_2$.

To extend the methodology from the previous experiment, the transesterification

of 4-methyl-2-phenyl-1,3,2-dioxaborolane (**3.12**), 1,5-dihydro-3-phenyl-2,4,3-

benzodioxaborepin (**3.13**), and 2,4-diphenyl-1,3,2-dioxaborolane (**3.14**) with diol **3.2**

were investigated in the presence of different amounts of BF$_3$·OEt$_2$ (Figure 41). These

reactions were carried out in NMR tubes and the esters were made in situ by mixing

phenylboronic acid with the corresponding diol in CDCl$_3$ (see chapter II section 2). Then

an equimolar amount of catechol **3.2** was added to the NMR tube, and the solution was

titrated with different amounts of BF$_3$·OEt$_2$ (Figure 42).
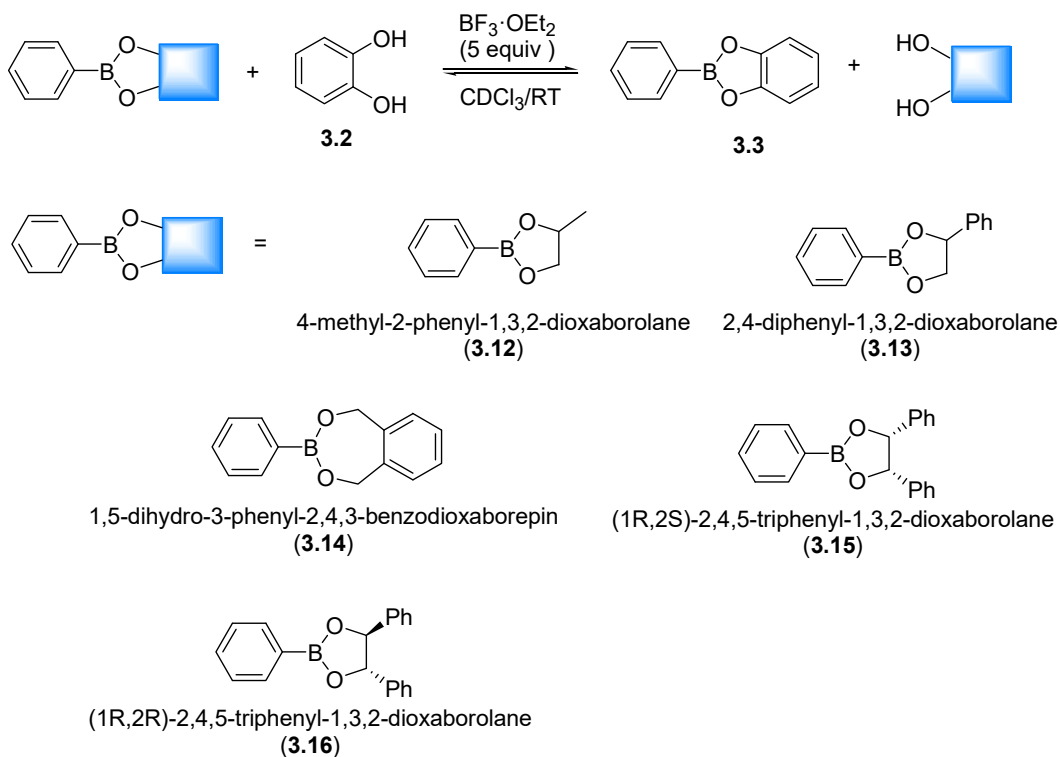
Figure 41. Reactions of boronate esters **3.12**, **3.13**, and **3.14** with catechol **3.2** in the

presence of BF$_3$·OEt$_2$.
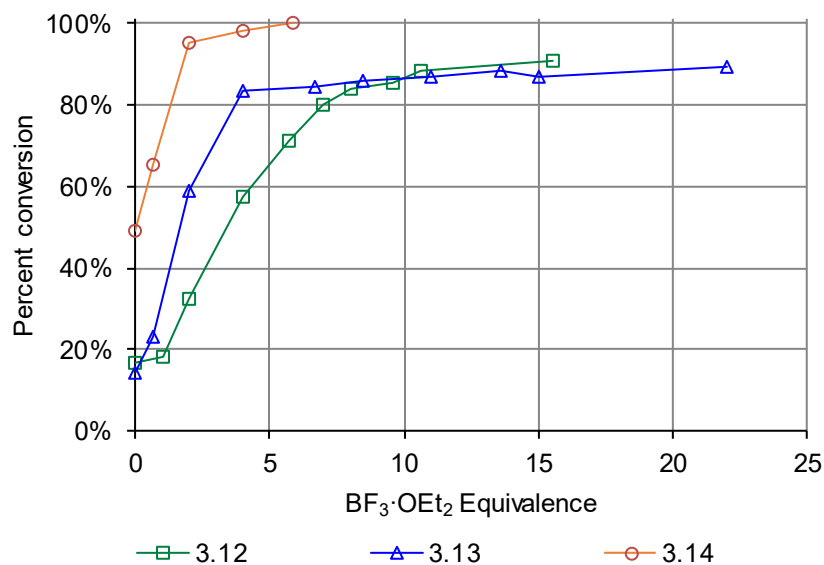
Figure 42. Transesterification of boronate esters **3.12**, **3.13**, and **3.14** with catechol **3.2** in

the presence of varying amounts of BF$_3$·OEt$_2$.

Without BF$_3$·OEt$_2$, there was only about 17% and 15% transesterification of esters **3.12** and **3.13**, respectively. In contrast, 49% transesterification of ester **3.14** with catechol was observed. This reflects the fact that esters **3.14** and **3.3** have similar stabilities. With the higher equivalents of BF$_3$·OEt$_2$, all the esters showed an increase in the transesterification with diol **3.2**. With 5 equiv of BF$_3$·OEt$_2$ there was 100% conversion of ester **3.14** into ester **3.3**. However, the maximum attainable transesterification of esters **3.12** and **3.13** were about 91% and 87%, respectively.

To avoid the effect of residual water from the *in situ* synthesis of boronate ester starting materials, the above described transesterification reactions were carried out with pre-synthesized boronate esters (see chapter II section 3). Therefore, the boronate esters were added to an NMR tube with catechol **3.2**, CDCl$_3$, and 5 equiv of BF$_3$·OEt$_2$ (Figure 43). This study also included esters **3.15** and **3.16**. Table 2 shows the summary of the results.
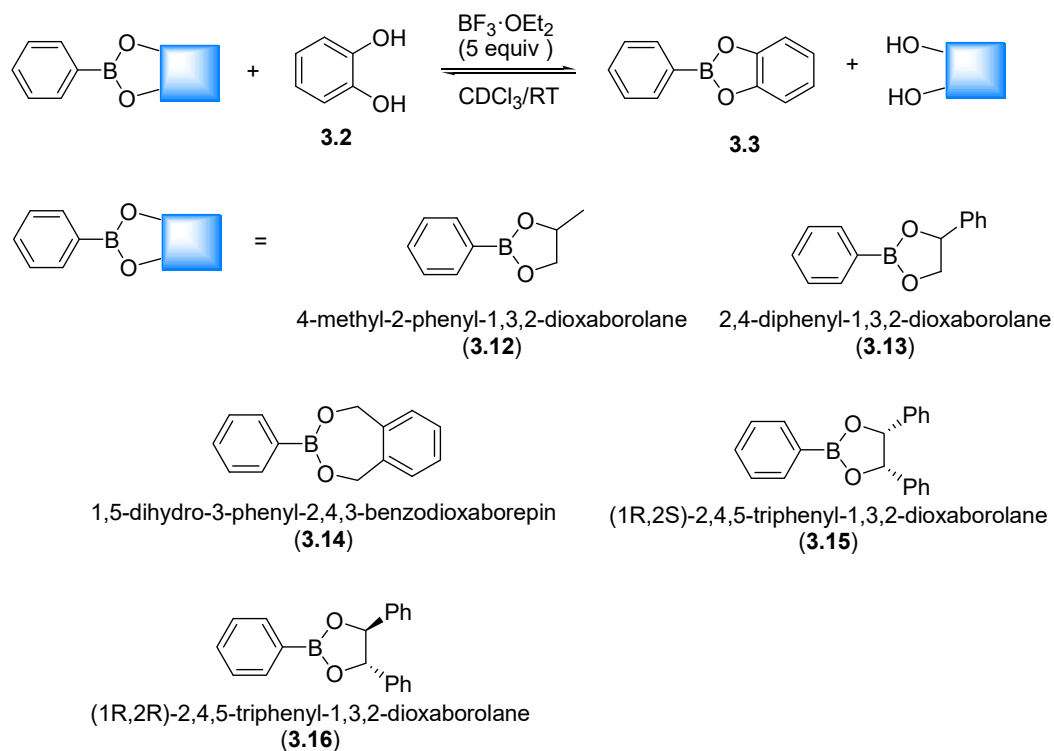
Figure 43. The reaction of different boronate esters **3.12**-**3.16** with catechol **3.2** in the presence of BF$_3$·OEt$_2$.

Table 2

Transesterification of different dioxaboroles with catechol

Ester	% Transesterification		Time (h)
	Without BF$_3$·OEt$_2$	With 5 equiv BF$_3$·OEt$_2$	
3.9	27%	90%	0.1
3.12	16%	83%	0.1
3.13	19%	92%	0.1

| Ester | % Transesterification | | Time (h) |
	Without BF$_3$·OEt$_2$	With 5 equiv BF$_3$·OEt$_2$	
3.14	49%	100%	0.1
3.15	0%	98%	3
3.16	5%	85%	11

Without BF$_3$·OEt$_2$, all esters underwent varying amounts of transesterification. In the presence of BF$_3$·OEt$_2$, all boronate esters showed an improvement in transesterification. The reaction of boronate esters **3.9**, **3.12**, **3.13**, and **3.14** reached equilibrium effectively instantaneously. On the other hand, esters **3.15** and **3.16** took 3 h and 11 h to reach equilibrium, respectively. At 0.1 h, there was only 66% and 45% transesterification of esters **3.15** and **3.16**, respectively. These results indicate that **3.16** is more stable than ester **3.15**, as well as the other esters studied. An additional observation from this study was that the co-product hydrobenzoins undergo a pinacol-type rearrangement in the presence of BF$_3$·OEt$_2$ (see chapter IV for further evidence of this rearrangement).

To investigate the effect of substituents on the phenyl ring, the transesterification of different substituted pinacol boronate esters with catechol was studied in the presence of 5 equiv of BF$_3$·OEt$_2$ (Figure 44). The reaction progress was monitored by ^{1}H NMR.
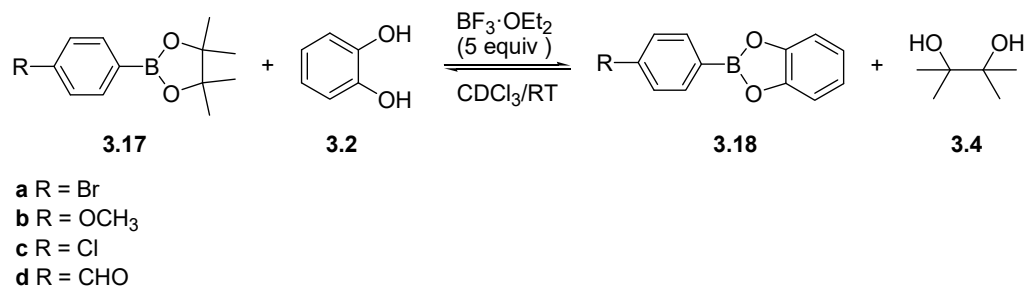
Figure 44. The reaction of different substituted pinacol boronate esters with catechol in the presence of BF$_3$·OEt$_2$.

Boronate esters **3.17a** and **3.17b** were synthesized *in situ* and separately by the condensation reaction between relevant phenylboronic acid and pinacol (**3.4**) (see chapter II), whereas esters **3.17c** and **3.17d** were purchased from commercial sources

All boronate esters used for this study underwent 100% transesterification with catechol in the presence of 5 equiv of BF$_3$·OEt$_2$. Bromo and methoxy pinacol boronate esters **3.17a** and **3.17b** showed slower transesterification with the separately synthesized pinacol esters than *in situ* synthesized pinacol esters. The lower rate of transesterification of esters **3.17c** and **3.17d** may be due to the difference in water content in the reaction medium. Therefore, we assumed water, formed from the condensation reaction between phenylboronic acid and pinacol, may increase the rate of the BF$_3$·OEt$_2$-facilitated transesterification. To confirm this idea, pre-synthesized boronate esters **3.17a** and **3.17b** were dried under vacuum before subjecting them to transesterification with **3.2**. Boronate ester **3.17b** took 47 h to give 100% transesterification with 5 equiv BF$_3$·OEt$_2$. Wherein, ester **3.17a** gave only 76% transesterification with 5 equiv BF$_3$·OEt$_2$ after 23 h of the reaction. The results of this study are summarized Table 3.

Table 3

*Summary of the transesterification of esters **3.1** and **3.17** with catechol*

Ester	% Transesterification		Time (h)
	Without BF$_3\cdot$OEt$_2$	With 5 equiv BF$_3\cdot$OEt$_2$	
3.1[*]	5%	100%	0.3
3.17a[‡]	0%	100%	14
3.17a[*]	0%	76%	23
3.17b[‡]	0%	100%	14
3.17b[*]	0%	100%	47
3.17c[†]	0%	100%	48
3.17[†]	0%	100%	51

Note. [*]*pre-synthesized,* [‡]*Synthesized in situ,* [†]*commercially available*

3.3.3 Preparative scale transesterification

Next, the preparative scale transesterification of ester **3.1** with diol **3.2** in the presence of BF$_3\cdot$OEt$_2$ was investigated (Figure 45). The transesterification of ester **3.1** was carried out with an equivalent of catechol **3.2** in the presence of 5 equiv of BF$_3\cdot$OEt$_2$ in chloroform. After 24 h the solvent was removed under reduced pressure and complete conversion to ester **3.3** and pinacolone was observed using ^{1}H NMR spectroscopy (Figure 46). The sample was then heated under vacuum for 1 h. Subsequent NMR analysis

revealed that these conditions were sufficient enough to remove the pinacolone and allow

the isolation of ester **3.3**.
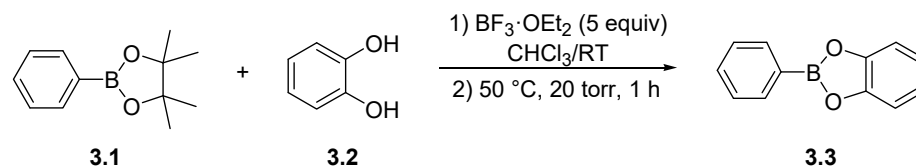
Figure 45. The reaction of ester **3.1** and catechol **3.2** in the presence of BF$_3$·OEt$_2$ in

chloroform.
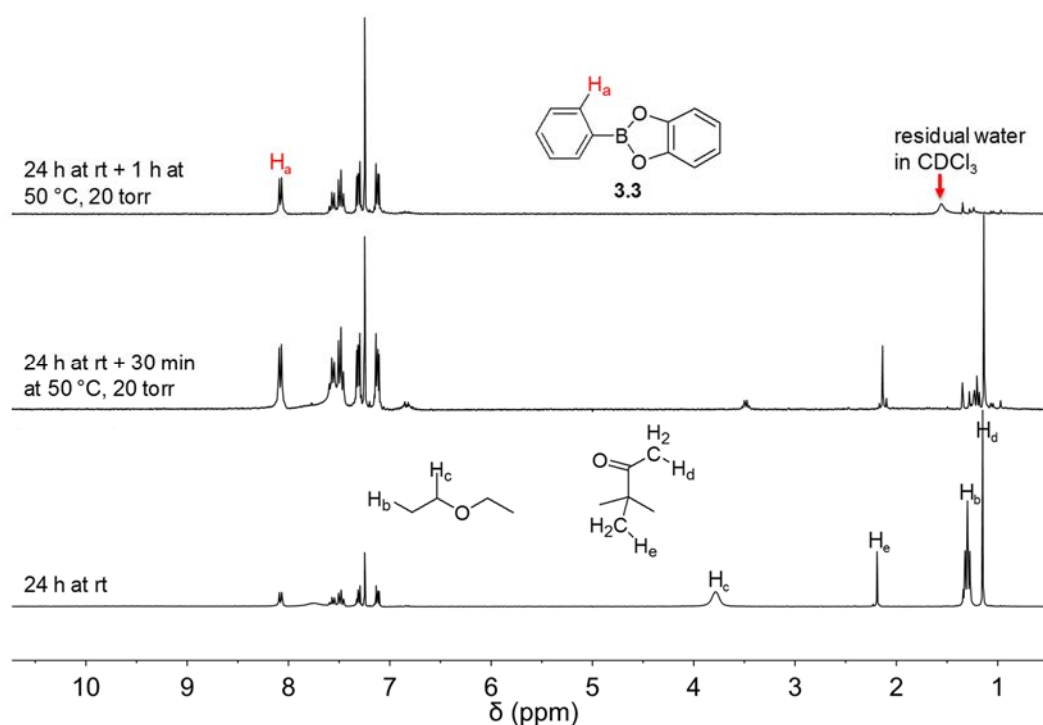
Figure 46. ^{1}H NMR spectra (in CDCl$_3$) of the transesterification of ester **3.1** and catechol

3.2 in the presence of 5 equiv of BF$_3$·OEt$_2$ in chloroform.

3.3.4 Transesterification of bis-boronate esters

Ester **3.1** and commercially available pentaerythritol **3.19** (2:1 mol ratio) were

mixed in a vial with toluene and BF$_3$·OEt$_2$ (10 equiv) (Figure 47). Tetraol **3.19** is

sparingly soluble in toluene. However, all starting materials dissolved after 3 days. At

that point, the toluene was removed under reduced pressure at 45 °C and NMR analysis

in CDCl3 confirmed 100% transesterification of ester **3.1** into ester **3.20** (Figure 48).
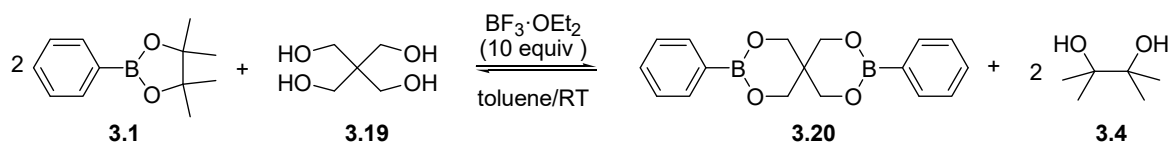
Figure 47. The reaction of ester **3.1** and tetraol **3.19** in the presence of BF3·OEt2.
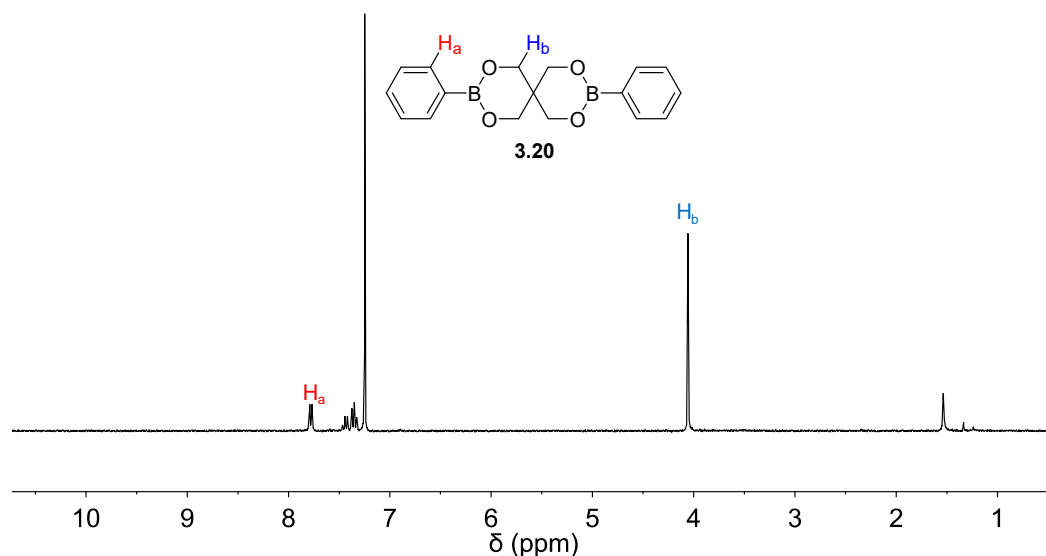
Figure 48. ^{1}H NMR spectrum of the transesterification product **3.20**.

The same reaction was examined in chloroform, which resulted in the same

product. However, deborylation of ester **3.1** occurs if the reaction mixture is heated or if

the reaction time is extended (Figure 49).
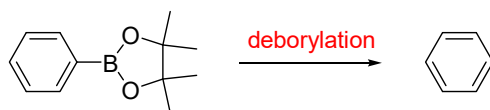
Figure 49. Deborylation of boronate ester **3.1**.

The transesterification of ester **3.1** pentaerythritol **3.19** showed similar behavior to

that of neopentyl glycol, with ester **3.1** in the presence of BF3·OEt2 in our previous

studies, where we found that neopentyl glycol gives 100% conversion of ester **3.1** to the

neopentyl glycol boronate ester with 5 equiv of BF$_3$·OEt$_2$.

Then, bis(dioxaborole) **3.21** and diol **3.2** (2 equiv) were mixed in CDCl$_3$ in an

NMR tube (Figure 50). There was no evidence of transesterification even after 24 h.

Then, BF$_3$·OEt$_2$ (10 equiv) was added and the sample was analyzed periodically (Figure

51). With time, crystals formed in the NMR tube and the NMR signals decreased in

intensity (Figure 52).
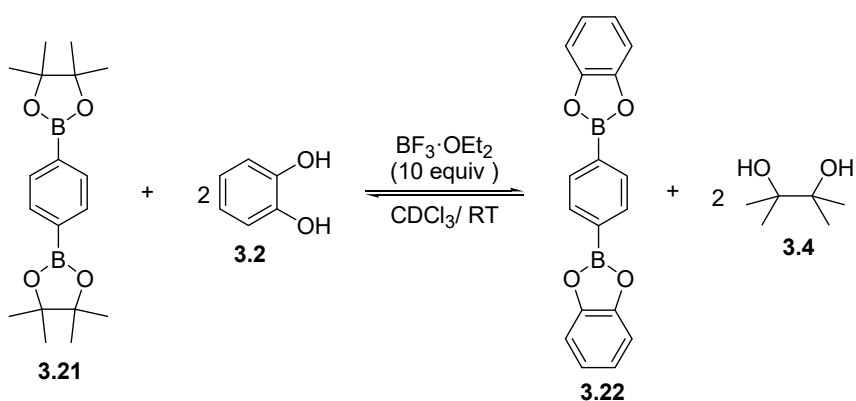
Figure 50. The reaction of ester **3.21** and catechol **3.2** in the presence of BF$_3$·OEt$_2$.
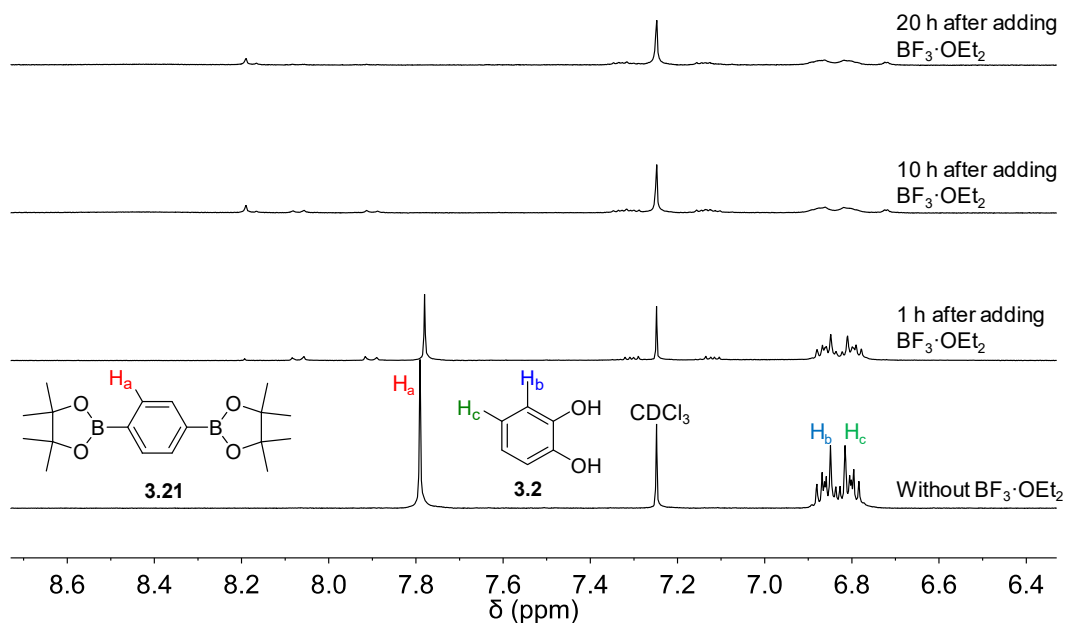
Figure 51. The aromatic region of the ^{1}H NMR spectrum of the reaction between ester **3.21** and catechol **3.2** in the presence of BF$_3$·OEt$_2$ in CDCl$_3$.
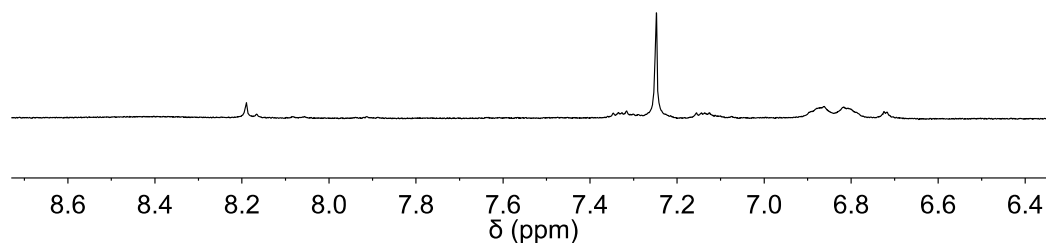
Figure 52. The zoomed in aromatic region of the ^{1}H NMR spectrum after 20 h of the reaction between ester **3.21** and catechol **3.2** in the presence of BF$_3$·OEt$_2$ in CDCl$_3$.

After 20 h of reaction time, the crystals were isolated and analyzed separately using ^{1}H NMR in CDCl$_3$. According to the ^{1}H NMR spectrum, the formation of bis-catechol ester **3.22** was confirmed (Figure 53).
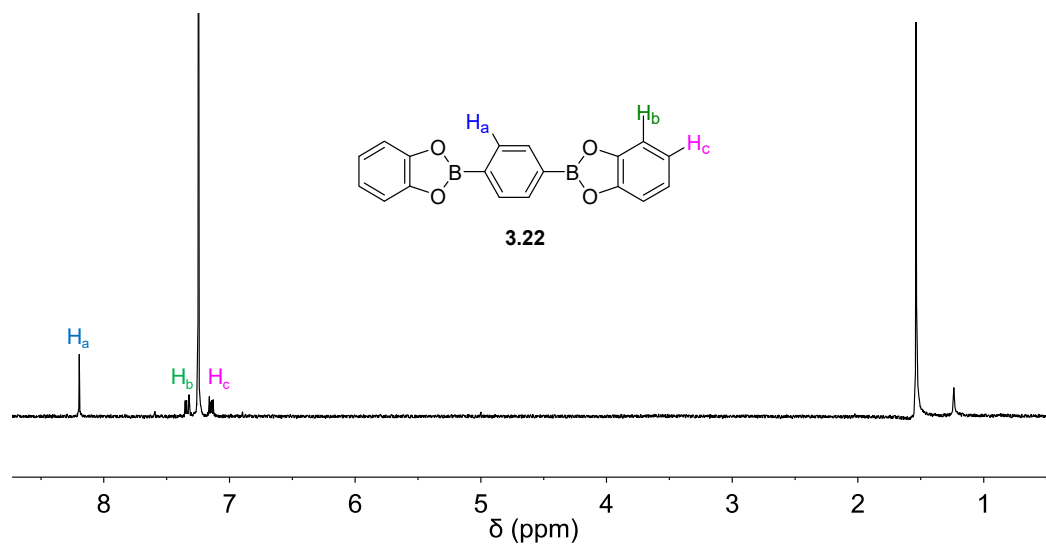
Figure 53. ¹H NMR spectrum of isolated bis-catechol ester **3.22** in CDCl₃.

Ester **3.23** and catechol **3.2** (2 equiv) were added to an NMR tube with BF₃·OEt₂ (10 equiv) and CDCl₃ (Figure 54). Initially, there was no evidence of transesterification between ester **3.23** and catechol **3.2**. However, after adding BF₃·OEt₂ (10 equiv), crystals formed with time in the NMR tube and the NMR signals decreased in intensity (Figure 55).
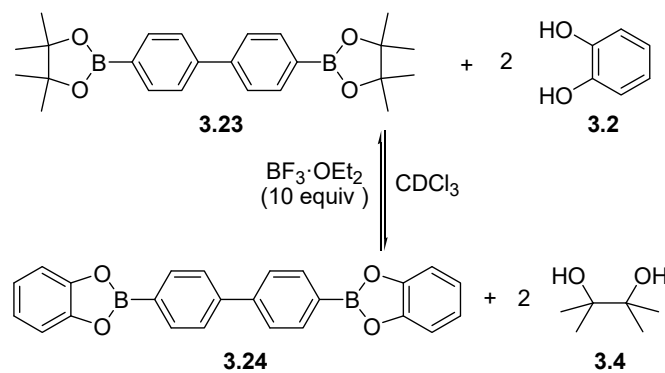
Figure 54. Reaction of ester **3.23** and catechol **3.2** in the presence of BF₃·OEt₂.
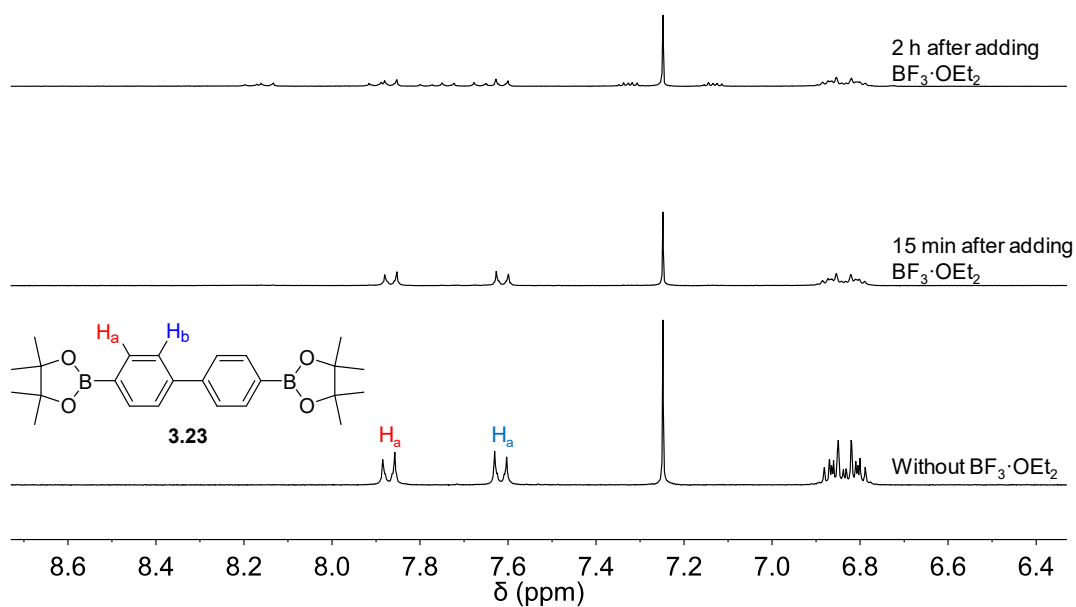
Figure 55. The aromatic region of the ¹H NMR spectrum of the reaction between ester

3.23 and catechol **3.2** in the presence of BF₃·OEt₂.

Then, after 24 h the crystals (mp: 299 °C -300 °C) were isolated and analyzed

separately by ¹H NMR in CDCl₃. Formation of bis-catechol ester **3.24** was supported by

the signals observed in the NMR spectrum (Figure 56).
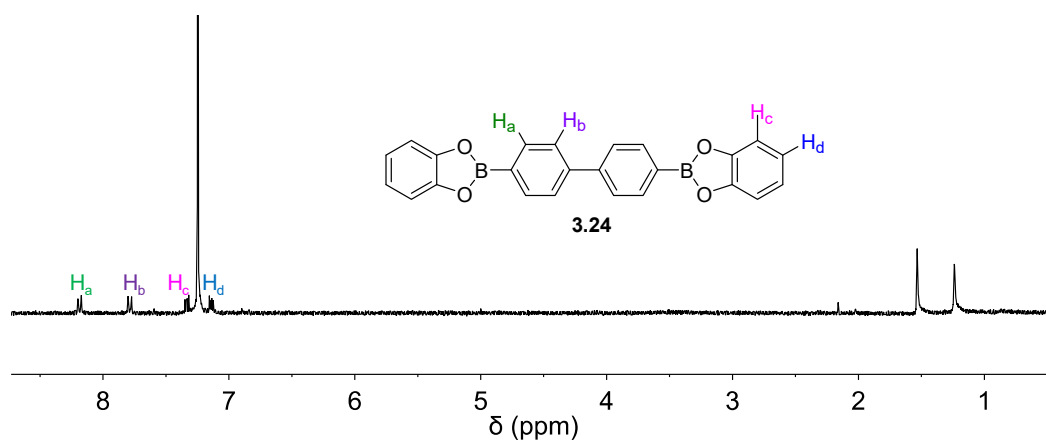
Figure 56. ¹H NMR spectrum of isolated bis-catechol ester **3.24** in CDCl₃.

As a final example of bis-pinacol ester transesterification, commercially available fluorene-based ester **3.25** and catechol **3.2** (2 equiv) were mixed in CDCl$_3$ in an NMR tube (Figure 57). The reaction progress was monitored by NMR spectroscopy and there was no evidence of transesterification. However, 53 h after adding 10 equiv of BF$_3$·OEt$_2$ 100% transesterification was observed (Figure 58).
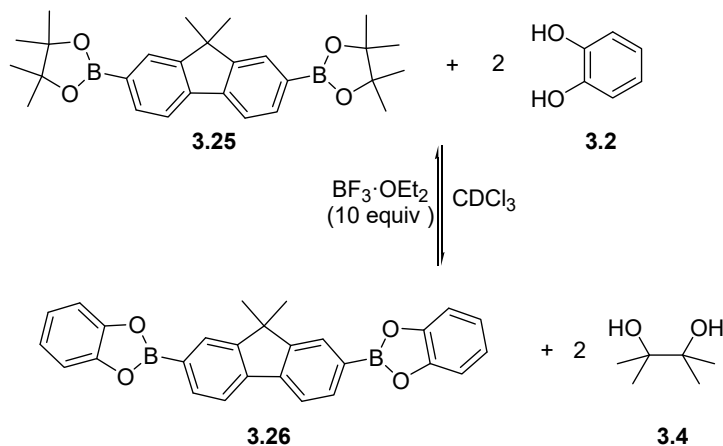
Figure 57. The reaction of fluorene-based ester **3.25** and catechol **3.2** in the presence of BF$_3$·OEt$_2$.
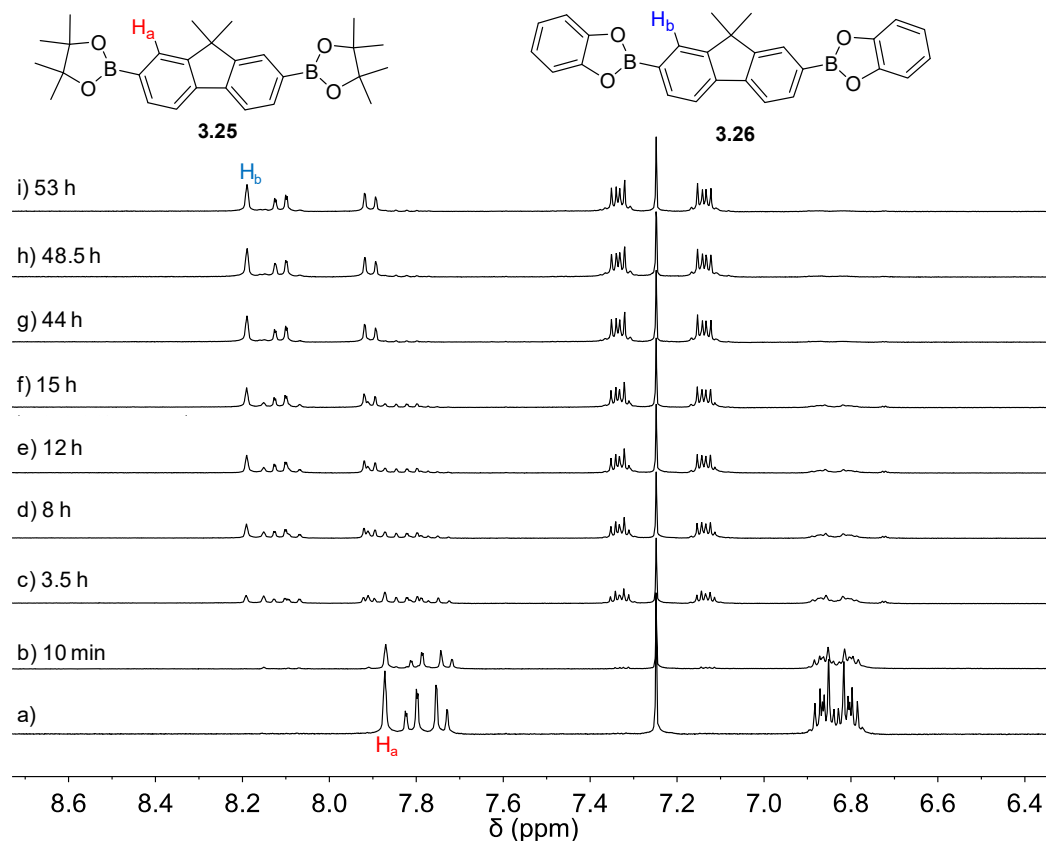
Figure 58. The aromatic region of the ^{1}H NMR spectrum of the reaction between fluorene-based ester **3.25** and catechol **3.2** a) without BF$_3$·OEt$_2$, b-i) with BF$_3$·OEt$_2$.

3.3.5 Transesterification with benzene tetraol

The transesterification of ester **3.1** with tetrahydroxybenzene **3.27** was studied in the presence of BF$_3$·OEt$_2$ (Figure 59). However, this transesterification was partially successful with only about 40% transesterification. The major concern with this reaction was to find a better solvent. Tetraol **3.27** is sparingly soluble in most organic solvents. The transesterification reaction was carried out in toluene. After three days of adding BF$_3$·OEt$_2$ all the starting materials dissolved. At that point, the toluene was removed under reduced pressure at 45 °C and an NMR spectrum was obtained in CDCl$_3$ (Figure 60).
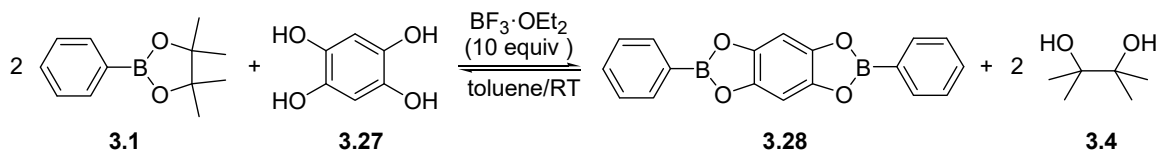
Figure 59. Reactions of ester **3.1** and tetraol **3.27** in toluene in the presence of BF$_3$·OEt$_2$.
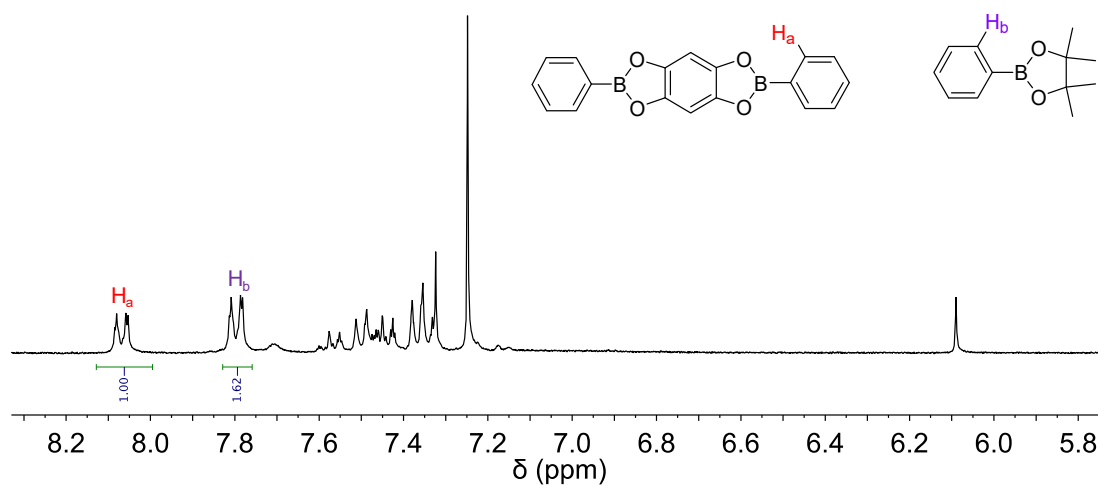
Figure 60. ^{1}H NMR spectrum of ester **3.1** and tetraol **3.27** in the presence of BF$_3$·OEt$_2$ in toluene.

The transesterification of ester **3.1** with tetraol **3.27** was also studied in CDCl$_3$ (Figure 61). However, it took five days to dissolve all the starting materials and eventually deborylation of ester **3.1** was observed (Figure 62).
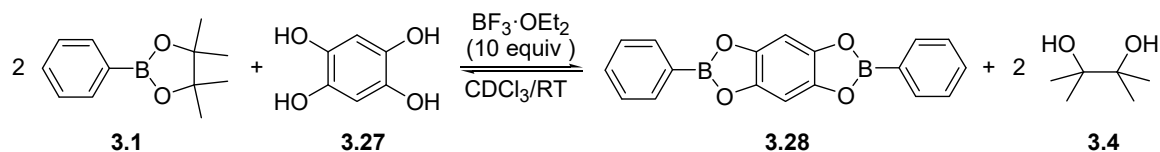
Figure 61. Reaction of ester **3.1** and tetraol **3.27** in CDCl$_3$ in the presence of BF$_3$·OEt$_2$.
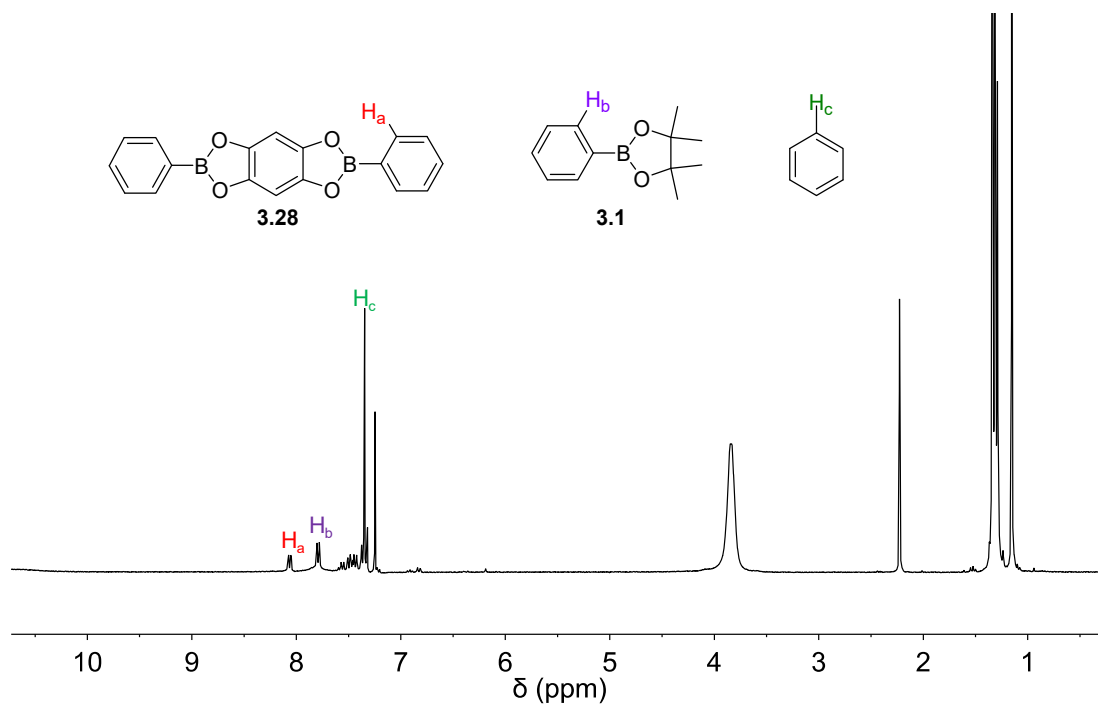
Figure 62. ^{1}H NMR spectrum of ester **3.1** and tetraol **3.27** in the presence of BF$_3$·OEt$_2$ in CDCl$_3$.

3.3.6 Attempted esterification with HHTP

Then, we tried to use the effect of BF$_3$·OEt$_2$ on the formation of tris boronate esters. For that, the transesterification reaction between ester **3.1** and hexaol **3.29** was carried out in order to attempt to synthesize tris boronate ester **3.30**. The hexaol **3.29** is sparingly soluble in most organic solvents. First, ester **3.1** and hexaol **3.29** were subjected to reaction in chloroform (Figure 63). However, even after adding 15 equiv of BF$_3$·OEt$_2$, hexaol **3.29** did not dissolve.
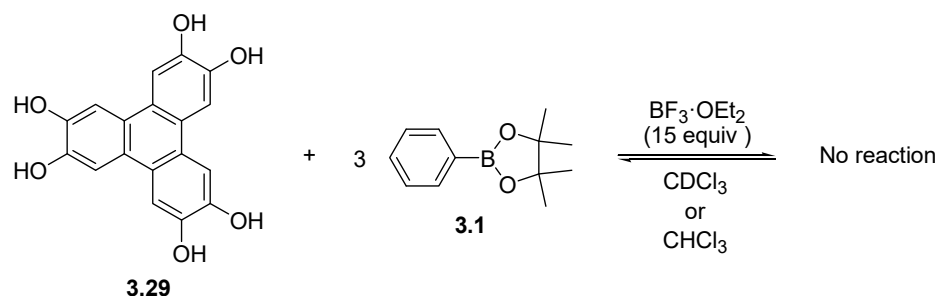
Figure 63. Reaction of ester **3.1** and hexaol **3.29** in the presence of BF$_3$·OEt$_2$ in CDCl$_3$ or

CHCl$_3$.

Then, the reaction was carried out under similar conditions which were used in

the synthesis of COF-5 and COF-10.[39] Instead of mesitylene/dichloroethane solvent

mixture used by Dichtel and coworkers, xylene/dichloroethane was used (Figure 64). The

reaction mixture was heated at 50 °C for 6 days. Although the starting materials dissolved

after 6 days, it did not give the desired product. The harsh conditions may cause

deborylation of ester **3.1**.
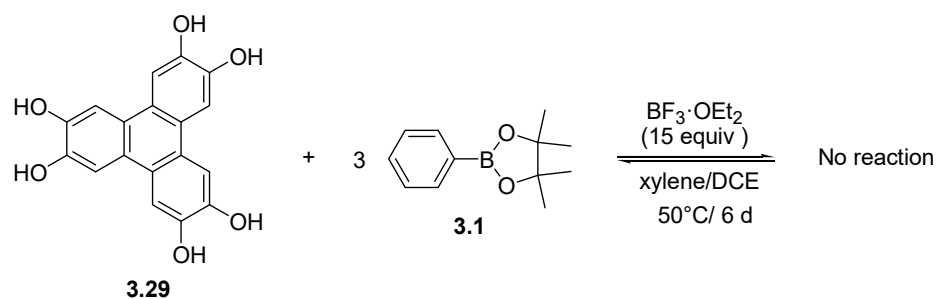
Figure 64. Reaction of **3.1** and **3.29** in the presence of BF$_3$·OEt$_2$.

3.4 Conclusions

Diol **3.8**, which forms during the transesterification of ester **3.9** and catechol **3.2** is

removed by BF$_3$·OEt$_2$, which is likely due to coordination. This causes the forward

reaction to increase generating more of the catechol ester. According to the

transesterification of boronate esters **3.12-3.14**, 1,2-propane diol, 1-phenyl-1,2-ethane

diol, and 1,2-benzenedimethanol coordinate with BF$_3$·OEt$_2$, which causes an increase in

the transesterification of boronate esters **3.12-3.14** with catechol **3.2**. In addition, the

transesterification of hydrobenzoins (**3.15** and **3.16**) seems to be facilitated by

coordination followed by rearrangement.

Boron trifluoride also facilitated transesterification reactions of substituted

pinacol boronate esters **3.17a-3.17d** with catechol **3.2**. The results indicate that there is

little effect from substituent groups on the activity of BF$_3$·OEt$_2$. However, the amount of

water present in the reaction mixture influences the rate of transesterification.

Boronate ester **3.3**, which formed from the transesterification of ester **3.1** and

catechol **3.2** in the presence of BF$_3$·OEt$_2$, was successfully isolated. Finally, BF$_3$·OEt$_2$

was successfully used for the synthesis of several bis(dioxaborole)s. However, the

complete formation of bis(dioxaborole) **3.28** has yet to be achieved.

3.5 Experimental

3.5.1 The effect of boron trifluoride on the transesterification of boronate esters.

Diol **3.8** was commercially available and it was dried with Na$_2$SO$_4$. Diol **3.8** (4

mL) was dried using Na$_2$SO$_4$ (2 g) for 6 h.

The transesterification reactions of ester **3.9** with catechol **3.2** were carried out in

NMR tubes using CDCl$_3$ as the solvent. An equimolar mixture of boronate ester **3.9** (8.6

mg, 0.058 mmol, 1 equiv) and catechol **3.2** (6.4 mg, 0.058 mmol, 1 equiv) in CDCl$_3$ (0.7

mL) was subjected to different equivalents (1 drop: 1 equiv, 3 drops: 3 equiv, 5 drops: 5

equiv, 10 drops: 10 equiv) of BF$_3$·OEt$_2$. The equivalents of BF$_3$·OEt$_2$ were determined

based on the ^{1}H-NMR integrations of the relevant proton signals (Table 4).

The transesterification reaction of esters **3.12**, **3.13**, and **3.14** with catechol **3.2**

were carried out in NMR tubes using CDCl$_3$ as the solvent. An equimolar mixture of

boronate esters (8.6 mg, 0.058 mmol, 1 equiv) and catechol **3.2** (6.4 mg, 0.058 mmol, 1

equiv) in CDCl$_3$ (0.7 mL) was subjected to reactions using different equivalents (1 drop:

1 equiv, 3 drops: 3 equiv, 5 drops: 5 equiv, 10 drops: 10 equiv) of BF$_3$·OEt$_2$ as the

catalyst. The equivalents of BF$_3$·OEt$_2$ were determined based on the ^{1}H-NMR

integrations of the relevant proton signals (Table 4).

The transesterification reaction of esters **3.12**, **3.13**, **3.14**, **3.15**, and **3.16** with

catechol **3.2** were carried out in NMR tubes using CDCl$_3$ as the solvent. An equimolar

mixture of boronate esters (8.6 mg, 0.058 mmol, 1 equiv) and catechol **3.2** (6.4 mg, 0.058

mmol, 1 equiv) in CDCl$_3$ (0.7 mL) was subjected to reactions. BF$_3$·OEt$_2$ (5 drops, 0.29

mmol, 5 equiv) was added and reaction progress was monitored by ^{1}H NMR

spectroscopy. The percent transesterification was determined based on the ^{1}H NMR

integrations of the relevant proton signals (Table 4).
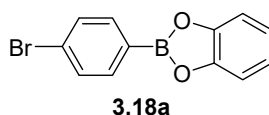
3.18a

2-(4-Bromophenyl)-1,3,2-benzodioxaborole (3.18a). An equimolar amount of

boronate ester **3.17a** (3.3 mg, 0.0116 mmol, 1 equiv) and diol **3.2** (1.3 mg, 0.0116 mmol,

1 equiv) were mixed in NMR tube in CDCl$_3$ (0.7 mL). BF$_3$·OEt$_2$ (1 drop, 0.0580 mmol, 5

equiv) was added and reaction progress was monitored by ^{1}H NMR spectroscopy. The

percent transesterification was determined based on the ^{1}H NMR integrations of the

relevant proton signals (Table 4). ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.93 (d, 2H), 7.63 (d, 2H), 7.31-7.27 (m, 4H), 7.13-7.10 (m, 4H).
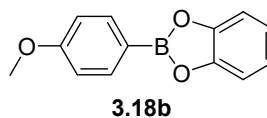
3.18b

2-(4-Methoxyphenyl)-1,3,2-benzodioxaborole (3.18b). An equimolar amount of boronate ester **3.17b** (2.7 mg, 0.0116 mmol, 1 equiv) and diol **3.2** (1.3 mg, 0.0116 mmol, 1 equiv) were mixed in NMR tube in CDCl$_3$ (0.7 mL). BF$_3$·OEt$_2$ (1 drop, 0.0580 mmol, 5 equiv) was added and reaction progress was monitored by ^{1}H NMR spectroscopy. The percent transesterification was determined based on the ^{1}H NMR integrations of the relevant proton signals (Table 4). ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 8.04 (d, 2H), 7.02 (d, 2H), 7.11-7.09 (m, 4H), 7.29-7.28 (m, 4H), 3.87 (s, 3H).
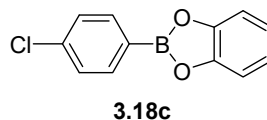
3.18c

2-(4-Chlorophenyl)-1,3,2-benzodioxaborole (3.18c). An equimolar amount of boronate ester **3.17c** (2.8 mg, 0.0116 mmol, 1 equiv) and diol **3.2** (1.3 mg, 0.0116 mmol, 1 equiv) were mixed in NMR tube in CDCl$_3$ (0.7 mL). BF$_3$·OEt$_2$ (1 drop, 0.0580 mmol, 5 equiv) was added and reaction progress was monitored by ^{1}H NMR spectroscopy. The percent transesterification was determined based on the ^{1}H NMR integrations of the relevant proton signals (Table 4). ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 8.04 (d, 2H), 7.48 (d, 2H), 7.32-7.28 (m, 4H), 7.14-7.11 (m, 4H).
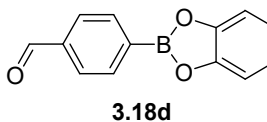
3.18d

4-(1,3,2-Benzodioxaborol-2-yl)-benzaldehyde (3.18d). An equimolar amount of boronate ester **3.17d** (2.7 mg, 0.0116 mmol, 1 equiv) and diol **3.2** (1.3 mg, 0.0116 mmol, 1 equiv) were mixed in NMR tube in CDCl$_3$ (0.7 mL). BF$_3$·OEt$_2$ (1 drop, 0.0580 mmol, 5 equiv) was added and reaction progress was monitored by ^{1}H NMR spectroscopy. The percent transesterification was determined based on the ^{1}H NMR integrations of the relevant proton signals (Table 4). ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 10.09 (s, 1H), 8.29 (d, 2H), 8.04 (d, 2H), 7.36-7.32 (m, 4H), 7.17-7.14 (m, 4H).

Table 4

^{1}H-NMR signals used to determine the percent transesterification

Reaction	starting material	product
3.1 + 3.2	δ 7.80 (**3.1**)	δ 8.10 (**3.3**)
3.9 + 3.2	δ 7.80 (**3.9**)	δ 8.10 (**3.3**)
3.12 + 3.2	δ 7.79 (**3.12**)	δ 8.10 (**3.3**)
3.13 + 3.2	δ 7.90 (**3.13**)	δ 8.10 (**3.3**)
3.14 + 3.2	δ 7.76 (**3.14**)	δ 8.10 (**3.3**)
3.15 + 3.2	δ 8.00 (**3.15**)	δ 8.10 (**3.3**)
3.16 + 3.2	δ 7.99 (**3.16**)	δ 8.10 (**3.3**)
3.17a + 3.2	δ 7.60 (**3.17a**)	δ 7.90 (**3.18a**)
3.17b + 3.2	δ 7.75 (**3.17b**)	δ 8.00 (**3.18b**)
3.17c + 3.2	δ 7.70 (**3.17c**)	δ 8.00 (**3.18c**)

Reaction	starting material	product
3.17d + 3.2	δ 7.96 (**3.17d**)	δ 8.30 (**3.18d**)

3.5.2 Isolation of dioxaborole 3.3

Ester **3.1** (0.1 g, 0.49 mmol, 1 equiv) and diol **3.2** (0.054 g, 0.49 mmol, 1 equiv) were mixed in CHCl$_3$ (15 mL) in a vial. Chloroform was washed with distilled water (3×30 mL) before using it for the reaction. Then, BF$_3$·OEt$_2$ (0.3 mL, 2.45 mmol, 5 equiv) was added and the reaction mixture was stirred for 24 h at room temperature. The product was concentrated by removing the solvent under reduced pressure. The collected product was heated at 50 ˚C under vacuum (20 torr) for 1 h.

3.5.3 Effect of BF$_3$·OEt$_2$ on the oligo(dioxaborole) formation

The reaction progress was monitored by ^{1}H NMR spectroscopy. The percent transesterification was determined based on the ^{1}H NMR integrations of the relevant proton signals (Table 5).

Table 5

^{1}H-NMR signals used to determine the percent transesterification

Reaction	starting material	product
3.1 + 3.19	δ 7.80 ppm (**3.1**)	δ 7.79 ppm (**3.20**)
3.1 + 3.21	δ 7.79 ppm (**3.21**)	δ 8.19 ppm (**3.22**)
3.1 + 3.23	δ 7.88 ppm (**3.23**)	δ 8.18 ppm (**3.24**)
3.1 + 3.25	δ 7.90 ppm (**3.25**)	δ 8.20 ppm (**3.26**)

Reaction	starting material	product
3.1 + **3.27**	δ 7.90 ppm (**3.1**)	δ 8.20 ppm (**3.28**)

3.20
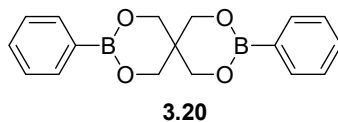
3,9-Bis(phenyl)-2,4,8,10-tetraoxa-3,9-diboraspiro[5.5]undecane (3.20). Tetraol

3.19 (1.6 mg, 0.0116 mmol, 1 equiv) and ester **3.1** (4.7 mg, 0.0232 mmol, 2 equiv) were

mixed in toluene-d_8 (0.7 mL) in an NMR tube. Then, BF$_3$·OEt$_2$ (2 drops, 0.1160 mmol,

10 equiv) was added. It took 3 days to dissolve all the starting materials. After 3 days of

the reaction, ^{1}H NMR was obtained. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 7.79 (d, 4H), 7.44-

7.35 (m, 6H), 4.06 (s, 8H).

3.22
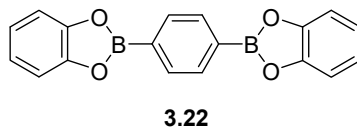
2,2'-(1,4-Phenylene)bis-1,3,2-benzodioxaborole (3.22). Ester **3.21** (3.8 mg,

0.0116 mmol, 1 equiv) and catechol **3.2** (2.5 mg, 0.0232 mmol, 2 equiv) were mixed in

CDCl$_3$ (0.7 mL) in an NMR tube. Then, BF$_3$·OEt$_2$ (2 drops, 0.1160 mmol, 10 equiv) was

added and the reaction progress was monitored by ^{1}H NMR spectroscopy. ^{1}H-NMR

(CDCl$_3$, 300 MHz) δ: 8.20 (s, 4H), 7.35-7.33 (m, 4H), 7.16-7.13 (m, 4H).

3.24
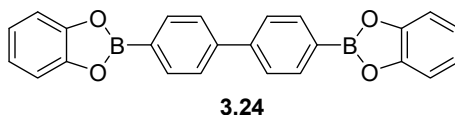
2,2'-[1,1'-Biphenyl]-4,4'-diylbis-1,3,2-benzodioxaborole (3.24). Ester **3.23** (3.8

mg, 0.0058 mmol, 1 equiv) and catechol **3.2** (1.3 mg, 0.0116 mmol, 2 equiv) were mixed

in CDCl$_3$ (0.7 mL) in an NMR tube. Then, BF$_3$·OEt$_2$ (1 drops, 0.0580 mmol, 10 equiv) was added and the reaction progress was monitored by ^{1}H NMR spectroscopy. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 8.20 (d, 4H), 7.80 (d, 4H), 7.35-7.32 (m, 4H), 7.16-7.13 (m, 4H).

3.26
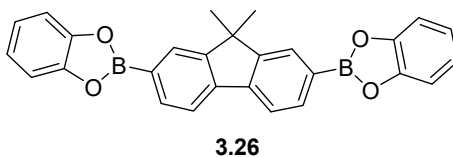
*2,2'-(9,9-Dimethyl-9H-fluorene-2,7-diyl)bis[1,3,2-benzodioxaborole] (**3.26**).*

Ester **3.25** (5.2 mg, 0.0116 mmol, 1 equiv) and catechol **3.2** (2.5 mg, 0.0232 mmol, 2 equiv) were mixed in CDCl$_3$ (0.7 mL) in an NMR tube. Then, BF$_3$·OEt$_2$ (2 drops, 0.1160 mmol, 10 equiv) was added and the reaction progress was monitored by ^{1}H NMR spectroscopy. ^{1}H-NMR (CDCl$_3$, 300 MHz) δ: 8.19 (s, 2H), 8.12 (d, 2H), 7.92 (d, 2H), 7.35-7.32 (m, 4H), 7.15-7.12 (m, 4H).

3.28
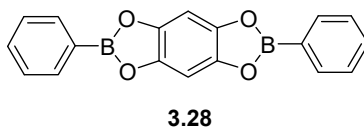
*2,6-Diphenyl-benzo[1,2-d;4,5-d']bis[1,3,2]dioxaborole (**3.28**).* Tetraol **3.27** (1.6 mg, 0.0116 mmol, 1 equiv) and ester **3.1** (4.7 mg, 0.0232 mmol, 2 equiv) were mixed in toluene (3 mL) in a vial. Then, BF$_3$·OEt$_2$ (2 drops, 0.1160 mmol, 10 equiv) was added. After 3 days of the reaction, toluene was removed under reduced pressure (45 °C). ^{1}H NMR spectroscopy of the product was obtained in CDCl$_3$.

Tetraol **3.27** (1.6 mg, 0.0116 mmol, 1 equiv) and ester **3.1** (4.7 mg, 0.0232 mmol, 2 equiv) were mixed in CDCl$_3$ (0.7 mL) in an NMR tube. Then, BF$_3$·OEt$_2$ (2 drops, 0.1160 mmol, 10 equiv) was added and the ^{1}H NMR was obtained after 3 days.
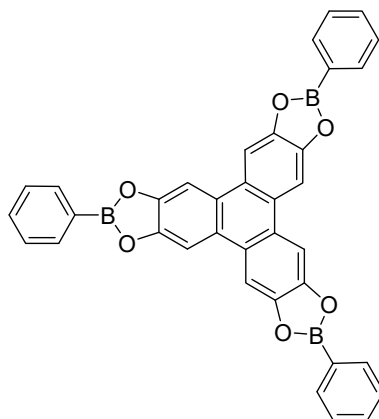
3.30

Attempted synthesis of 2,7,12-triphenyl-triphenyleno[2,3-d:6,7-d':10,11-d'']tris[1,3,2]dioxaborole (3.30). Hexaol **3.29** (3.8 mg, 0.0116 mmol, 1 equiv) and ester **3.1** (7.1 mg, 0.0348 mmol, 3 equiv) were mixed in CHCl₃ (3 mL) in a vial. Then, BF₃·OEt₂ (3 drops, 0.1740 mmol, 15 equiv) was added.

Hexaol **3.29** (1.6 mg, 0.0116 mmol, 1 equiv) and ester **3.1** (4.7 mg, 0.0232 mmol, 3 equiv) were mixed in CDCl₃ (0.7 mL) in an NMR tube. Then, BF₃·OEt₂ (3 drops, 0.1740 mmol, 15 equiv) was added and the ¹H NMR was obtained after 3 days.

Hexaol **3.29** (3.8 mg, 0.0116 mmol, 1 equiv) and ester **3.1** (7.1 mg, 0.0348 mmol, 3 equiv) were mixed in xylene (1 mL) and dichloroethane (3 mL) solvent mixture in a vial. Then, BF₃·OEt₂ (3 drops, 0.1740 mmol, 15 equiv) was added. The reaction mixture was heated at 50 °C for 6 days.

CHAPTER IV

PINACOL REARRANGEMENT

4.1 Background

In chapter III we showed that the addition of $BF_3 \cdot OEt_2$ to transesterification

reactions facilitated conversion to the product esters. In some of those reactions the

subsequent rearrangement of pinacol caused a shift in equilibrium by removing pinacol

via the pinacol rearrangement. The pinacol rearrangement is an acid catalyzed

transformation which converts 1,2-diols to ketones (Figure 65). Here $BF_3 \cdot OEt_2$ acts as a

Lewis acid, which facilitates the rearrangement.[41]

R= alkyl or aryl
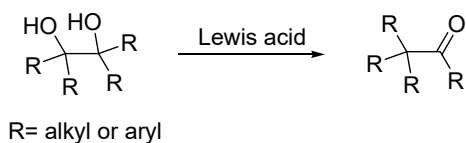
Figure 65. Acid catalyzed rearrangement reaction of 1,2-diols.

The rearrangement proceeds through a positively charged intermediate, which

undergoes a 1,2-alkyl shift. Mechanistically, the hydroxyl group gets protonated in the

presence of a Bronsted acid or coordinated by a Lewis acid. Next, a relatively stable

carbocation is formed after the removal of a water molecule. Then, a rearrangement takes

place as the alkyl group shifts to the positively charged carbon generating an even more

stable carbocation. Finally, a proton is removed to generate the pinacolone product

(Figure 66).
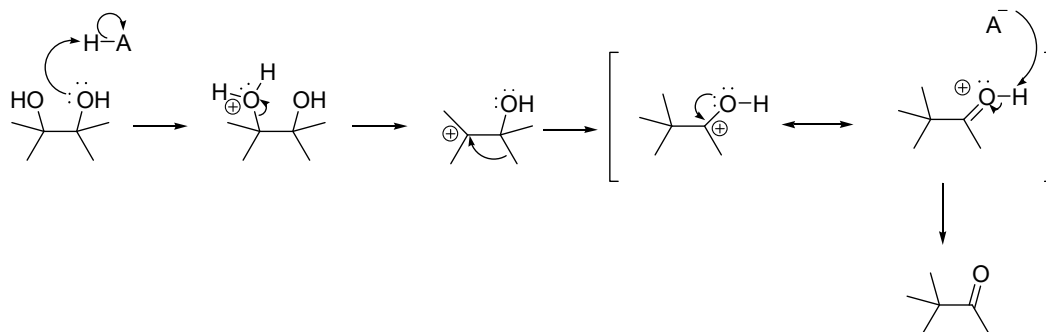
Figure 66. Mechanism of the Bronsted acid catalyzed pinacol rearrangement.

To date, many studies regarding the pinacol rearrangement have been reported using different acid catalysts or dehydrating agents. In 1988, Kakimoto and group investigated the pinacol rearrangement of various diols with polyphosphoric acid trimethylsilyl ester (PPSE) under mild conditions (80 °C).[42] They observed the formation of tetraphenylethylene oxide (**4.2**) in addition to benzpinacolone (**4.3**) during the rearrangement of benzpinacol (**4.1**) (Figure 67). However, at 150 °C benzpinacolone was the only product.
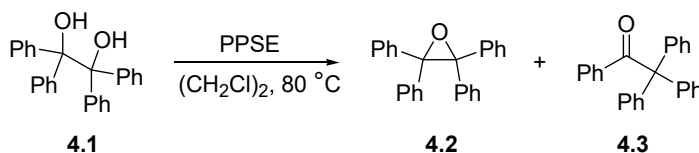
Figure 67. Benzpinacol rearrangement in the presence of PPSE.

Yamamoto and coworkers studied the benzpinacol rearrangement with 4-methylpyridine N-oxide SbCl$_5$ (1:1) complex (complex A) and pyridine N-oxide-SbCl$_5$ (1:1) (complex B).[43] They observed the formation of benzpinacolone along with a small amount of tetraphenylethylene oxide with complex A and B (Figure 68).
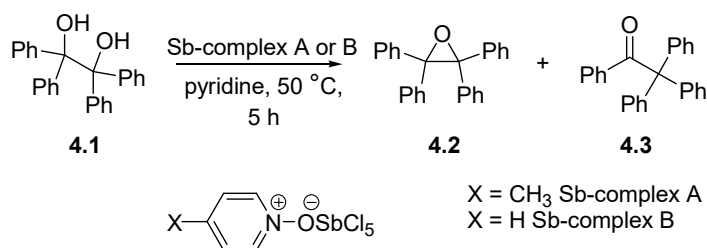
Figure 68. Benzpinacol rearrangement in the presence of complex A and B.

Robinson and coworkers used a dehydrating agent, diethoxytriphenylphosphoran (DTPP).[44] In their study, they experienced cis and trans epoxide formation of meso- or d-1,2-diphenylethane-1,2-diol with DTPP (Figure 69).
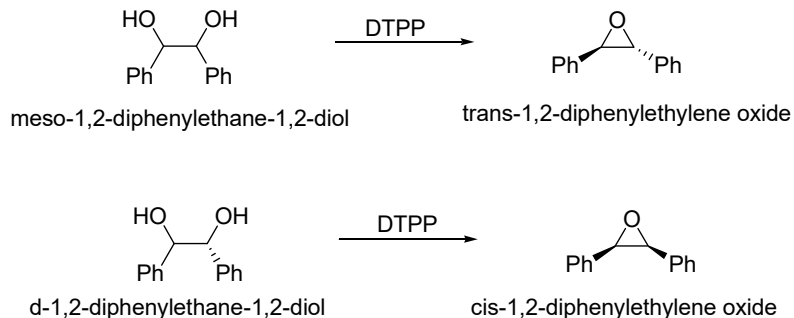
Figure 69. Meso- and d-1,2-diphenylethane-1,2-diol reaction with DTPP.

Sands has used $BF_3 \cdot OEt_2$ for the rearrangement of various cyclic diols (Figure 70).[45] This method gave the ketone as the major product instead of the expected diene formation which occurs in H_2SO_4.[46]
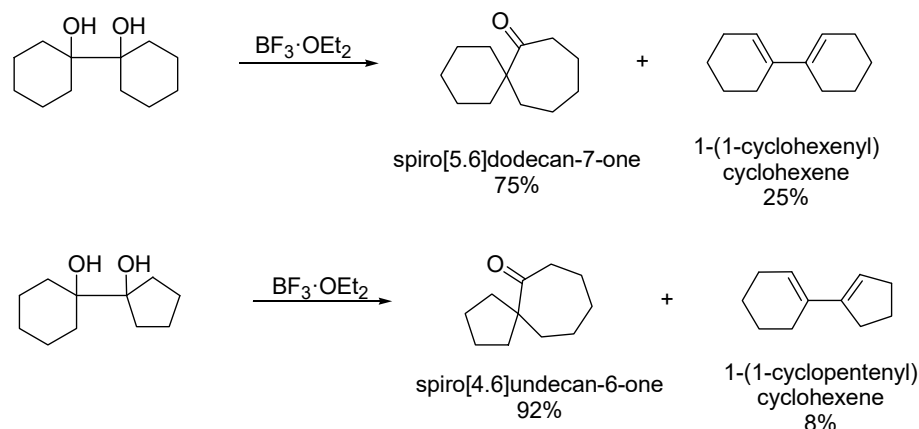
Figure 70. The reaction of cyclic diols with BF$_3$·OEt$_2$.

Walsh and coworkers experienced a pinacol-type rearrangement of R-hydroxy cyclopropyl carbinols while they were trying diastereoselective synthesis of cis- and trans-2,3-disubstituted cyclobutanone.[47] The rearrangement of cyclopropane diol with sulfonyl chlorides in pyridine (py) and with a series of Lewis and Brønsted acids (Figure 71). Methanesulfonyl chloride (MsCl) and mesitylene sulfonyl chloride (MesSO$_2$Cl) in pyridine, both favoring the trans diastereomer. The major product with catalytic p-toluenesulfonic acid (PTSA) was trans-2,3-disubstituted cyclobutanone and BF$_3$·OEt$_2$ favors the cis product.
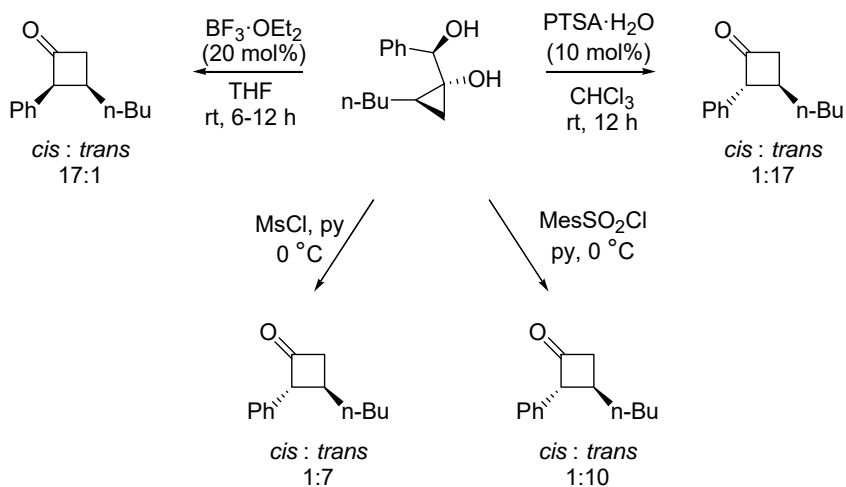
Figure 71. Reaction of cyclopropane diol with Lewis and Brønsted acids.

4.2 Objective

Study the effect of Lewis acids on the dehydration/rearrangement of pinacol and various 1,2-diols.

4.3 Results and Discussion

Toward this goal, the rearrangement of benzpinacol, pinacol, meso-hydrobenzoin, and d-hydrobenzoin was studied with common organic soluble Lewis acid catalysts, *para*-toluene sulfonic acid (PTSA) and boron trifluoride diethyl etherate (BF$_3$·OEt$_2$) (Figure 72).
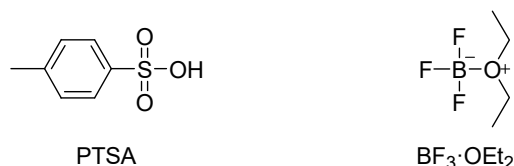
Figure 72. The acid catalysts used in the current study.

4.3.1 Pinacol rearrangement with PTSA

To begin, the rearrangement of benzpinacol, pinacol, meso-hydrobenzoin, and d-hydrobenzoin was studied using PTSA as the catalyst and toluene as the solvent.

The rearrangement of benzpinacol (**4.1**) was investigated in toluene with catalytic amounts (10 mol %) of PTSA at different temperatures. ^{1}H NMR analysis revealed the formation of two products, tetraphenylethylene oxide (**4.2**) and benzpinacolone (**4.3**) (Figure 73). The results are summarized in Table 6. These results are similar to that of Yamamoto.[43]
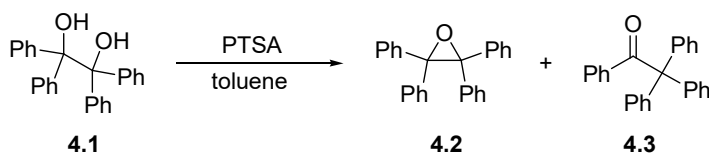
Figure 73. The reaction of benzpinacol and PTSA.

Table 6

*Summary of the extent of benzpinacol (**4.1**) rearrangement in the presence of PTSA*

Entry	4.1 mM	PTSA mol%	Condition		Composition (%)		
			Temp. (°C)	Time (h)	4.1	4.2	4.3
1	0.06	10%	22	44	100	ND	ND
2	0.06	10%	120	24	ND	31	69
3	0.06	10%	110	1	ND	100	ND
4	0.06	10%	80	1.5	ND	100	ND
5	0.05	10%	50	20	40	60	ND
6	0.06	1%	80	6	94	ND	6
7	0.06	5%	80	4.5	ND	61	39
8	0.06*	10%	80	6	ND	59	41
9	0.05*	10%	80	1.5	ND	85	15
10	0.05*	10%	80	3.5	4	95	1
11	0.05*	10%	80	1	42	55	3
12	0.05*	10%	80	20	ND	46	54

*Note. ND: Not Detected, reactions were run using 5 mL toluene, *50 mL scale reaction*

At room temperature, there was no rearrangement. At 80 °C, the complete conversion of diol **4.1** into epoxide **4.2** after 90 min with 10 mol% of PTSA was observed (entry 4). The formation of epoxide **4.2** starts with time. At 50 °C, the formation of

ketone **4.3** was not observed (entry 5). However, similar results on a large-scale (1 g of

diol **4.1**) study could not be obtained. This may be because large-scale reactions were

carried out in a 100 mL round bottom flask instead of 25 mL round bottom flask, and it

was heated in an 80 °C oil bath. The temperature through the whole reaction mixture may

not be continuous. The stirring speed may also affect the rate of the reaction. In

conclusion, the rearrangement of benzpinacol with PTSA depends on the amount of the

PTSA, and temperature has higher influence for the formation of ketone **4.3**. We

identified product epoxide **4.2** as the kinetic product and product **4.3** as the

thermodynamic product. The mechanism for the benzpinacol rearrangement with PTSA

is shown in Figure 74. This reaction proceeds through a carbocation intermediate.

Epoxide **4.2** forms by donating the lone pair of electrons on the oxygen of hydroxyl

group to the carbocation and this reaction is reversible. With high temperature and time,

the epoxide converts into the carbocation intermediate. Finally, the ketone product **4.3** is

obtained after the aryl shift.
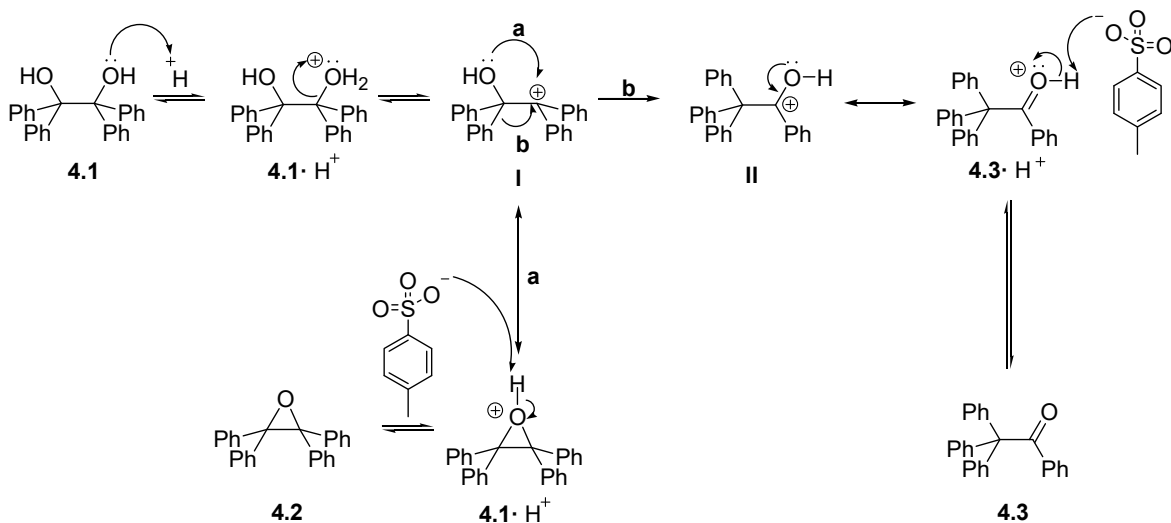
Figure 74. The proposed mechanism for the reaction: (a) to form epoxide **4.2** and (b) to form ketone **4.3**.

Next, the rearrangement of pinacol (**4.4**) was studied with a catalytic amount of the PTSA in toluene. There was no rearrangement of pinacol with 10% PTSA in toluene at room temperature (Figure 75). Further, rearrangement was not observed even after refluxing the reaction mixture for 24 h. This may be because alkyl substituents are a less strong electron-donating group than aryl substituents.
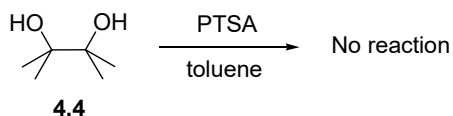
Figure 75. The reaction of pinacol with PTSA.

To support the notion that aryl substituted diols help to facilitate the rearrangement, meso-hydrobenzoin (**4.6**) was studied with a catalytic amount of the PTSA in toluene. There was no rearrangement of these diols with 10% PTSA in toluene at room temperature. However, after refluxing in toluene for 24 h with 10% PTSA

product was obtained (Figure 76). According to ¹H-NMR analysis, the reaction mixture

contained ketone (**4.8**), aldehyde (**4.7**), and epoxide (**4.9**) (Figure 77). The proposed

mechanism is shown in Figure 78.

Figure 76. The reaction of diol **4.6** with PTSA.

Figure 77. ¹H NMR spectra of a) meso-hydrobenzoin and b) reaction of diol **4.6** with
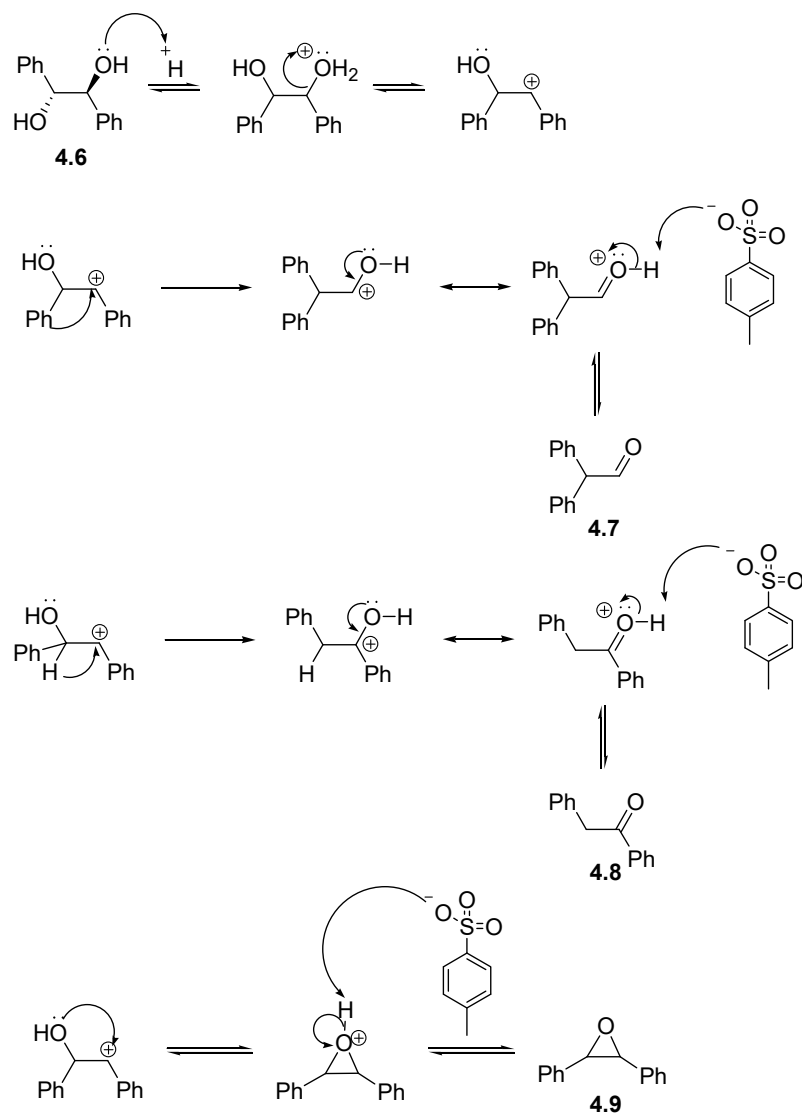
PTSA.

Figure 78. The proposed mechanism for the reaction of diol **4.6** with PTSA.

The rearrangement of d-hydrobenzoin (**4.10**) was studied with a catalytic amount of the PTSA in toluene. Again, there was no rearrangement with 10% PTSA in toluene at room temperature. The reaction mixture was refluxed in toluene for 24 h with 10% PTSA (Figure 79). After 24 h, toluene was removed under reduced pressure and NMR of the product was obtained. According to the NMR spectrum, the rearrangement of diol **4.10** resulted in three major products (Figure 80).
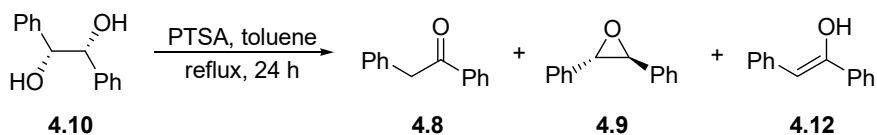
Figure 79. The reaction of diol **4.10** with PTSA.
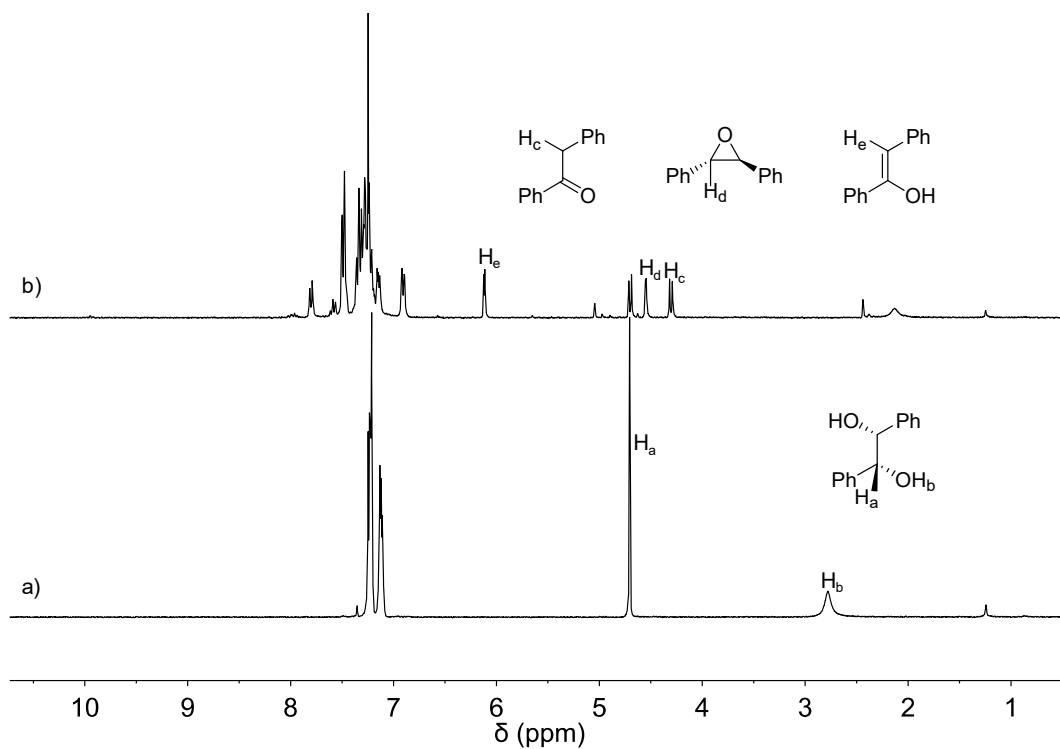
Figure 80. ^{1}H NMR spectra of a) d-hydrobenzoin and b) reaction of diol **4.10** with PTSA.

4.3.1 Pinacol rearrangement with BF$_3$·OEt$_2$

Next, BF$_3$·OEt$_2$ was investigated for the rearrangement of benzpinacol, pinacol, meso-hydrobenzoin, and d-hydrobenzoin (Figure 81). All reactions were carried out in an NMR tube in CDCl$_3$. First, the rearrangement of benzpinacol **4.1** with 0.3, 2.5, and 7 equiv of BF$_3$·OEt$_2$ was studied. The results are shown in Figure 82.
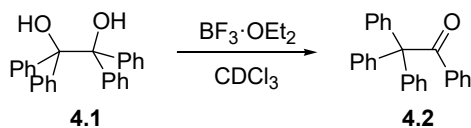
Figure 81. The reaction of benzpinacol with BF$_3$·OEt$_2$.
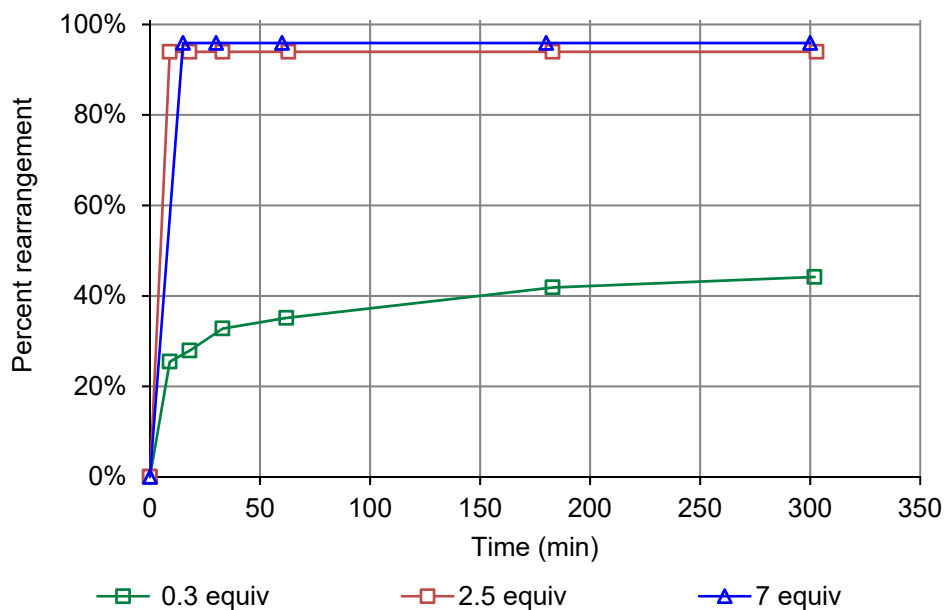
Figure 82. Benzpinacol rearrangement with the different equivalents of BF₃·OEt₂.

The reactions were monitored for 5 h. There was only 44% benzpinacolone with 0.3 equiv of the catalyst. Wherein, there was no big difference in the rearrangement with 2.5 and 7 equiv of BF₃·OEt₂ with having 94% and 96% rearrangement, respectively. This rearrangement reaction may have reached 100% conversion. Since the percent conversion was calculated using the integration values of relevant ^{1}H NMR signals, which may have been overlapping with solvent signals.

Then, rearrangement of pinacol **4.4** with six different equivalents of BF₃·OEt₂ was studied (Figure 83). The results are shown in Figure 84.
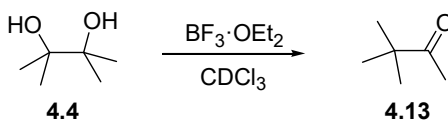
Figure 83. The reaction of pinacol with BF₃·OEt₂.
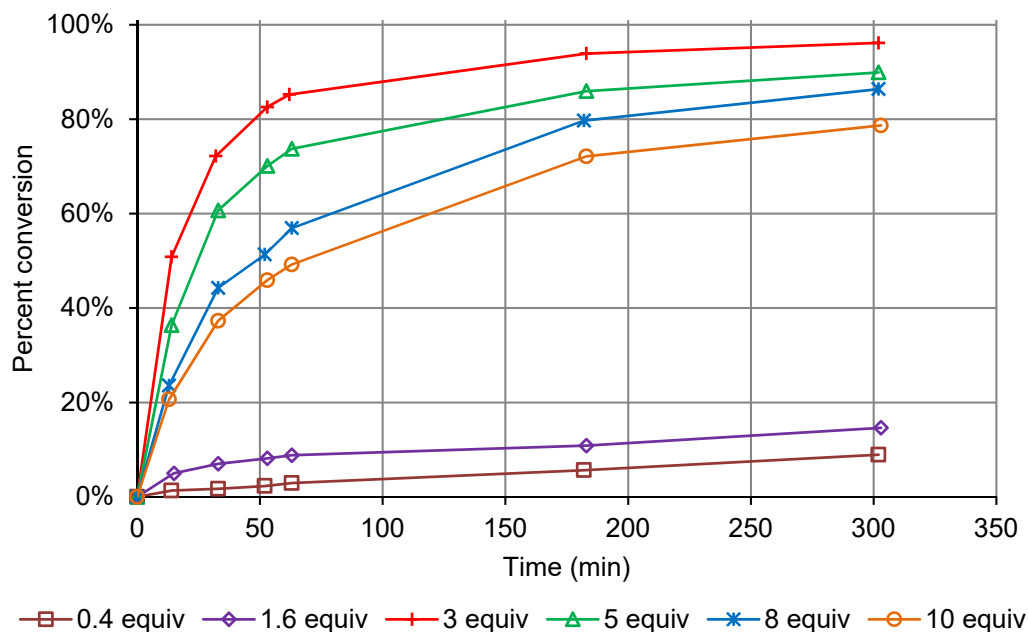
Figure 84. Pinacol rearrangement with six different equivalents of BF₃·OEt₂.

After 5 h, the highest rearrangement of pinacol was observed with 3 equiv of

BF₃·OEt₂. With 0.4 and 1.6 equiv of BF₃·OEt₂ there were only 9% and 15% pinacolone,

respectively. By increasing the amount of BF₃·OEt₂ to more than 3 equiv, the rate and the

amount of rearrangement decreased.
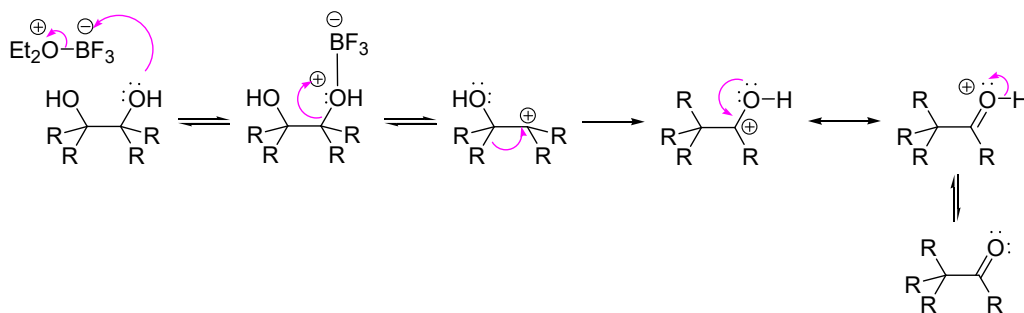
Figure 85. The proposed mechanism of the pinacol rearrangement in the presence of

BF₃·OEt₂.

The rearrangement of meso-hydrobenzoin (**4.6**) was studied with 0.5, 1, 3, 5, 7, and 10 equiv BF$_3$·OEt$_2$ (Figure 86). The reaction was monitored over 7 h using ^{1}H NMR (Figure 87).
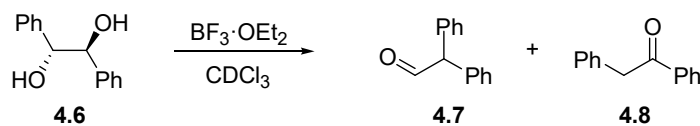
Figure 86. The reaction of diol **4.6** with BF$_3$·OEt$_2$.
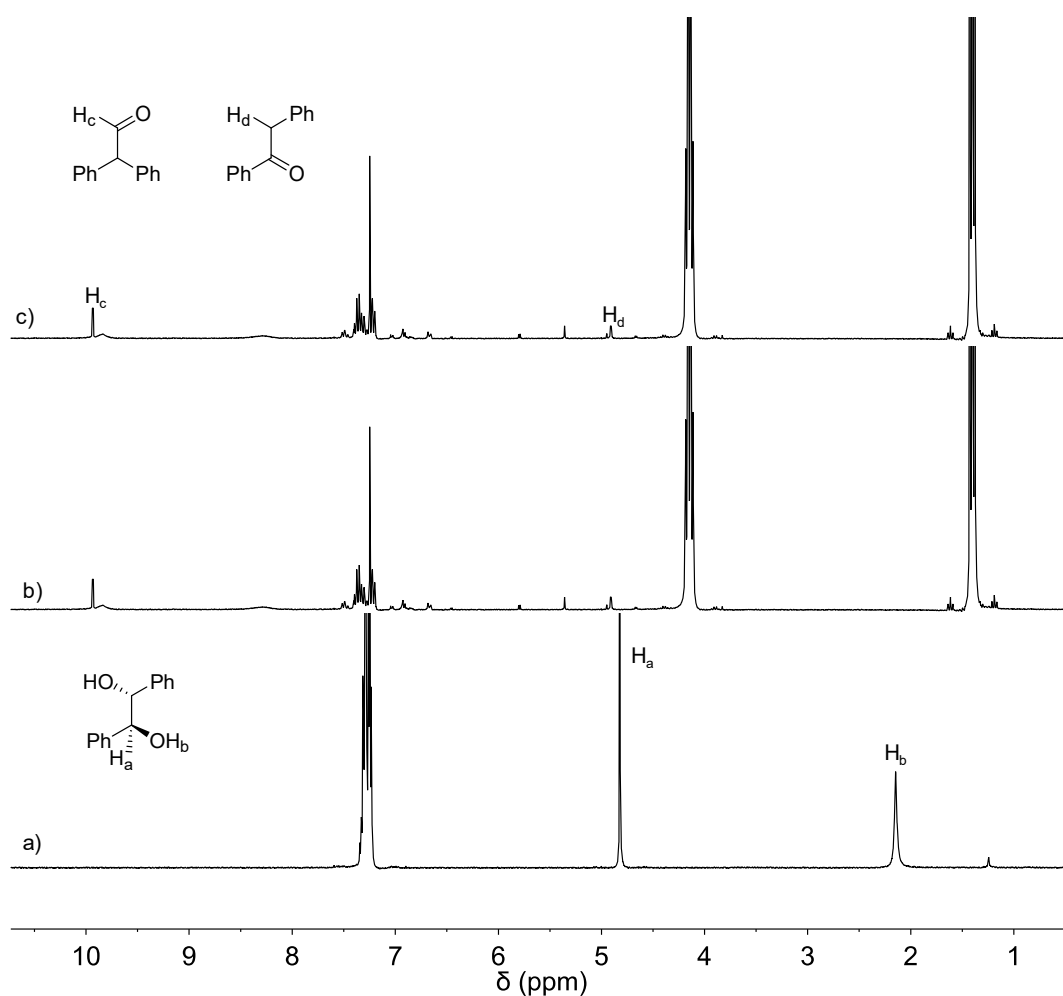
Figure 87. ^{1}H NMR spectra of a) meso-hydrobenzoin **4.6**, b) with 5 equiv BF$_3$·OEt$_2$, and c) with 10 equiv BF$_3$·OEt$_2$.

According to the ^{1}H NMR spectra, BF$_3$·OEt$_2$ catalyzed the rearrangement of diol **4.6**. It formed different products with time and with the different equivalents of BF$_3$·OEt$_2$. The major product was aldehyde **4.7**. NMR spectra (Figure 87) show the different product formation of diol **4.6** with the different equivalence of BF$_3$·OEt$_2$. However, with 7 equiv of BF$_3$·OEt$_2$, it formed only its aldehyde **4.7** (Figure 88).
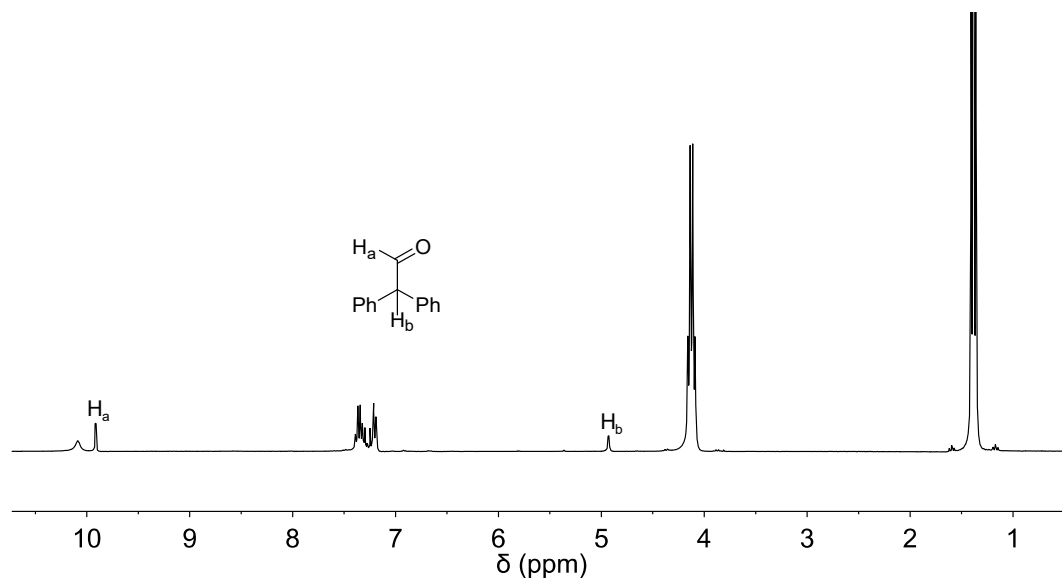
Figure 88. ^{1}H NMR spectrum of the rearrangement reaction of diol **4.6** with 7 equiv of BF$_3$·OEt$_2$.

The rearrangement hydrobenzoin (**4.10**) with 5 and 10 equiv of BF$_3$·OEt$_2$ was studied (Figure 89).
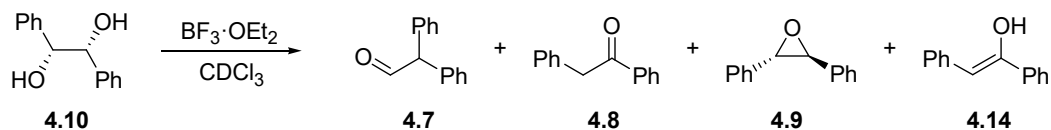
Figure 89. The reaction of diol **4.10** with BF$_3$·OEt$_2$.

Several products were observed with this reaction as well. Figure 90 shows the ^{1}H NMR spectra of these reactions that were obtained after 7 h of the reaction.
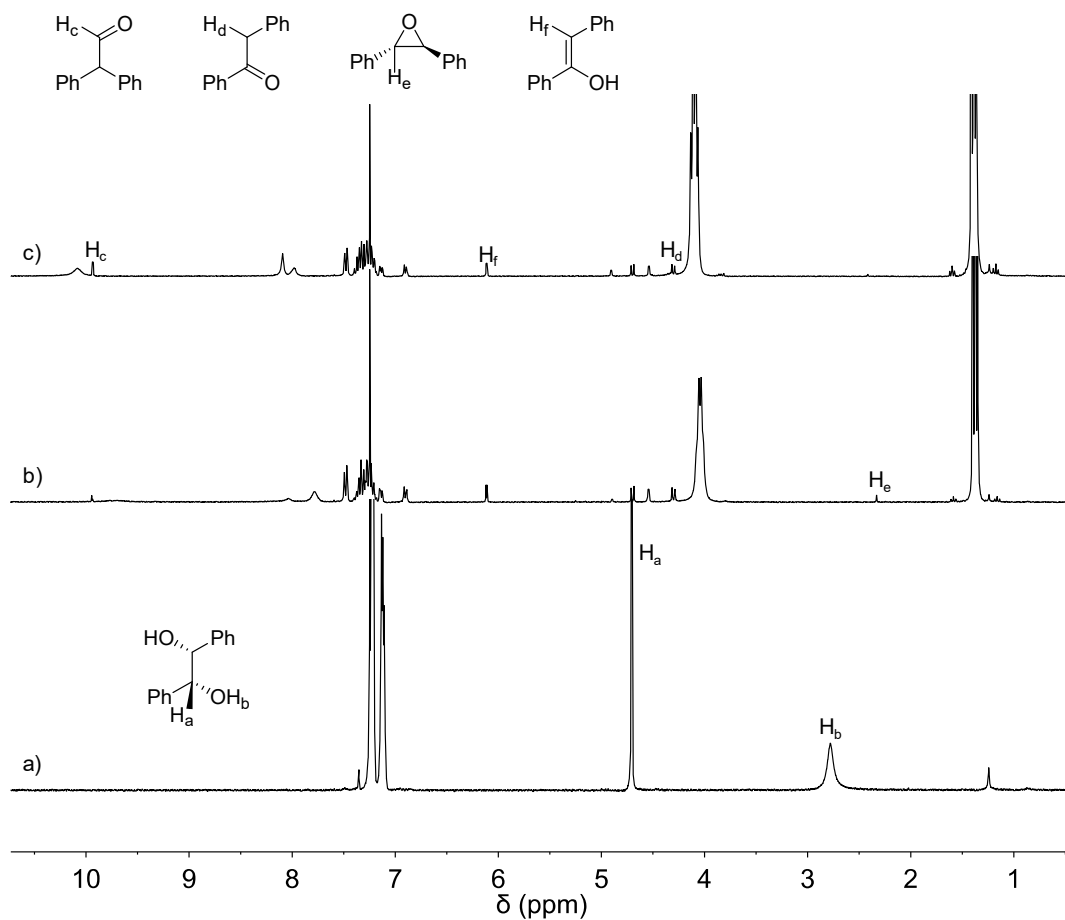
Figure 90. ^{1}H NMR spectra of a) d-hydrobenzoin **4.10**, b) with 5 equiv BF$_3$·OEt$_2$, and c) with 10 equiv BF$_3$·OEt$_2$.

4.4 Conclusions
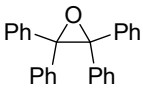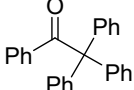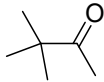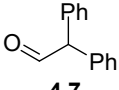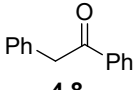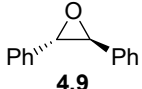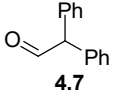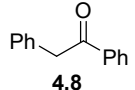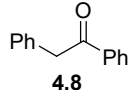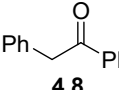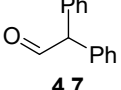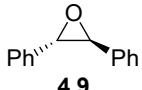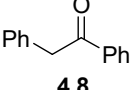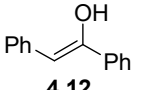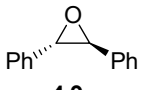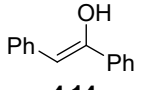
Although PTSA catalyzed the rearrangement of benzpinacol, meso-hydrobenzoin, and d-hydrobenzoin, it did not facilitate the rearrangement of pinacol. This may be because alkyl substituents are less electron donating groups than aryl groups. It is well known than benzylic cations are more stable than the alkyl cation intermediates.

In sharp contrast, BF$_3$·OEt$_2$ catalyzed the rearrangement of pinacol, benzpinacol, meso-hydrobenzoin, and d-hydrobenzoin even at room temperature. These diols undergo rearrangement reactions in the presence of BF$_3$·OEt$_2$, which supports the

transesterification reactions of the boronate esters in chapter III. See table 7 for a

summary of pinacol rearrangement products.

Table 7

Different rearrangement products of pinacol, benzpinacol, and hydrobenzoin

1,2-diol	PTSA	BF₃·OEt₂
benzpinacol (**4.1**)	**4.2** **4.3**	**4.3**
pinacol (**4.4**)	No rearrangement	**4.13**
meso-hydrobenzoin (**4.6**)	**4.7** **4.8** **4.9**	**4.7** **4.8**
hydrobenzoin (**4.10**)	**4.8** **4.9** **4.12**	**4.7** **4.8** **4.9** **4.14**

4.5 Experimental

*Rearrangement of 1,1,2,2-tetraphenylethane-1,2-diol (benzpinacol, **4.1**) with*

PTSA. Small scale and large scale reactions were carried out in 25 mL and 100 mL round

bottom flasks, respectively. Diol **4.1** and PTSA (1–13 mol %) were mixed in toluene. The

reaction mixture was heated in an oil bath. The reaction mixtures were monitored by TLC (ethyl acetate: hexane (1:4)) until completion and then by ^{1}H –NMR spectroscopy.

*Rearrangement of 2,3-dimethylbutane-2,3-diol (pinacol, **4.4**) with PTSA.* Diol **4.4** (20 mg, 0.093 mmol) was mixed with toluene (5 mL) and PTSA (10 mol %) in a 25 mL round bottom flask. The reaction mixture was refluxed using an oil bath set to 110 °C.

*Rearrangement of (1R,2S)-1,2-diphenylethane-1,2-diol (meso-hydrobenzoin, **4.6**) with PTSA.* Diol **4.6** (20 mg, 0.093 mmol) was mixed with toluene (5 mL) and PTSA (10 mol %) in a 25 mL round bottom flask. The reaction mixture was refluxed in an oil bath.

*Rearrangement of (1R,2R)-1,2-diphenylethane-1,2-diol (d-hydrobenzoin, **4.10**) with PTSA.* Diol **4.10** (100 mg, 0.85 mmol) was mixed with toluene (5 mL) and PTSA (10 mol %) in a 25 mL round bottom flask. The reaction mixture was refluxed in an oil bath.

The rearrangement reactions with $BF_3 \cdot OEt_2$ were carried out in NMR tubes using $CDCl_3$ as the solvent and the reaction progress was monitored by ^{1}H-NMR spectroscopy. The equivalence of $BF_3 \cdot OEt_2$ and the extent of rearrangement were determined based on the ^{1}H-NMR integrations of the relevant proton signals (Table 8).

Table 8

^{1}H-NMR signals used to determine the percent rearrangement

Reaction	starting material	product
4.1 + PTSA	δ 7.33-7.26 ppm (**4.1**)	δ 7.68 ppm (**4.3**) δ 7.14- 7.05 ppm (**4.2**)
4.4 + PTSA	δ 1.3 ppm (**4.4**)	δ 2.3 + 1.13ppm

Reaction	starting material	product
4.1 + BF$_3$·OEt$_2$	δ 7.33-7.26 ppm (**4.1**)	δ 7.68 ppm (**4.3**)
4.4 + BF$_3$·OEt$_2$	δ 1.3 ppm (**4.1**)	δ 2.3 + 1.13ppm

Rearrangement of 1,1,2,2-tetraphenylethane-1,2-diol (4.1) with BF$_3$·OEt$_2$. Diol **4.1** (0.0311 g, 0.085 mmol) was reacted with five different equivalence (1 drop: 0.3 equiv, 3 drops: 1 equiv, 6 drops: 2.5 equiv, 12 drops: 7 equiv, 20 drops: 14 equiv) of BF$_3$·OEt$_2$ in CDCl$_3$ (0.6 mL).

Rearrangement of 2,3-dimethylbutane-2,3-diol (4.4) with BF$_3$·OEt$_2$. Diol **4.4** (0.01 g, 0.085 mmol) was reacted with six different equivalence (1 drop: 0.4 equiv, 1.5 drops: 1.6 equiv, 6 drops: 3 equiv, 10 drops: 5 equiv, 18 drops: 8 equiv, 22 drops: 10 equiv) of BF$_3$·OEt$_2$ in CDCl$_3$ (0.6 mL).

Rearrangement of (1R,2S)-1,2-diphenylethane-1,2-diol (4.6) with BF$_3$·OEt$_2$. Diol **4.6** (2.5 mg, 0.016 mmol) was reacted with five different equivalence (0.5 equiv, 1 equiv, 3 equiv, 5 equiv, 10 equiv) of BF$_3$·OEt$_2$ in CDCl$_3$ (0.7 mL).

Rearrangement of (1R,2R)-1,2-diphenylethane-1,2-diol (4.10) with BF$_3$·OEt$_2$. Diol **4.10** (2.5 mg, 0.016 mmol) was reacted with two different equivalence (5 equiv, 10 equiv) of BF$_3$·OEt$_2$ in CDCl$_3$ (0.7 mL).

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VITA

EDUCATION
Master of Science in Chemistry   Anticipated summer 2017
      Sam Houston State University, Huntsville, TX
- Thesis title: "The Effect of Boron Trifluoride on the Transesterification of Boronate Esters"
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Bachelor of Science (Joint Major) in Chemistry and Physics (4 years)   06/12
Rajarata University, Sri Lanka
- Final year research project: "Purification and Characterization of the Clay from Giant Tank", Advisor: Dr. Ajith Herath
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AWARDS
- Sam Houston State University Graduate Scholarship (2015 and 2016)
- Sam Houston State University College of Science and Engineering Technology Summer Stipend for Thesis Research (2016)
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RESEARCH EXPERIENCE
      I am investigating the effect of Lewis acids on the dehydration/rearrangement of pinacol and other 1,2- diols. Concurrently, I am investigating the effect of Lewis acids on the transesterification of dioxaboroles

PRESENTATIONS
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TEACHING EXPERIENCE
Graduate Teaching Assistant   09/2015 – Present
Department of Chemistry, Sam Houston State University
- Conducted General Chemistry laboratory classes and tutoring classes (CHEM 1406 and CHEM 1411)
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Assistant Lecturer in Chemistry   12/2014 – 07/2015
National Institute of Education, Maharagama, Sri Lanka
The National Institute of Education (NIE), Sri Lanka is the prime institute in the country responsible for providing leadership for the development of general education

- Assisted in designing and developing curriculum for the general education and teacher education system in chemistry
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Instructor in Chemistry   06/2013 – 08/2014
General Sir John Kotelawala Defence University, Sri Lanka
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Faculty of Applied Sciences, Rajarata University of Sri Lanka
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