2013

Synthesis of donor-acceptor benzobis(oxazole) small molecules

James Scott Klimavicz
Iowa State University

Synthesis of donor-acceptor benzobis(oxazole) small molecules

by

James Scott Klimavicz

A thesis submitted to the graduate faculty

In partial fulfillment of the requirements of the degree of

MASTER OF SCIENCE

Major: Organic Chemistry

Program of Study Committee:
Malika Jeffries-EL, Major Professor
Javier Vela
Arthur Winter

Iowa State University
Ames, Iowa
2013

DEDICATION

Dedicated to my wonderful parents, Paul and Nancy Klimavicz, who always believed in me, even when I did not, my dear family and friends (especially Dana Drochner and Kirsten Johnson) for all of their support, and to everyone who has had to listen to me rant to no end about chemistry.

CONTENTS

DEDICATION ii

NOMENCLATURE v

ACKNOWLEDGEMENTS vi

CHAPTER 1. INTRODUCTION TO CONJUGATED MOLECULES AND BENZOBISOXAZOLES 1

1.1. Background of Conjugated Polymers and Dyes 1

1.2. Small Molecule Dyes and Monodisperse Oligomers 2

1.3. Donor-Acceptor Compounds 2

1.4. Benzobisoxazoles 3

1.4.1. *trans*-BBO 4

1.4.2. *cis*-BBO 4

1.4.3. Electronic uses 5

1.5. References 9

CHAPTER 2. SYNTHESIS OF SYMMETRIC D-π-A-π-D BENZOBISOXAZOLE ORGANIC CHROMOPHORES 13

2.1. Introduction 13

2.2. Synthetic Approach 13

2.3. Optical Properties and Solvatochromism 17

2.4. Electronic Properties 22

2.5. Results and Discussion 26

2.6. Experimental Methods 28

2.7. References 33

CHAPTER 3. TOWARDS THE SYNTHESIS OF ASYMMETRIC BENZOBISOXAZOLE DYES 35

3.1. Introduction 35

3.2. Retrosynthetic Approaches 36
3.3. Results and Discussion 39
3.3.1. Troubles of asymmetric *t*-BBOs 39
3.3.2. Synthesis of asymmetric *c*-BBO 49
3.3.3. Orthoester work 54
3.4. Future Work 59
3.5. Experimental Methods 60
3.6. References 79

NOMENCLATURE

Bn	benzyl
Boc	*N*-*tert*-butoxycarbonyl
Bz	benzoyl
c-BBO	benzo[1,2-*d*:5,4-*d*']bis(oxazole), or *cis*-BBO
BBZT	benzo[1,2-*d*:4,5-*d*']bis(thiazole)
CP	conjugated polymer
DAHQ	2,5-diaminohydroquinone dihydrochloride
DMAc	*N*,*N*-dimethylacetamide
DMF	*N,N*-dimethylformamide
HOMO	highest occupied molecular orbital
HRMS	high resolution mass spectrometry
LUMO	lowest unoccupied molecular orbital
NMR	nuclear magnetic resonance
OFET	organic field effect transitor
OLED	organic light emitting diode
OPV	organic photovoltaic
RBF	round-bottom flask
t-BBO	benzo[1,2-*d*:4,5-*d*']bis(oxazole), or *trans*-BBO
TFA	trifluoroacetic acid
THF	tetrahydrofuran

ACKNOWLEDGEMENTS

I thank the 3M Foundation and the National Science Foundation (DMR-0846607) and 12 Teragrid (TG-CHE100148) for partial support of this work. I also thank Dr. Kamel Harrata and the Mass Spectroscopy Laboratory of Iowa State University (ISU) for analysis of our compounds, and Atta Gueye, Dr. Elena Sheina and Dr. Christopher Brown of Plextronics for providing UPS measurements.

I would also like to thank the Jeffries-EL research group for their work and advice through my years in the group, with specific thanks to Dana Drochner, Dr. Jared Mike, Mathew Hirsch, Dawn Knoble, Achala Bhuwalka, Brian Tlach, Brandon Kobilka, and Dr. Malika Jeffries-EL.

CHAPTER 1. INTRODUCTION TO CONJUGATED MOLECULES AND BENZOBISOXAZOLES

1.1. Background of Conjugated Polymers and Dyes

Since the discovery of the conductance of doped poly(acetylene) in 1977,[1] the semiconducting and conducting properties of π-conjugated organic compounds has garnered much attention. Presently, most semiconducting materials used are inorganically-based, using high-purity silicon, germanium, arsenic, and other metalloids.[2] However, organic analogues have the potential to provide much cheaper alternatives provided that devices can be made efficient enough. Furthermore, due to the seemingly infinite potential structure variation, electronic properties of organic molecules can be fine-tuned to a higher degree than can inorganic compounds.[3]

The original π-CPs developed were relatively simple in nature, and included poly(*para*-phenylene),[4] polyaniline,[5] polythiophene,[6] poly(2,5-pyrrole),[5] and polyphenylenevinylene (Figure 1).[7] Conducting polymers have a conjugated backbone, allowing for the delocalization of charges to produce solitons and bipolarons, and thus allowing for charge transport along the molecule.[8] However, due to these polymers' rigid-rod structure, as well as strong π-stacking interactions,[9] the solubility of these compounds was low, though this problem was later assuaged by the inclusion of solubilizing alkyl chains to interrupt packing and aggregation.[10-11]

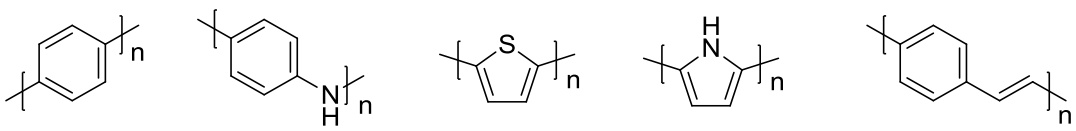


Figure 1: From left to right: poly(*para*-phenylene), polyaniline, polythiophene, poly(2,5-pyrrole), and polyphenylenevinylene .

1.2. Small Molecule Dyes and Monodisperse Oligomers

While CPs have many potential benefits, such as long conjugation lengths to carry charges in devices, there are also possible difficulties involved in their use. Although new synthetic methods allow for better control of the chain length of polymers, the resultant polymeric compound is not monodisperse, and instead shows a Poisson ditribution in chain length.[12-13] As these distributions are dependent on time, [14]monomer concentration,[15] and catalyst loadings,[16] it can be reasonably expect that there will be variability between different batches of polymer. Small molecule dyes, on the other hand, are well-defined structures that eliminate this problem whilst still maintaining many of the desirable properties of their polymeric analogs.[17-18] Monodisperse oligomers, which are oligomers with the same number of repeat units, can serve as models for the longer CPs,[19-20] particularly when effective conjugation length is reached.[21]

1.3. Donor-Acceptor Compounds

Presently, a common technique to adjust the HOMO, LUMO, and band gap of conjugated molecules by including electron-donating and electron-accepting groups, as hybridization between the HOMO of the donor and the LUMO of the acceptor produces a relatively narrow band gap. [17, 22] Indeed, using this method, it is possible to obtain CPs and dyes with band gaps below 1 eV.[23-24] The combined effect of conjugation and donor-acceptor effects can be seen in Figure 2 upon comparing retinol and β-carotene to retinal and astaxanthin, respectively, where the former have no electron-withdrawing carbonyls,

while the latter compounds of the same length do, and absorb longer wavelengths of light, red-shifting the observed color.

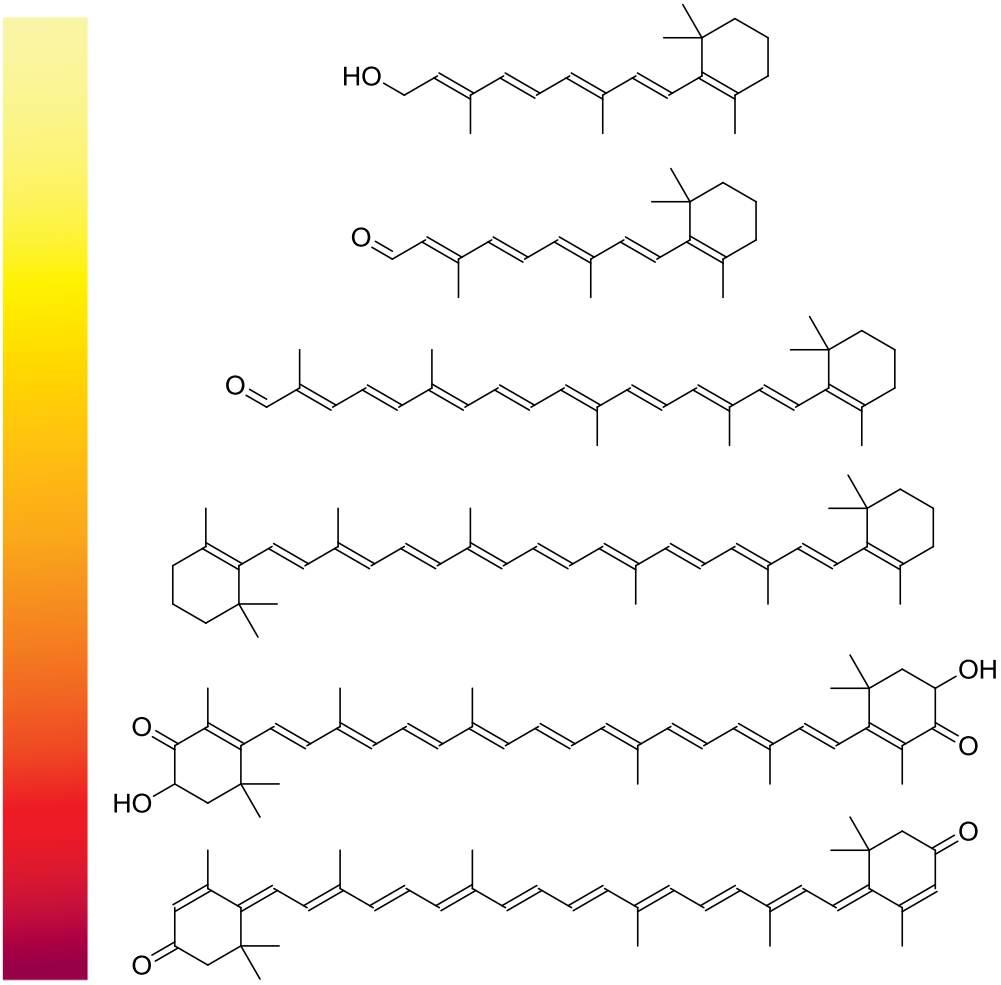


Figure 2: Naturally-occurring polyenes are common as pigments in plants and some animals. From the top: retinol, retinal, apocarotenal, β-carotene, astaxanthin, rhodoxanthin. These dyes range from light yellow, to yellow, then shades of orange and red, and finally to a violet-red.

1.4. Benzobisoxazoles

Benzobisoxazoles have been of interest recently due to many beneficial properties, both within and outside of the field of organic electronics. Polymers made

with BBOs have attracted much attention for their uses as high-performance materials, with poly(p-phenylene-2,6-benzobisoxazole), previously sold under the trade name Zylon®,[25] being perhaps the best-known example. Zylon was well known for its ability to be used to create extremely strong fibers,[26] and was used to make bulletproof vests, as the tensile strength of the polymer was 1.6 times that of Kevlar®.[27] The polymer is also known for its chemical[28] and heat resistance.[29] BBOs have also been used in CPs to synthesize organic electronic devices.

1.4.1. *trans*-BBO

The herein-named *t*-BBO, or benzo[1,2-d:4,5-d']bis(oxazole), is the more commonly seen isomer of BBO, due to its easy synthesis from chloranil.[30-31] Additionally, the *trans*- arrangement, which colloquially refers to the fact that the oxazole rings are oriented opposite from each other; that is, there is no vertical plane of symmetry, though there is a rotational axis, giving the molecule C_{2h} symmetry. The 1,4-positioning of the imine-nitrogens allows for the drawing of a valid quinoid structure through the BBO molecule.

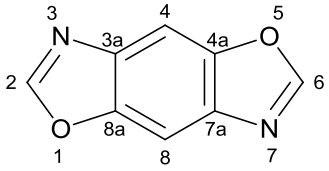


Figure 3: A numbered *t*-BBO molecule. All substitutions herein occur at the 2- and 6-positions.

1.4.2. *cis*-BBO

c-BBO, or benzo[1,2-*d*:5,4-*d*']bis(oxazole), is less commonly seen than its aforementioned isomer, but has similar optical and electronic properties, despite the fact

that the imine-nitrogens are not *para*, which precludes the drawing of valid quinoid structures. The *cis*-isomer possesses C_{2v} symmetry, and has an inherent dipole present, which the *trans*-isomer does not.

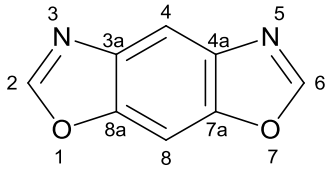


Figure 4: A numbered *t*-BBO molecule. All substitutions herein occur at the 2- and 6-positions.

1.4.3. Electronic uses

Conjugated molecules containing BBO have seen numerous uses in the field of organic electronics, as the BBO moiety serves as a good acceptor in donor-acceptor systems. Additionally, compounds containing BBOs have been known to show significant non-linear optical properties,[32-33] high quantum yields,[34] and high hole mobilities[35-36], allowing for their use in a wide range of devices, including single-electron switches,[37] as well as OFETs, OLEDs, and OPVs, discussed below. Furthermore, BBOs can be beneficial for electron transport improving device performance and efficiency.[38-39]

1.4.3.1. OFETs

Most organic analogs to OFETs have been done with polymeric materials; [40-42] however, some progress has been made towards transistors which contain small molecules.[43] The chromophoric aspect of dyes is not as important here as in OPVs or OLEDs, as emission or absorption of photons is not the main goal, and instead the focus

is on hole or electron mobilities. Though the contacts used are different, the typical device architecture for a thin-film OFET is shown in Figure 5, and is the same for both n- and p-type transitors.

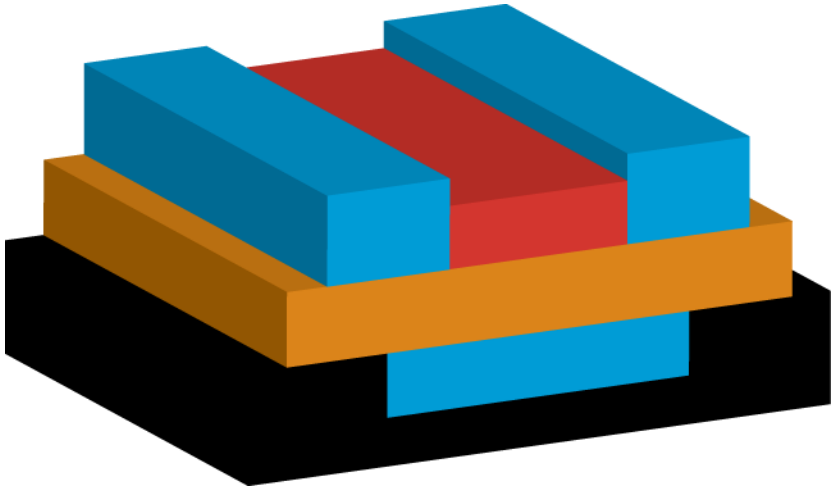


Figure 5: A typical layout of a thin-film OFET. The top blue portions are the source and drain, the red portion is the semiconductor, the orange is a dielectric insulator, and the bottom blue is the gate. Not to scale.

1.4.3.2. OLEDS

OLEDs have become another major interest, and both BBO polymers and small molecules can be used to synthesize them;[44-45] it has been shown that the inclusion of BBO polymers can improve the electron transport of such devices.[46] Polymer OLEDs can be quickly and cheaply made by spin-coating a polymer on to a conductive substrate, and building the rest of the device from that point; however, the efficiency of the final OLED may be poor if the film morphology is not ideal. Small molecules are potentially beneficial to OLED design as they can be thermally deposited onto a flexible substrate, allowing for careful control of the thickness and morphology of the emissive layer.[45] Deposition of additional layers also allows for the creation of highly-structured devices,

improving efficiency. Of particular interest in designing OLEDs is the synthesis of efficient blue-emitting devices, as the currently available materials that emit in the blue region tend to have poor color purity, as well as a shorter lifetime.[47-48] Additionally, an increase in brightness is also desired, as the human retina has a lower sensitivity to blue light, and, as a result, brighter devices are required.[49-50] A typical OLED is shown in Figure 6; note that the glass substrate is on the bottom, where light is emitted.

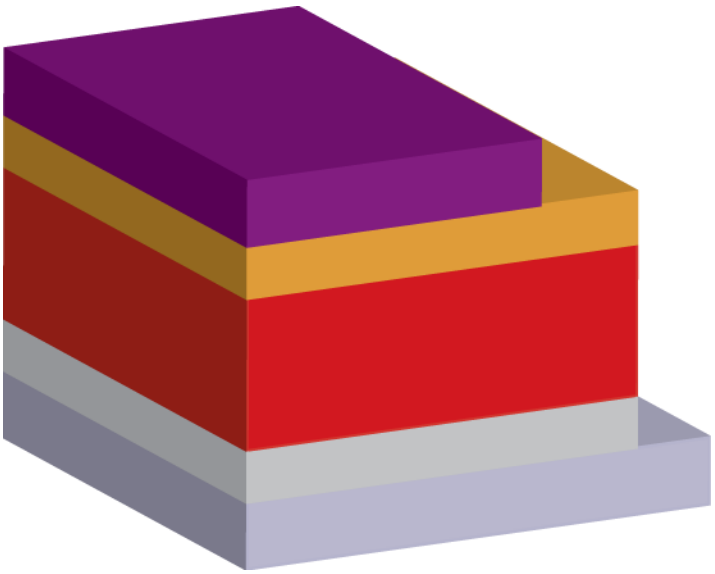


Figure 6: A typical OLED. The purple top layer is the metal cathode, followed by the electron transport layer, orange, the emissive layer containing the CP, red, and the hole transport layer, grey, and the anode on the bottom, mauve. The bottom substrate is transparent, as theis is where light is emitted. Not to scale. The emissive layer is occasionally combined with either the hole or electron transport layer to simplify the device architecture.

1.4.3.3. OPVs

BBO dyes can also be used for OPVs, and much work has gone into the development of this technology, as polymeric OPVs may be printed on a flexible substrate, allowing for bendable solar cells. [51-53] A typical bulk heterojunction OPV layout is shown Figure 7, where the active layer consists of both a polymeric electron

donor and an electron acceptor, often a fullerene derivative.[54] Dye-sensitized solar cells are a variation upon this in which small-molecule dyes are in included in the active layer to absorb more of the solar spectrum to improve efficiency.[55-57]

BBO-containing–dye-sensitized OPVs potentially have the beneficial effect higher photostability than BBO-containing CPs, as it is theorized that BBO eximer formation is the leading cause of photodegredation in current BBO systems.[58] π-stacked BBOs can form an eximer upon exposure to light, which then forms a radical ion pair capable of reducing oxygen to the superoxide radical, which then reacts with the polymer.

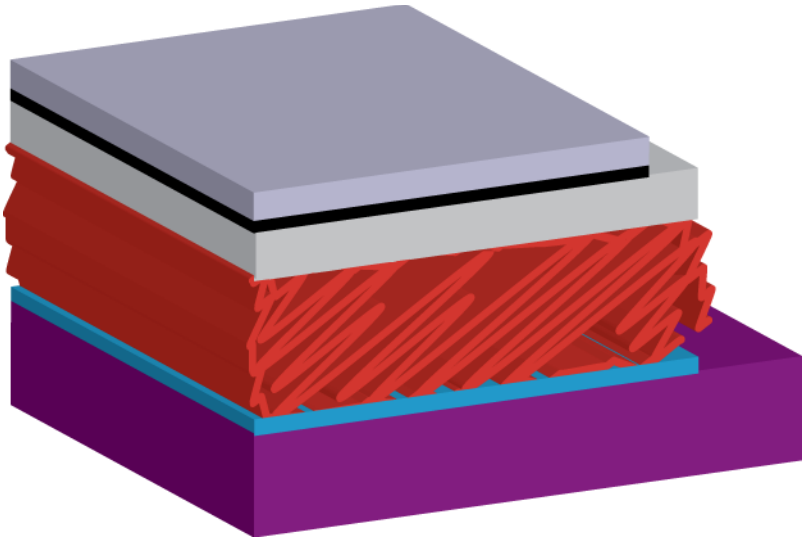


Figure 7: A Typical bulk heterojunction OPV. Light enters through the top layer, which is glass, onto which the next layer, a transparent conductive layer, often indium tin oxide, has been coated. A hole-transport layer, light grey, is often included, followed by a layer consisting of the donor and acceptor mixed together. A hole-blocking layer, cyan, may be included before the bottom metal cathode, purple. Not to scale.

1.5. References

1. Chiang, C. K.; Fincher, C. R.; Park, Y. W.; Heeger, A. J.; Shirakawa, H.; Louis, E. J.; Gau, S. C.; MacDiarmid, A. G., *Phys. Rev. Lett.* **1977,** *39* (17), 1098.

2. Streetman, B. G.; Banerjee, S. K., *Solid State Electronic Devices*. 6 ed.; Pearson Prentice Hall Upper Saddle River, NJ, 2006.

3. Kraft, A.; Grimsdale, A. C.; Holmes, A. B., *Angewandte Chemie International Edition in English* **1998,** *37* (4), 403-428.

4. Schluter, A. D., Synthesis of Poly(para-phenylene)s. In *Handbook of Conducting Polymers*, 2nd ed.; Skotheim, T. A., Elsenbaumer,Ronald L., Reynolds, John R., Ed. Marcell Dekker: New York, 1998; pp 209-224.

5. Reddinger, J. L.; Reynolds, J. R., *Adv. Polym. Sci.* **1999,** *145*, 57-122.

6. Roncali, J., *Chem. Rev.* **1992,** *92* (4), 711-38.

7. Moratti, S. C., The Chemistry and Uses of Polyphenylenevinylenes. In *Handbook of Conducting Polymers*, 2nd ed.; Skotheim, T. A., Elsenbaumer, Ronald L., Reynolds, John R., Ed. Marcell Dekker: New York, 1998; pp 343-361.

8. Bredas, J. L.; Street, G. B., *Acc. Chem. Res.* **1985,** *18* (10), 309-315.

9. Skotheim, T. A.; Reynolds, J. R., *Handbook of conducting polymers*. 3rd ed / edited by Terje A. Skotheim and John Reynolds. ed.; London: Boca Raton, Fla., 2007; p (various pagings).

10. Elsenbaumer, R.; Jen, K.; Oboodi, R., *Synth. Met.* **1986,** *15* (2), 169-174.

11. Yamamoto, T.; Takagi, M.; Kizu, K.; Maruyama, T.; Kubota, K.; Kanbara, H.; Kurihara, T.; Kaino, T., *J. Chem. Soc., Chem. Commun.* **1993,** (9), 797-8.

12. Flory, P. J., *J. Am. Chem. Soc.* **1942,** *64* (9), 2205-2212.

13. Granek, R.; Cates, M., *The Journal of chemical physics* **1992,** *96*, 4758.

14. Bras, J.; Guillerez, S.; Pepin-Donat, B., *Chem. Mater.* **2000,** *12* (8), 2372-2384.

15. Daoud, M.; Cotton, J., *JPhys* **1982,** *43* (3), 531-538.

16. Wautelet, P.; Moroni, M.; Oswald, L.; Le Moigne, J.; Pham, A.; Bigot, J. Y.; Luzzati, S., *Macromolecules* **1996,** *29* (1), 446-55.

17. Qian, G.; Dai, B.; Luo, M.; Yu, D.; Zhan, J.; Zhang, Z.; Ma, D.; Wang, Z. Y., *Chem. Mater.* **2008,** *20* (19), 6208-6216.

18. Ellinger, S.; Graham, K. R.; Shi, P.; Farley, R. T.; Steckler, T. T.; Brookins, R. N.; Taranekar, P.; Mei, J.; Padilha, L. A.; Ensley, T. R., *Chem. Mater.* **2011,** *23* (17), 3805-3817.

19. Martin, R. E.; Diederich, F., *Angew. Chem. Int. Ed.* **1999,** *38* (10), 1350-1377.

20. Chen, A. C.; Culligan, S. W.; Geng, Y.; Chen, S. H.; Klubek, K. P.; Vaeth, K. M.; Tang, C. W., *Adv. Mater.* **2004,** *16* (9-10), 783-788.

21. Meier, H.; Stalmach, U.; Kolshorn, H., *Acta Polym.* **1997,** *48* (9), 379-384.

22. van Mullekom, H. A. M.; Vekemans, J. A. J. M.; Havinga, E. E.; Meijer, E. W., *Mater. Sci. Eng., R* **2001,** *32* (1), 1-40.

23. Brockmann, T. W.; Tour, J. M., *J. Am. Chem. Soc.* **1995,** *117* (16), 11.

24. Zhang, Q. T.; Tour, J. M., *J. Am. Chem. Soc.* **1997,** *119* (21), 5065-5066.

25. Natsuhara, T., *Kako Gijutsu (Processing Technology)* **1996,** *31* (9), 566.

26. Bourbigot, S.; Flambard, X., *Fire Mater.* **2002,** *26* (4-5), 155-168.

27. Seely, L.; Zimmerman, M.; McLaughlin, J., *Adv. Space Res.* **2004,** *33* (10), 1736-1740.

28. Ishikawa, H.; Chen, Q.; Bin, Y.; Komatsu, K.; Matsuo, M., *JMatS* **2007,** *42* (18), 7772-7779.

29. Kuroki, T.; Tanaka, Y.; Hokudoh, T.; Yabuki, K., *J. Appl. Polym. Sci.* **1997,** *65* (5), 1031-1036.

30. Wolfe, J. F.; Arnold, F. E., *Macromolecules* **1981,** *14*, 909-915.

31. Mike, J. F.; Makowski, A. J.; Mauldin, T. C.; Jeffries-El, M., *J. Polym. Sci., Part A: Polym. Chem.* **2010,** *48* (6), 1456-1460.

32. Ulrich, D. R., *MCLC* **1988,** *160* (1), 1-31.

33. Reinhardt, B. A.; Unroe, M. R.; Evers, R. C., *Chem. Mater.* **1991,** *3*, 864-71.

34. Jenekhe, S. A., *Adv. Mater.* **1995,** *7* (3), 309-311.

35. Yu, S. C.; Gong, X.; Chan, W. K., *Macromolecules* **1998,** *31* (17), 5639-5646.

36. Mike, J. F.; Nalwa, K.; Makowski, A. J.; Putnam, D.; Tomlinson, A. L.; Chaudhary, S.; Jeffries-El, M., *PCCP* **2011,** *13* (4), 1338-1344.

37. Simonian, N.; Mayr, A.; Likharev, K. K. In *Design and simulation of molecular single-electron resistive switches*, Nanotechnology (IEEE-NANO), 2012 12th IEEE Conference on, IEEE: 2012; pp 1-6.

38. Ahmed, E.; Subramaniyan, S.; Kim, F. S.; Xin, H.; Jenekhe, S. A., *Macromolecules* **2011,** *44* (18), 7207-7219.

39. Ahmed, E.; Kim, F. S.; Xin, H.; Jenekhe, S. A., *Macromolecules* **2009,** *42* (22), 8615-8618.

40. Usta, H.; Lu, G.; Facchetti, A.; Marks, T. J., *J. Am. Chem. Soc.* **2006,** *128* (28), 9034-9035.

41. Mas-Torrent, M.; Rovira, C., *Chem. Soc. Rev.* **2008,** *37* (4), 827-838.

42. Dimitrakopoulos, C. D.; Malenfant, P. R. L., *Adv. Mater.* **2002,** *14* (2), 99-117.

43. Wu, W.; Liu, Y.; Zhu, D., *Chem. Soc. Rev.* **2010,** *39* (5), 1489-1502.

44. Friend, R. H.; Gymer, R. W.; Holmes, A. B.; Burroughes, J. H.; Marks, R. N.; Taliani, C.; Bradley, D. D. C.; Dos Santos, D. A.; Bredas, J. L.; Logdlund, M.; Salaneck, W. R., *Nature* **1999,** *397* (6715), 121-128.

45. Tang, C. W.; VanSlyke, S. A., *Appl. Phys. Lett.* **1987,** *51* (12), 913-915.

46. Kulkarni, A. P.; Tonzola, C. J.; Babel, A.; Jenekhe, S. A., *Chem. Mater.* **2004,** *16* (23), 4556-4573.

47. Wen, S.-W.; Lee, M.-T.; Chen, C. H., *J. Display Tech.* **2005,** *1* (1), 90.

48. Shaheen, S.; Jabbour, G.; Morrell, M.; Kawabe, Y.; Kippelen, B.; Peyghambarian, N.; Nabor, M.-F.; Schlaf, R.; Mash, E.; Armstrong, N., *J. Appl. Phys.* **1998,** *84* (4), 2324-2327.

49. Green, D. G., *J. Physiol.* **1968,** *196* (2), 415-429.

50. Vak, D.; Lim, B.; Lee, S.-H.; Kim, D.-Y., *Org. Lett.* **2005,** *7* (19), 4229-4232.

51. Thompson, B. C.; Frechet, J. M. J., *Angew. Chem. Int. Ed.* **2008,** *47* (1), 58-77.

52. Coakley, K. M.; McGehee, M. D., *Chem. Mater.* **2004,** *16* (23), 4533-4542.

53. Scharber, M.; Mühlbacher, D.; Koppe, M.; Denk, P.; Waldauf, C.; Heeger, A.; Brabec, C., *Adv. Mater.* **2006,** *18* (6), 789-794.

54. Scharber, M. C.; Mühlbacher, D.; Koppe, M.; Denk, P.; Waldauf, C.; Heeger, A. J.; Brabec, C. J., *Adv. Mater.* **2006,** *18* (6), 789-794.

55. Hagfeldt, A.; Boschloo, G.; Sun, L.; Kloo, L.; Pettersson, H., *Chem. Rev.* **2010,** *110* (11), 6595-6663.

56. Grätzel, M., *J. Photochem. Photobiol. C: Photochem. Rev.* **2003,** *4* (2), 145-153.

57. Petritsch, K.; Dittmer, J. J.; Marseglia, E. A.; Friend, R. H.; Lux, A.; Rozenberg, G. G.; Moratti, S. C.; Holmes, A. B., *Sol. Energy Mater. Sol. Cells* **2000,** *61* (1), 63-72.

58. So, Y.-H.; Martin, S. J.; Bell, B.; Pfeiffer, C. D.; Van Effen, R. M.; Romain, B. L.; Lefkowitz, S. M., *Macromolecules* **2003,** *36* (13), 4699-4708.

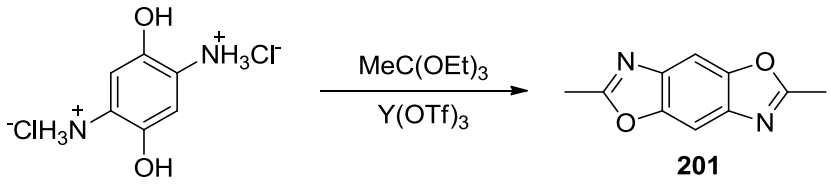
CHAPTER 2. SYNTHESIS OF SYMMETRIC D-Π-A-Π-D BENZOBISOXAZOLE ORGANIC CHROMOPHORES

2.1. Introduction

A series of chromophoric dyes was synthesized and characterized to determine the effect of electron-donating strength on the electric and optical properties vinylene-linked *t*-BBOs, as summarized in the paper published on the topic. [1] The goal was to synthesize small molecules with a D-π-A-π-D model, as has been done previously,[2-3] with benzobisoxazole as the core acceptor, and vinylene linkages as a π-spacer. The purpose of the spacer is to reduce steric strain in the system, thereby diminishing torsion along the conjugated backbone that would otherwise cause decreased planarity, and therefore effective conjugation.[4-6]

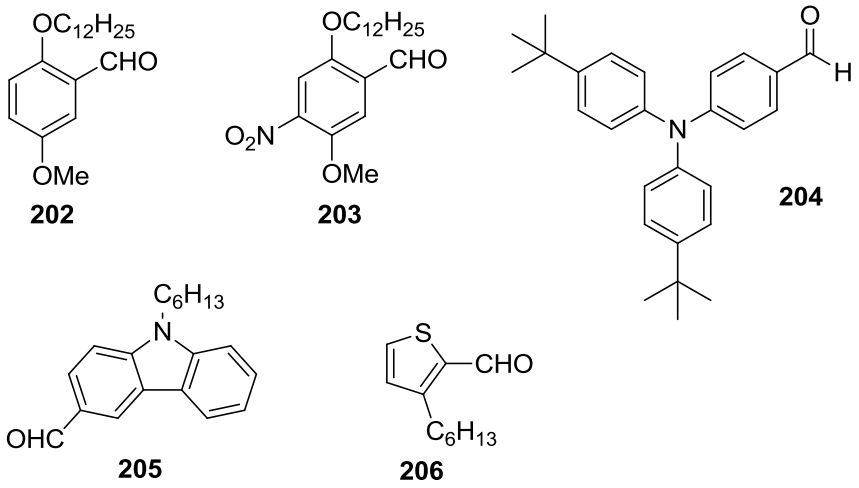
2.2. Synthetic Approach

The presence of the vinylene linkages allows for the simple introduction of aromatic moieties into the molecule, as a base-catalyzed condensation, in this case, a Knoevenagel condensation,[7] with an aldehyde can be used to make the conjugated system. 2,6-Dimethyl-*t*-BBO (**201**), which has been synthesized previously (Scheme 1),[8] was chosen as the core substrate as the methyl groups can be deprotonated by base to form a resonance-stabilized anion,[9] which is capable of condensing with an aldehyde to produce a conjugated vinylene.



Scheme 1: Synthesis of 2,6-dimethyl-*t*-BBO from DAHQ.

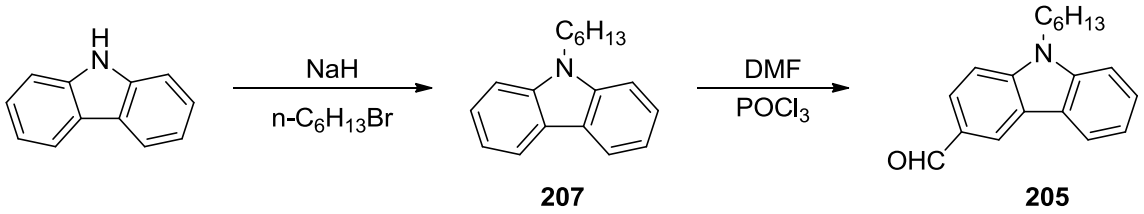
To test the effect of donor strength on the optical and physical properties of *t*-BBOs, a variety of aromatic aldehydes (**202 – 206**) were synthesized or obtained from colleagues, which are shown in Scheme 2.



Scheme 2: The aromatic aldehydes used in the Knoevenagel condensation with **201**.

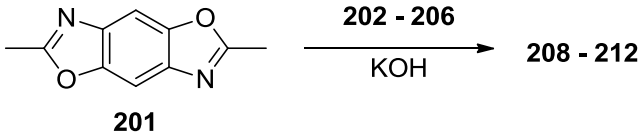
9-Hexylcarbazole-3-carboxaldehyde (**205**) was obtained from 9-hexylcarbazole (**207**), which was in turn obtained from carbazole and *n*-hexyl bromide in high yield after deprotonation with sodium hydride (Scheme 3). The conversion to the

carboxaldehyde was previously reported in literature,[10] though significant improvement in yield was obtained by slight changes in the procedure.

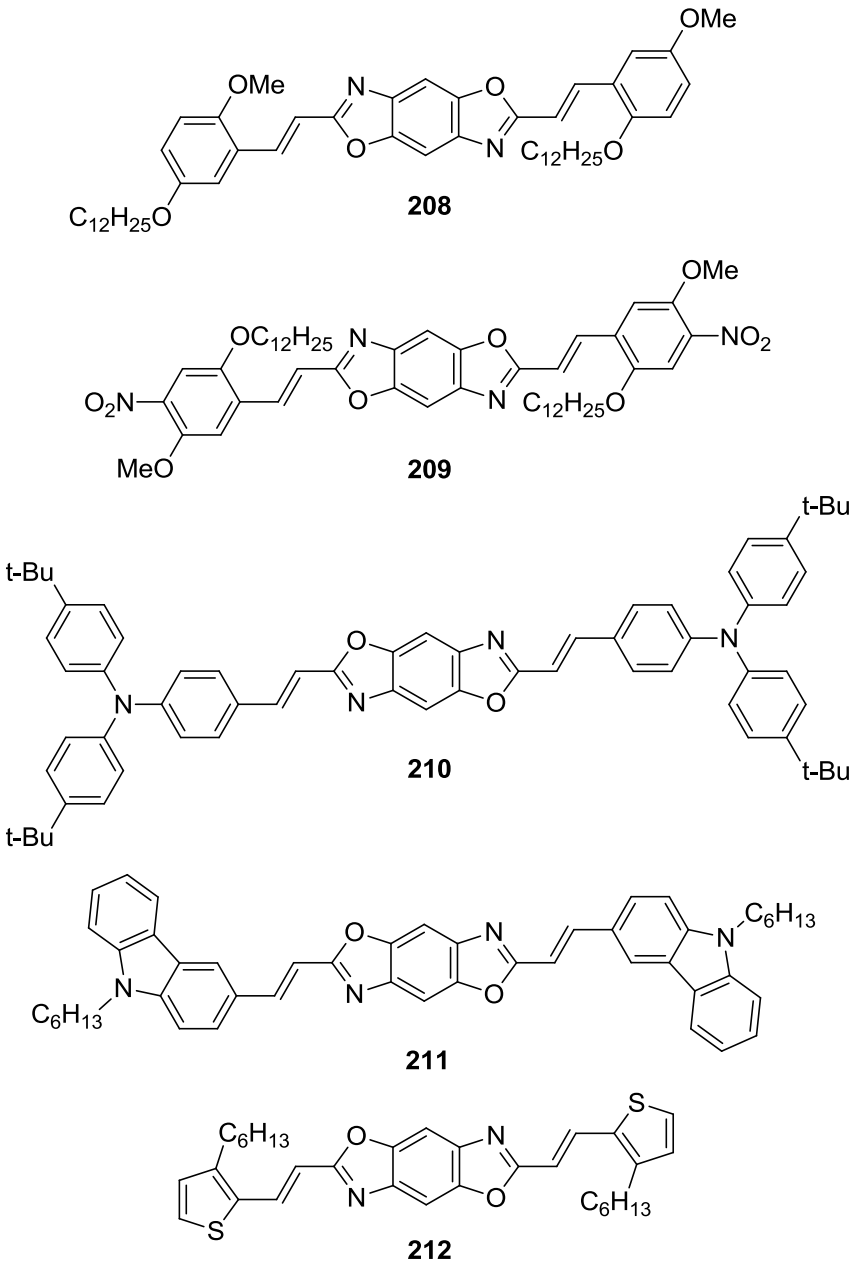


Scheme 3: Synthesis of 9-hexylcarbazole-3-carboxaldehyde.

The selected aldehydes were dissolved in DMF, and powdered potassium hydroxide was added to begin the deprotonation. The aldehyde was then added neat (Scheme 4), and the reaction was permitted to proceed at room temperature for fifteen minutes, before the product was precipitated out by addition of water, followed by rinsing and recrystallization from ethanol to give the disubstituted dyes, shown in Scheme 5.



Scheme 4: The synthesis of benzobisoxazole chromophores **208-212**.



Scheme 5: The benzobisoxazole dyes which were produced and characterized.

2.3. Optical Properties and Solvatochromism

The optical properties of the synthesized dyes were studied with UV-Vis absorbance and solution fluorescence spectroscopy. Figure 8 shows the absorbance and emission spectra of the dyes in chloroform, while numerical information regarding the spectra is shown in Table 1. All of the dyes had small absorbance bands below 350 nm, due to the absorbance of the *t*-BBO core,[11] and all had maximum absorbances between 403-453 nm, as well has high extinction coefficients up to nearly 90,000 M^{-1} cm^{-1}. Compounds **208**, **210**, and **211** all had fairly high fluorescent quantum yields, while **209** had a very low quantum yield, perhaps due to intramolecular charge transfer in the excited state as a result of the electron-deficient nitro group on the aromatic ring.[12] Dye **212** also possessed a relatively low quantum yield, which is presumably due to the presence of sulfur on the aromatic ring. Sulfur is known to promote the quantumly forbidden intersystem crossing $S^1 \rightarrow T^1$ via the heavy atom effect, which causes orbital mixing.[13] All dyes, when excited in their main absorption band, showed a significant Stokes shift, with the triphenylamine derivative **210** possessing a difference of nearly 100 nm between its absorption and emission maxima.

Compound	λ_{abs} max (nm)	ε_{max} (L mol^{-1} cm^{-1})	λ_{ems} max (nm)	Φ_{fl}	Stokes shift (nm)	Onset (nm)	Decomp (ºC)
208	403	58300	476	0.58	73	450	333
209	453	43600	502	0.002	49	509	314
210	431	81500	530	0.64	99	482	389
211	422	88900	470	0.25	48	469	364
212	410	65600	479	0.067	69	451	311

Table 1: The optical data of BBO chromophores **208-212**.

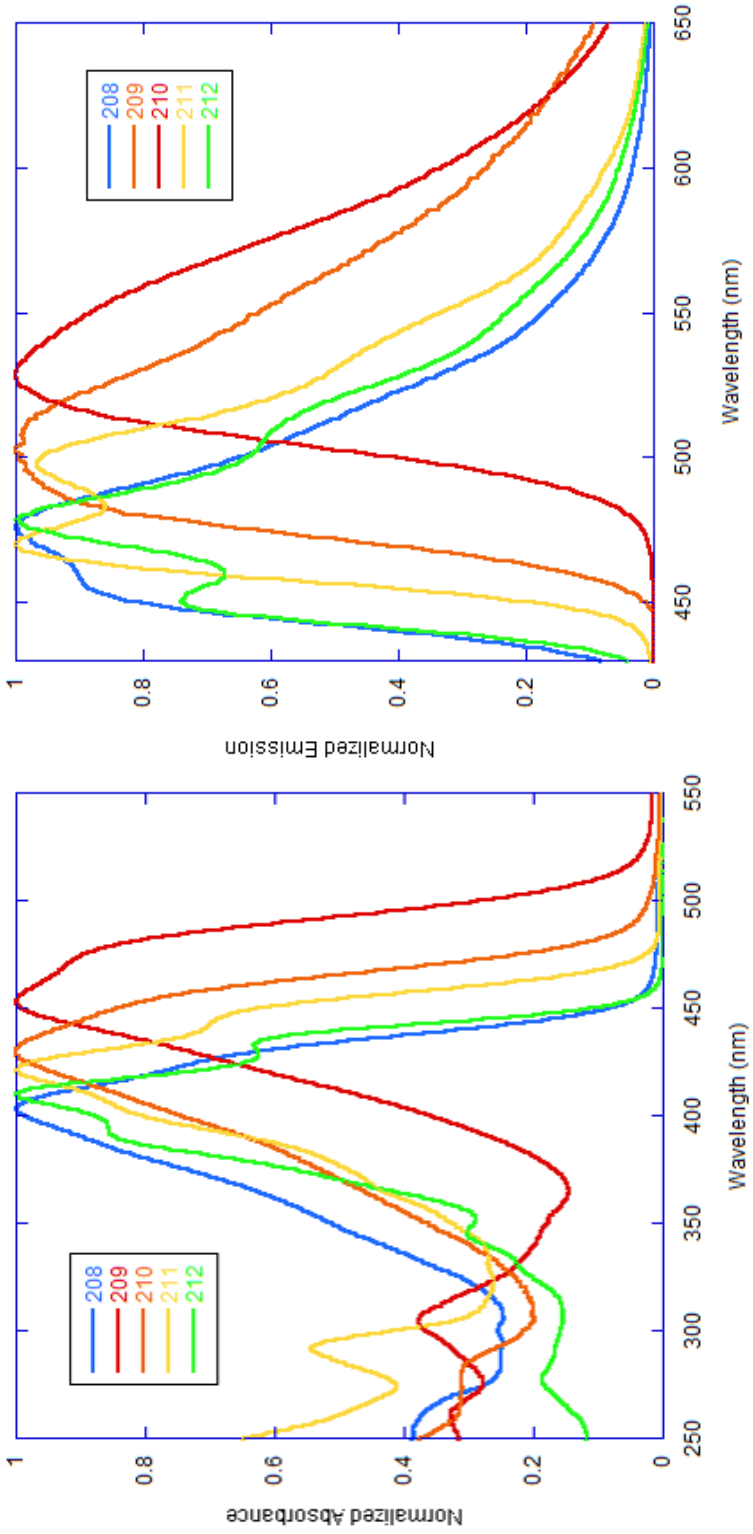


Figure 8: The UV-Vis absorption and fluorescence emission spectra of *t*-BBO dyes **208-212** in chloroform.

The nitrogen-containing **210** and **211** showed the lowest onsets, likely due to the strongly-donating nature of the heteroatom, in addition to the larger extent of conjugation in the molecule, while **208** showed a significantly lower onset. The nitro-containing **209**, despite having an electron-withdrawing group, possessed the highest onset of 509 nm.

Dyes **208**, **210**, and **211** were also selected for use in solvatochormatic studies[14] (Figure 9 and Figure 10) due to their high fluorescent quantum yields compared to **209** and **212**. Compound **210** showed an astounding bathochromic shift of 96 nm upon increasing the solvent polarity from hexane to methanol, with emission maxima at 475 and 571, respectively. **208** and **211** showed slightly less impressive shifts of 20 nm and 53 nm when increasing the solvent polarity, though both of these compounds appear to have some aggregation in butanol, as determined by the presence of a small shoulder in the emission spectra caused by eximer formation.[15]

The large difference in solvatochromism between the triphenylamine dye **210** and the carbazole dye **211** is likely due to greater degrees of freedom of the former.[16] The triphenylamine moiety likely exists as a propeller shape in solution,[17-18] as opposed to the planar carbazole group. This decreased planarity increases the importance of solvent polarity, as the solvent cage must reorient itself around the excited molecule, thereby reducing the emitted photons' energy in highly polar solvents.[19]

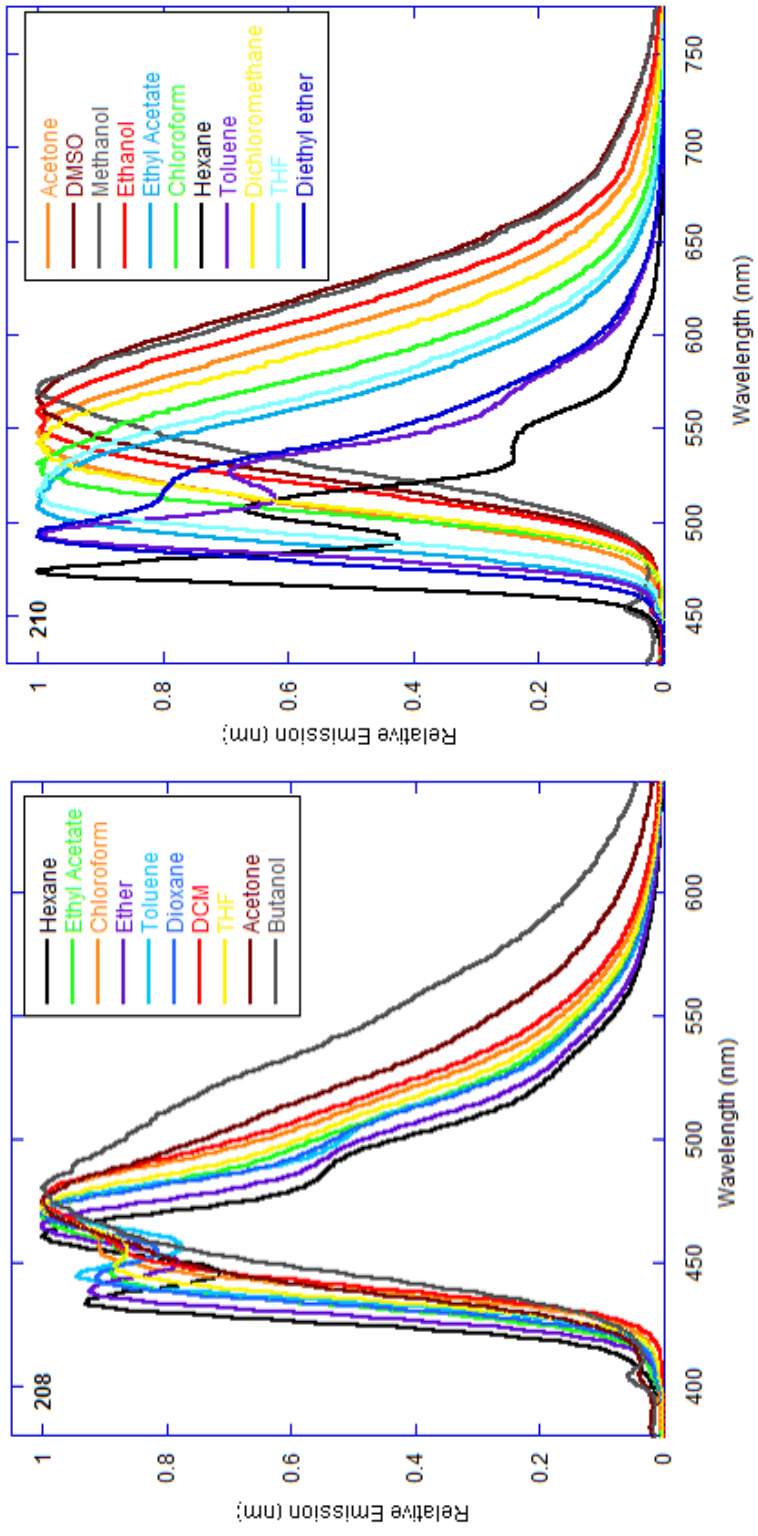


Figure 9: The solvatochromism the emission spectra of **208** and **210** in various solvents. The emission maximum shifts to higher wavelengths in more-polar solvents.

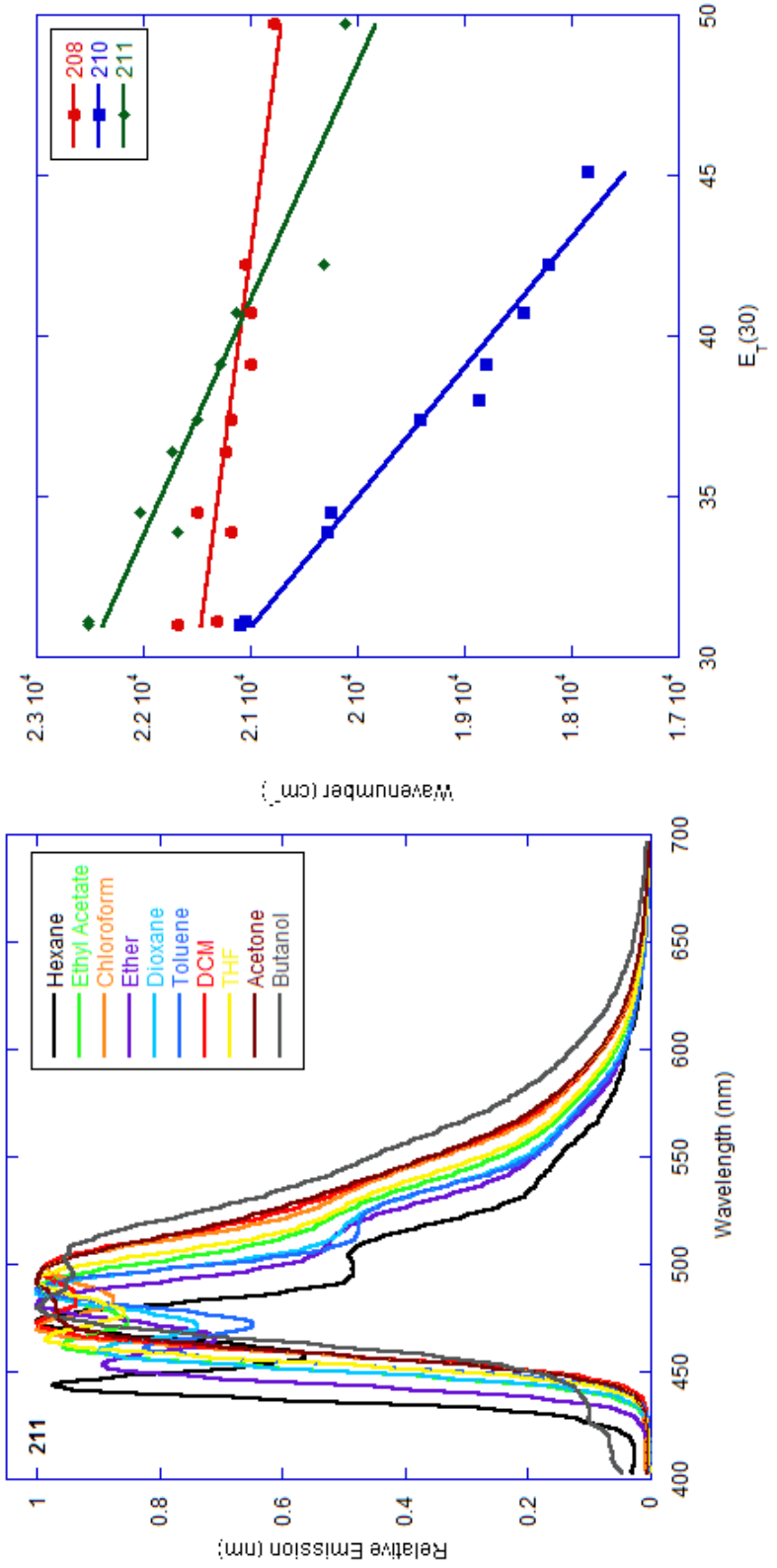


Figure 10: The solvatochromism the emission spectra of **211** in various solvents (left). The emission maximum shifts to higher wavelengths in more-polar solvents. The $E_t(30)$ plot shows how solvent-dependent the emission spectrum is for **208**, **210**, and **211**.

Rearrangement of the solvent cage around the excited state of the dyes is also readily apparent by observing the shape of the emission spectra. In the nonpolar solvents hexane, as well as those solvents with only slight polarity, such as diethyl ether or toluene, defined structures can be seen in the emission spectra due to the separate vibrational energies. However, this structure is diminished in the more-polar solvents such as THF and ethyl acetate, and lost completely upon dissolution in the most polar solvents, like methylene chloride or acetone.

A quantitative measurement of the dependence of the emission spectra on the solvent polarity was made by plotting the emission maxima in wavenumbers against the $E_t(30)$ solvent parameter[20] and finding the line of best fit (Figure 10).[19] A linear regression gave slopes of 40, 247, and 136 cm^{-1} for **208**, **210**, and **211**, confirming the great effect of solvent polarity on the emission spectrum on 210.

2.4. Electronic Properties

The electrical properties of the benzobisoxazole dyes were explored experimentally, and compared to theoretical values. Because the synthesized dyes have HOMO values outside of the solvent level of tetrabutylammonium tetrafluoroborate/acetonitrile, ultraviolet photoelectron spectroscopy was used to provide an absolute HOMO energy level.[21] Experimental band-gaps were determined by from the onset values of the absorption spectra of the dyes in chloroform, and the LUMO was determined by subtracting the band-gap from the HOMO.

Frontier orbitals were generated using B3LYP/6-31G* density functional theory, performed by Dr. Aimeé L. Tomlinson using Gaussia09 through the National Science

Foundation's Extreme Science and Engineering Discovery Environment on Sand Diego Supercomputer Center's Trestles cluster. Experimental and theoretical data are outlined in Table 2, while the calculated molecular orbitals are shown in **Figure 11**.

Compound	HOMO		LUMO		E_g (eV)	
	Exp.	Theory	Exp.	Theory	Exp.	Theory
208	5.77	5.00	3.01	1.95	2.76	2.78
209	5.99	5.68	3.55	2.93	2.44	2.50
210	5.37	4.70	2.79	1.86	2.58	2.51
211	5.25	5.17	2.60	2.54	2.65	1.72
212	5.46	5.13	2.81	2.17	2.75	2.75

Table 2: The theoretical and experimental HOMO and LUMO values for dyes **208-212**, as well as the band gaps, obtained from the UV-Vis spectra.

Discounting **209**, the HOMO level became more stabilized as the strength of the donor increased, from the dialkoxybenzene in **208** to the carbazole in **211**, and the LUMO decreased in a similar manner. It is interesting to note that, for most dyes, the experiment and theoretical band gaps are in good agreement. The notable exception to this is **211**, the dye with carbazole moiety, which had a much higher band gap that predicted. It is possible that these deviations occurred because the computer –optimized structures of these dyes do not match up with those found in practice. Twisting of the conjugated system would lead to a higher-energy band gap that predicted,[22] and this may be brought on by the presence of the alkyl chains used for solubility.

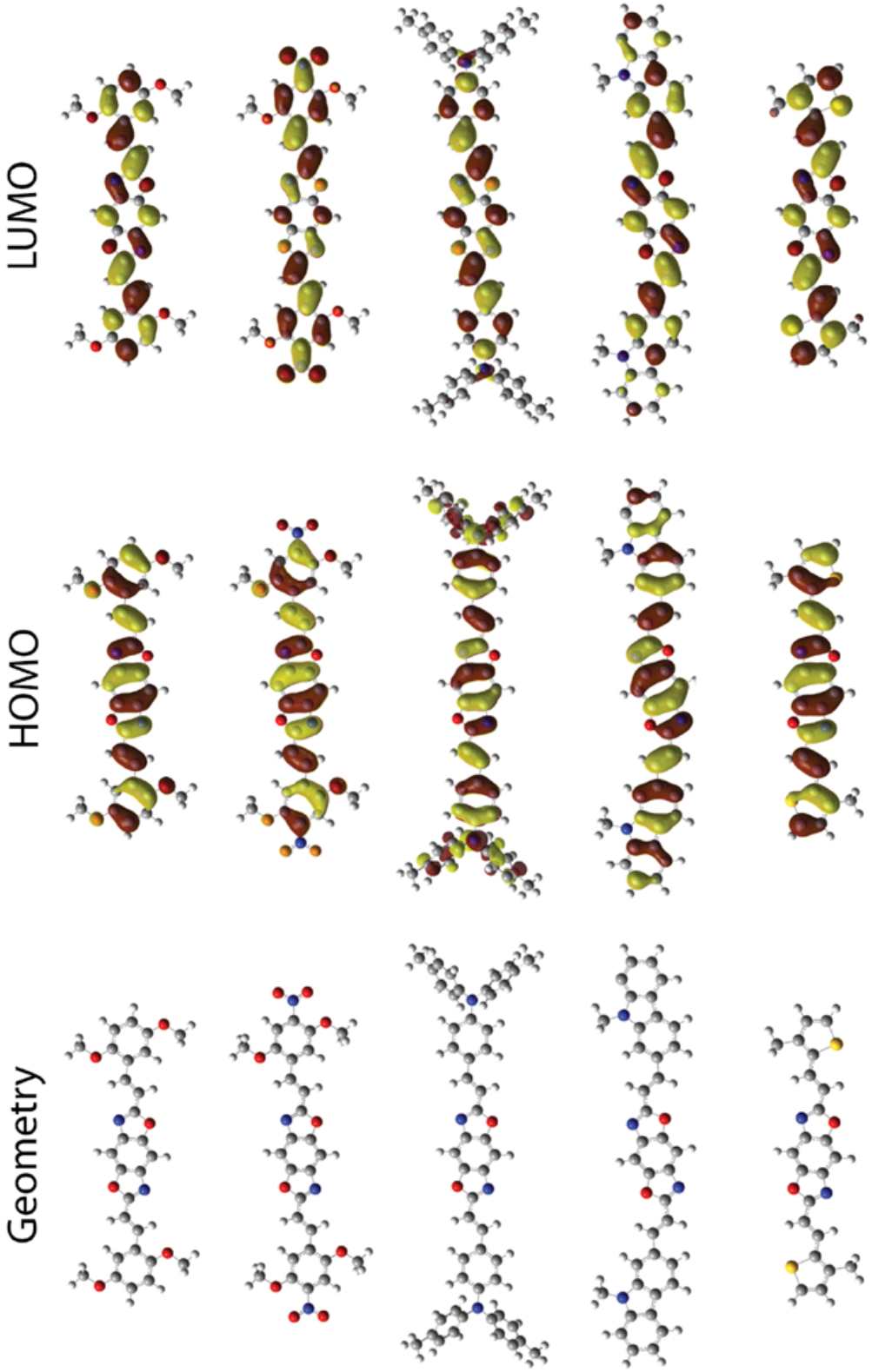


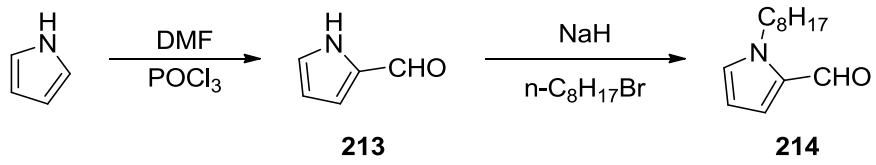
Figure 11: HOMO and LUMO orbitals for symmetric *t*-BBO dyes. Note that alkyl chains are truncated for purposes of computing. Molecular orbitals correspond to **208-212** from top to bottom.

Benzobisoxazole **209** was analogous to this trend due to the presence of the nitro-group, which caused the aromatic substituent to act as more of an acceptor than a donor, and thus, the resultant dye was not of the D-π-A-π-D architecture, causing it to behave in a manner inconstant with the other benzobisoxazoles. Evidence of the withdrawing powers of the nitro- group can be seen when looking at Hammett parameters, which are generally used for the determination of the effects of *meta* and *para* substitutions on benzoic acid derivatives.[23] However, Hammett parameters are still useful here to determine the relative strengths of the electron -inductive and resonance effects between the aryl substituents in **208** and **209**. The nitro- group is strongly electron-withdrawing ($\sigma_{para} = 0.78$) , while the methoxy group is a fairly weak electron-donating group when *para* ($\sigma = -0.27$), and slightly electron-withdrawing when *meta* ($\sigma = 0.12$). While, due to sterics, there are no *ortho* values, it can be assumed that the resonance effects will be similar to the σ_{para} value. This indicates that the aromatic ring is more electron-withdrawing than is benzene, and is therefore more of an acceptor in nature.

Upon looking at the molecular orbitals in **Figure 11**, it is evident that the chromophores **210** and **211** show donor-acceptor traits, as can be seen in the movement of electron density moving from triphenylamine or carbazole substituent, respectively, in the HOMO, to the relatively electron-poor benzobisoxazole core in the LUMO. **208**, **209**, and **212** did not show this movement, and instead only experienced a slight redistribution of electron density.

2.5. Results and Discussion

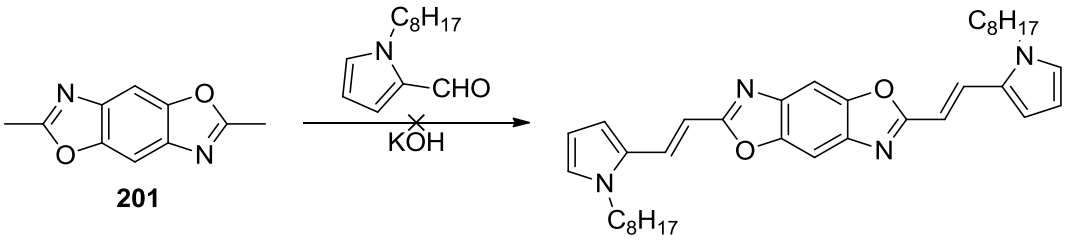
The attempt to make several other benzobisoxazoles for the purpose of comparison was met with failure. A pyrrole-derivative would have provided an electron-rich, nitrogen-containing heterocycle. This substituent would serve as an analogous compound to **211**, allowing for the effects of conjugation to be determined independently from the effects of the presence of a heteroatom. To this end, pyrrole was converted to pyrrole-2-carboxaldehyde (**214**) via a Vilsmeier-Haack reaction, which was then used to make *N*-octlypyrrole-2-carboxaldehyde (**214**) via deprotonation followed by alkylation.



213 **214**

Scheme 6: The synthesis of *N*-octlypyrrole-2-carboxaldehyde.

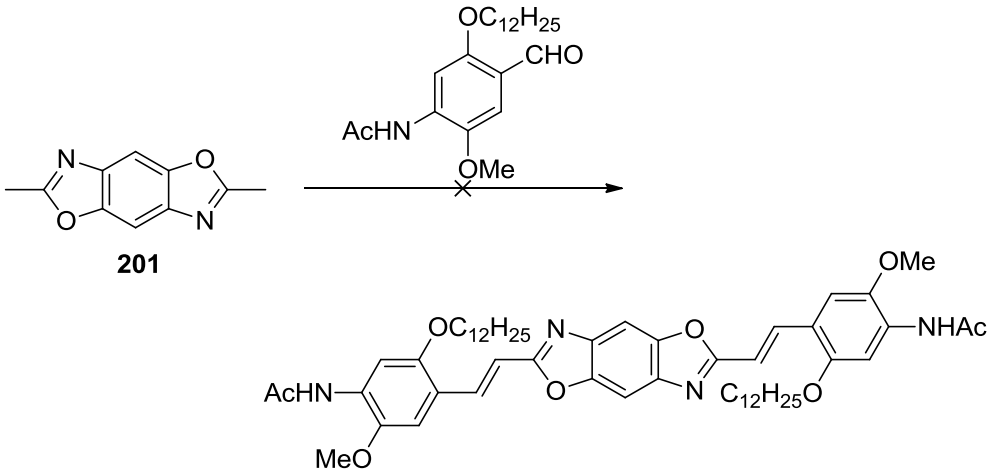
Unfortunately, upon the attempted condensation of **214** with **201**, no desired product was obtained despite several attempts (Scheme 7). It is hypothesized that the pyrrole may have polymerized or otherwise decomposed in the presence of the strongly basic conditions.



201

Scheme 7: The disubstituted benzobisoxazole bearing pyrrole could not be synthesized.

4-Acetimido-2-(dodecyloxy)-5-methoxybenzaldehyde was also an attractive candidate for use, as the presence of acetamido- group would cause the ring to serve as a more-electron–rich version of aldehyde **202**. Unluckily, this reaction also failed to produce the desired outcome (Scheme 8), which may be due to amide cleavage to form the free amine, which would then be susceptible to oxidation.



Scheme 8: The failed synthesis of an electron-rich version of **208**.

Overall, it was shown that diarylvinylene benzobisoxazoles are capable of showing high absorbances in the visible spectrum, as well as potentially high quantum yields, and their emission spectra are dependent upon solvent polarity. These compounds can be easily made from relatively simple starting materials, and depending on the aldehyde used, the HOMO and LUMO levels are easily varied to allow for the tuning of the band gaps, which would allow for the development of materials which are promising for use in OLEDs or OPVs.

2.6. Experimental Methods

Unless otherwise noted, all starting materials were purchased from commercial sources and used without further purification. All reactions were carried out under open air unless otherwise noted. Nuclear magnetic resonance spectra were obtained on a 400 MHz spectrometer (^{1}H at 400 MHz and ^{13}C at 100 MHz). ^{1}H NMR samples were referenced internally to residual protonated solvent. ^{13}C NMR samples were referenced to the central carbon peak of $CDCl_3$. In both instances, chemical shifts are given in δ relative to solvent. Coupling constants are reported in Hz. Fluorescence spectroscopy and UV-Visible spectra were obtained using solutions in $CHCl_3$, with concentrations of approximately 50 μM. Quantum yield measurements were taken using coumarin 152 in hexane as a standard (excitation at 375 nm; emission was taken from 390-700 nm; Φ = 1.00).[24] All values were corrected for the differences in the refractive index of the solvent using the following equation:

$$\boldsymbol{\Phi_X = \Phi_S \left(\frac{\int I_X}{\int I_S}\right)\left(\frac{A_S}{A_X}\right)\left(\frac{\eta_X^2}{\eta_S^2}\right)},$$

where *S* and *X* stand for the standard and the unknown, respectively, Φ is the quantum yield, $\int I$ is the integral of the fluorescence spectra, *A* is the absorbance at the excitation wavelength, and η is the refractive index of the solvents.

9-Hexyl-9*H*-carbazole (207): 9*H*-Carbazole (recrystallized from toluene/hexane) (16.72 g, 100 mmol) was dissolved in THF (100 mL) and cooled to 0 ºC. 60% Sodium hydride in mineral oil suspension (4.80 g, 120 mmol) was added, evolving hydrogen gas, and the solution was warmed to room temperature. 1-Bromohexane (33.01 g, 200 mmol)

was added, and the solution was refluxed for 12 hours. The reaction was quenched with 1M HCl (150 mL) and the organic layer was washed three times with brine (50 mL) and dried over sodium sulfate. The solvent was removed under vacuum, and the product was recrystallized from boiling methanol, producing white, columnar crystals. (23.16 g, 92% yield). ^{1}H NMR ($CDCl_3$): 8.11 (d, 2H), 7.48 (d, 2H), 7.43 (d, 2H), 7.22 (t, 2H), 4.31 (t, 2H), 1.88 (m, 2H), 1.44–1.27 (m, 6H), 0.87 (t, 3H). ^{13}C NMR ($CDCl_3$): 140.5, 125.7, 123.0, 120.4, 118.8, 108.8, 43.0, 31.7, 29.0, 27.0, 22.7, 14.2.

9-Hexyl-9*H*-carbazole-3-carboxaldehyde (205): DMF (1.75 g, 24.0 mmol) was cooled to 0 ºC, and phosphorus oxychloride (3.53 g, 23.0 mmol) was added drop-wise via an addition funnel over 15 minutes, keeping the temperature below 5 ºC. The reaction was stirred for 1 hour at 0 ºC, and then chlorobenzene (30 mL) was added. 9-Hexylcarbazole 5 (5.03 g, 20 mmol) dissolved in chlorobenzene (30 mL) was added drop-wise over 1 hour. The reaction was refluxed for 2 hours, and then at 75 ºC for 6 hours. The reaction was then quenched by the rapid addition of sodium acetate (100 g) dissolved in water (100 mL). The aqueous layer was extracted three times with ether (30 mL) and the combined organic layers were washed with saturated sodium bicarbonate solution until production of carbon dioxide ceased. The organic layer was dried over anhydrous sodium carbonate, boiled with activated carbon to remove colored impurities, and the solvent was removed by vacuum. The solid was recrystallized from heptane to produce beige, fibrous crystals. (5.22 g, 91% yield); mp: 53–54 °C ^{1}H NMR ($CDCl_3$): 10.06 (s, 1H), 8.52 (s, 1H), 8.10 (d, 1H), 7.97 (d, 1H), 7.52 (t, 1H), 7.41 (t, 1H), 7.38 (t, 1H), 7.30 (t, 1H), 4.21 (t, 2H), 1.82 (m, 2H) 1.41–1.27 (m, 6H), 0.88 (t, 3H). ^{13}C NMR ($CDCl_3$):

191.7, 144.0, 141.1, 128.4, 127.0, 126.7, 122.97, 122.93, 120.7, 120.3, 109.4, 108.9, 43.3, 31.5, 28.9, 26.9, 22.6, 14.0.

General Method of Symmetric Dye Synthesis: Potassium hydroxide (1.35 g, 24.0 mmol) was added to DMF (12 mL) and allowed to stir under open air for 15 minutes at room temperature. 2,6-Dimethylbenzo[1,2-d;4,5-d']bisoxazole 1 (376 mg, 2.00 mmol) was then added, turning the solution yellow, followed promptly by the addition of an aryl carboxaldehyde (3 eq., 6.00 mmol). The solution was then allowed to stir for 3 hours, after which the reaction was quenched with 1 M HCl solution (24 mL), causing the product to precipitate. The product was then filtered, and washed with water, followed by cold methanol. The products were then recrystallized from hot ethanol.

2,6-Bis((E)-2-dodecyloxy-5-methoxystyryl)benzo[1,2-d;4,5-d']bisoxazole (208): Bright yellow powder (0.96 g, 61% yield). mp: 91 °C. ^{1}H NMR ($CDCl_3$): 8.01 (d, J = 16.2, 2H), 7.85 (s, 2H), 7.49 (s, 2H), 7.35 (d, J = 16.2, 2H), 7.27 (s, 2H), 4.10 (t, 4H), 4.00 (s, 6H), 1.94 (m, 4H), 1.53 (m, 6H), 1.24 (m, 32H), 0.86 (t, 6H). ^{13}C NMR ($CDCl_3$): 164.6, 153.0, 152.1, 148.2, 140.6, 135.4, 131.2, 124.8, 117.5, 115.0, 113.7, 100.3, 69.4, 68.7, 31.9, 29.7, 29.23, 29.62, 29.60, 29.59, 29.41, 29.35, 26.1, 26.0, 22.7, 14.1. HRMS (+ESI): m/z calcd for $C_{50}H_{69}N_2O_6$ $[M+H]^+$, 793.5150; found 793.5153.

2,6-Bis((E)-2-dodecyloxy-5-methoxy-4-nitrostyryl)benzo[1,2-d;4,5-d']bisoxazole (208): Brick red powder (1.12 g; 63% yield). mp: 158 °C ^{1}H NMR ($CDCl_3$): 8.02 (d, J = 16.0, 2H), 7.85 (s, 2H), 7.49 (s, 2H), 7.30 (d, J = 16.0, 2H), 4.10 (t, 4H), 4.00 (s, 6H), 1.94 (m, 4H), 1.57 (m, 6H), 1.24 (m, 32H), 0.85 (t, 6H). ^{13}C NMR ($CDCl_3$): 163.8, 150.9, 148.3, 147.3, 140.9, 139.4, 133.5, 129.9, 118.0, 113.7, 109.6, 100.8, 69.7, 57.1,

38.4, 31.9, 29.66, 29.63, 29.58, 29.3, 29.0, 26.0, 22.7, 14.1. HRMS (+ESI): m/z calcd for $C_{50}H_{67}N_4O_{10}$ $[M+H]^+$, 883.4852; found 883.4856.

2,6-Bis((E)-4-(N,N-di(4-tert-butylphenyl)aminostyryl)benzo[1,2-d;4,5-d']bisoxazole (208): Orange powder (1.38 g, 75% yield). mp: 389 °C (dec.). ^{1}H NMR ($CDCl_3$): 7.73 (s, 2H), 7.73 (d, J = 15.5, 2H), 7.43 (d, 4H), 7.31 (d, 8H), 7.08 (d, 8H), 7.02 (d, 2H), 6.89 (d, J = 15.5, 2H), 1.33 (s, 36H). ^{13}C NMR ($CDCl_3$): 164.8, 150.2, 148.4, 147.2, 144.3, 140.6, 139.8, 128.9, 127.5, 126.5, 125.3, 121.1, 110.5, 100.1, 34.6, 31.6. HRMS (+ESI): m/z calcd for $C_{64}H_{67}N_4O_2$ $[M+H]^+$, 923.5259; found 923.5260.

2,6-Bis((E)-2-(9-hexylcarbazol-3-yl)vinylbenzo[1,2-d;4,5-d']bisoxazole (208): Orange-yellow powder (0.98 g, 69% yield). mp: 241 °C. ^{1}H NMR ($CDCl_3$): 8.31 (d, 2H), 8.15 (d, 2H), 8.01 (d, 2H), 7.79 (s, 2H), 7.76 (dd, 2H), 7.51 (td, 2H) 7.43 (d, 2H), 7.41 (d, 2H), 7.29 (td, 2H), 7.10 (d, 2H), 4.30 (t, 4H), 1.88 (m, 4H), 1.30 (m, 12H), 0.87 (t, 6H). ^{13}C NMR ($CDCl_3$): 164.7, 148.1, 141.5, 140.9, 126.2, 126.1, 125.3, 123.3, 122.7, 120.7, 120.6, 120.4, 119.6, 117.5, 110.0, 109.2, 109.1, 99.9, 43.3, 31.5, 28.9, 26.9, 22.5, 14.0. HRMS (+ESI): m/z calcd for $C_{48}H_{47}N_4O_2$ $[M+H]^+$, 711.3694; found 711.3703.

2,6-Bis((E)-2-(3-hexylthiophen-2-yl)vinylbenzo[1,2-d;4,5-d']bisoxazole (208): Bright yellow powder (0.58 g, 53% yield). mp: 126 °C. ^{1}H NMR ($CDCl_3$): 7.81 (d, J = 16.0, 2H), 7.72 (s, 2H), 7.10 (s, 2H), 6.97 (d, 2H), 6.79 (s, J = 16.0, 2H), 2.58 (t, 4H), 1.62 (m, 4H), 1.32 (m, 12H), 0.89 (t, 6H). ^{13}C NMR ($CDCl_3$): 163.8, 148.2, 144.5, 140.6, 140.1, 133.7, 131.2, 123.0, 112.0, 100.2, 31.6, 30.33, 30.30, 28.9, 22.6, 14.1. HRMS (+ESI): m/z calcd for $C_{32}H_{37}N_2O_2S_2$ $[M+H]^+$, 545.2291; found 545.2294

1*H*-Pyrrole-2-carboxaldehyde (213): DMF (20 mL) was cooled to 0 ºC, and phosphorus oxychloride (10.73 g, 70 mmol) was added drop-wise via an addition funnel over 15 minutes, keeping the temperature below 5 ºC. The reaction was stirred for 30 minutes at 0 ºC, and then dichloromethane (50 mL) was added. Pyrrole (4.23 g, 63 mmol) was dissolved in dichloromethane (20 mL) and added drop-wise. The reaction was stirred at room temperature for 15 minutes, refluxed for 15 minutes, cooled to 0 ºC, and quenched with 10% ammonium hydroxide. The product was extracted with methylene chloride, washed with sodium bicarbonate solution, and the organic layers were dried over sodium carbonate. Removal of solvent under vacuum gave a solid which was recrystallized from hot hexane (3.38 g, 56%).

1-octyl-1*H*-pyrrole-2-carbaldehyde (214): 1*H*-Pyrrole-2-carboxaldehyde (2.38 g, 25 mmol) was dissolved in DMF (8 mL), and was added to a suspension of sodium hydride (60% in mineral oil, 29 mmol) at 0 ºC over 15 minutes, and allowed to react for 30 minutes. Hexyl bromide (4.33 g, 26.25 mmol) was added drop-wise, and the reaction was stirred at room temperature. Reaction progress was monitored by GCMS. Upon completion (approximately 18 hours), the reaction was carefully quenched with ice water, and the product was extracted with hexane, which was dried over sodium sulfate. The solvent was removed under vacuum, and the crude product was purified by vacuum distillation to give a colorless oil (4.26 g, 95%).

2.7. References

1. Klimavicz, J. S.; Mike, J. F.; Bhuwalka, A.; Tomlinson, A.; Jeffries-El, M., *Pure Appl. Chem.* **2012,** *84* (4), 991-1004.

2. Pasker, F. M.; Le Blanc, S. M.; Schnakenburg, G.; Höger, S., *Org. Lett.* **2011,** *13* (9), 2338-2341.

3. Wang, X.; Zhou, Y.; Lei, T.; Hu, N.; Zhen, E.-Q.; Pei, J., *Chem. Mater.* **2010,** *22* (12), 3735-3745.

4. Lhost, O.; Brédas, J., *The Journal of chemical physics* **1992,** *96*, 5279.

5. Woo, H. S.; Lhost, O.; Graham, S. C.; Bradley, D. D. C.; Friend, R. H.; Quattrocchi, C.; Brédas, J. L.; Schenk, R.; Müllen, K., *Synth. Met.* **1993,** *59* (1), 13-28.

6. Ko, S.; Mondal, R.; Risko, C.; Lee, J. K.; Hong, S.; McGehee, M. D.; Bredas, J.-L.; Bao, Z., *Macromolecules (Washington, DC, U. S.)* **2010,** *43* (16), 6685-6698.

7. Knoevenagel, E., *Berichte der deutschen chemischen Gesellschaft* **1898,** *31* (3), 2596-2619.

8. Mike, J. F.; Makowski, A. J.; Jeffries-El, M., *Org. Lett.* **2008,** *10* (21), 4915-4918.

9. Houpis, I. N.; Molina, A.; Lynch, J.; Reamer, R. A.; Volante, R. P.; Reider, P. J., *J. Org. Chem.* **1993,** *58* (11), 3176-3178.

10. Chen, B.-S.; Chen, Y.-J.; Chou, P.-T., *J. Mater. Chem.* **2011,** *21* (12), 4090-4094.

11. Feng, D.; Wang, S.; Zhuang, Q.; Guo, P.; Wu, P.; Han, Z., *J. Mol. Struct.* **2004,** *707* (1), 169-177.

12. Ueno, T.; Urano, Y.; Kojima, H.; Nagano, T., *J. Am. Chem. Soc.* **2006,** *128* (33), 10640-10641.

13. Turro, N. J.; Ramamurthy, V.; Scaiano, J. C., *Principles of Molecular Photochemistry*. University Science Books: Sausalito, CA, 2009.

14. Kamlet, M. J.; Abboud, J. L.; Taft, R., *J. Am. Chem. Soc.* **1977,** *99* (18), 6027-6038.

15. Jenekhe, S. A. *Excimers and exciplexes of conjugated polymers*; DTIC Document: 1994.

16. Motoyoshiya, J.; Fengqiang, Z.; Nishii, Y.; Aoyama, H., *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* **2008,** *69* (1), 167-173.

17. Porrès, L.; Mongin, O.; Katan, C.; Charlot, M.; Pons, T.; Mertz, J.; Blanchard-Desce, M., *Org. Lett.* **2004,** *6* (1), 47-50.

18. He, C.; He, Q.; Yang, X.; Wu, G.; Yang, C.; Bai, F.; Shuai, Z.; Wang, L.; Li, Y., *The Journal of Physical Chemistry C* **2007,** *111* (24), 8661-8666.

19. Reichardt, C.; Welton, T., *Solvents and Solvent Effects in Organic Chemistry*. 4 ed.; Wiley-VCH: Weinheim, Germany, 2011.

20. Matyushov, D. V.; Ladanyi, B. M., *The Journal of chemical physics* **1998,** *108*, 6362.

21. Salaneck, W. R., *J. Electron. Spectrosc. Relat. Phenom.* **2009,** *174* (1-3), 3-9.

22. Bredas, J. L.; Heeger, A. J., *Chem. Phys. Lett.* **1994,** *217* (5-6), 507-12.

23. Hansch, C.; Leo, A.; Taft, R., *Chem. Rev.* **1991,** *91* (2), 165-195.

24. Nad, S.; Kumbhakar, M.; Pal, H., *J. Phys. Chem. A* **2003,** *107* (24), 4808-4816.

CHAPTER 3. TOWARDS THE SYNTHESIS OF ASYMMETRIC BENZOBISOXAZOLE DYES

3.1. Introduction

The synthesis of asymmetric benzobisoxazole dyes was the next logical step after making the symmetric versions. Previously, the goal was to produce a series of D-π-A-π-D molecules using benzobisoxazole as a core. However, as *t*-BBO is not a particularly strong acceptor, the design of asymmetric dyes would allow the BBO to act a part of the π-spacer, and a stronger acceptor could be included on one side of the molecule with a strong donor on the other. The D-π-A– type architecture has been employed to a significant extent, both in small molecules and in CPs.[1] The inclusion of two different aromatic groups would allow for a more controllable method of fine-tuning the HOMO and LUMO levels of the resultant dye, as either the donor or acceptor could be changed to adjust either without greatly affecting the other. This ability to tune these dyes may have applications in producing dye-pumped lasers[2] of a desired wavelength emission, and some benzoxazole and benzothiazole derivatives can emit in the near-IR region,[3] indicating that BBOs and BBZTs can be used to make near-IR devices. Additionally, the presence of electron-rich and electron-poor regions of a molecule can promote self-assembly,[4] which is of particular interest when designing complex electronic systems,[5-6] non-linear optical devices,[7] or artificial photosynthetic systems.[8]

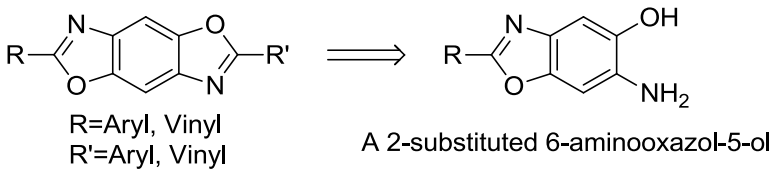
Further development of existing synthetic methods was needed, as a crucial step in asymmetric synthesis was to close a single side of the BBO core, and as such, a

variety of functional groups were needed, and orthogonal ring-closing methods proved useful.

3.2. Retrosynthetic Approaches

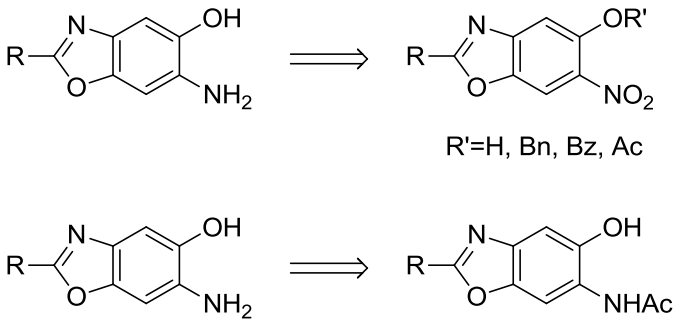
While the Knoevenagal condensation of an aldehyde with 2,6-dimethyl-*t*-BBO proved to be a simple method to make symmetrically-substituted dyes, condensing only one side in good yield proved to be problematic. Statistically, reacting 2,6-dimethyl-*t*-BBO with one equivalent of an aldehyde should give a 1:2:1 ratio of unreacted BBO to the desired mono-substituted product to the disubstituted BBO dye. However, due to the strongly basic conditions used in the condensation, the Cannizzaro reaction reduces the amount of aldehyde available for condensation due to disproportionation to a respective carboxylic acid and alcohol.[9] This necessitates a further sacrifice to the already-disappointing maximum yield of 50%, and further complicates the difficult isolation of the desired compound from the byproducts. Alternatively, more aldehyde could be used. This reduces the effect of the Cannizzaro reaction, and also increases the mole fraction of 2,6-dimethyl-*t*-BBO which will react, but at the cost of producing more of the disubstituted dye. Indeed, if x equivalents of the aldehyde are used for one equivalent of BBO, then it should be expected that a $1:2x:x^2$ ratio of the aforementioned products would be produced, with some deviation from this excepted due to not only the Cannizzaro reaction, but also due to changes in solubility. Unfortunately, modification of the basic procedure outlined in Chapter CHAPTER 2 proved ineffective for efficiently producing monosubstituted *t*-BBOs.

A retrosynthetic approach was used in an attempt to determine ideal starting materials as well as potentially difficult steps when synthesizing asymmetric *t*-BBOs. Working backwards from the final, desired product, it is clear that one must synthesize a 2-substituted 6-aminooxazol-5-ol, which can then be ring-closed to form the second oxazole ring via a reaction mild enough not to detrimentally affect the previously closed ring (Scheme 9).



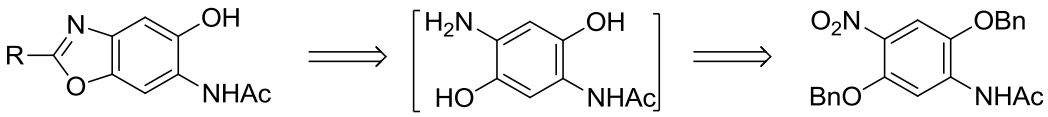
Scheme 9: Required precursor to asymmetric *t*-BBO.

The required 2-alkyl or -aryl 6-aminooxazol-5-ol could be synthesized by either reduction of a nitro group or the amide bond cleavage of an acetamido group. The nitro group reduction is also beneficial in that a benzyl protecting group on the phenolic oxygen could concomitantly be removed provided the selection of a suitable transition metal catalyst (Scheme 10). The difficulty, however, would lie in making this intermediate compound. Numerous other protecting groups could also be present on the phenolic oxygen, though only the acetoxy and benzoxy were also considered in synthesis due to their ease of introduction and low cost of reagents.



Scheme 10: Simple precursors to 2-substituted 6-aminooxazol-5-ol.

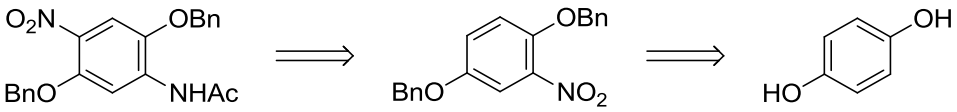
The 6-acetamido derivative of oxazole-5-ol could, in theory be produced from the nitrated, benzyl-protected acetanilide compound (Scheme 11), but the intermediary compound would likely be readily oxidized to a quinone or other oxidized compound by atmospheric oxygen due to its high electron density.[10-11] It is possible to work around this if both the reduction/deprotection and oxazole ring closure can be done in one pot.



Scheme 11: Production of 6-acetamidooxazol-5-ol from a dibenzylated, nitrated acetanilide.

2,5-Dialkoxy-4-nitroacetanilides can be easily synthesized from the 2,5-dialkoxyacetanilides by mild nitration, and this in turn comes from the 1,4-dialkoxynitrobenzene in two steps, which can be synthesized from hydroquinone in two more steps (Scheme 12). The purpose of choosing hydroquinone or readily available analogues, such as 1,4-dimethoxybenzene is two-fold. These compounds are very cheap and available in large quantities, which is important as some steps in the syntheses of

these compounds are not the best-yielding. They also have both of the oxygen atoms of *t*-BBO already present on the ring, which is crucial as there are very few reliable methods for introducing phenolic oxygens onto a benzene ring in high yield.



Scheme 12: The use of hydroquinone as a starting point.

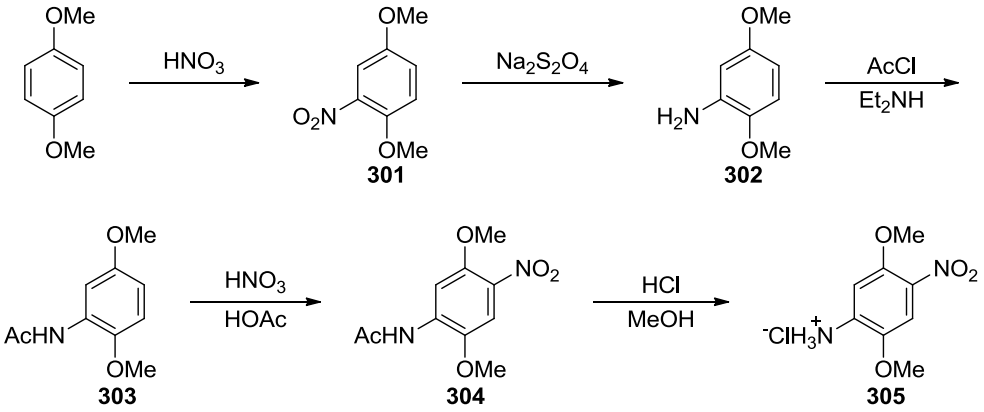
3.3. Results and Discussion

3.3.1. Troubles of asymmetric *t*-BBOs

3.3.1.1. The Methyl Protecting Group

The simplest protecting group, atomically speaking, for a phenol is a methyl ether, and, as such, 1,4-dimethoxybenzene was chosen as the first protected hydroquinone derivative. Nitration of 1,4-dimethoxybenzene in glacial acetic acid proceeded smoothly to yield 1,4-dimethoxy-2-nitrobenzene (**301**) in high yield (96%). Originally, this compound was reduced to 2,5-dimethoxyaniline (**302**) using catalytic hydrogenation over palladium on carbon, but it was later found that the reduction with sodium dithionite proceed smoothly and quickly. 2,5-Dimethoxyaniline may also be purchased at relatively low cost instead of being synthesized, but a sample obtained from a commercial source proved to be partially decomposed, as determined by a somewhat messy NMR as well as a dark purple discoloration, and freshly prepared compound gave

a better yield in the next step. Protection with acetyl chloride to give the acetanilide derivative (**303**) followed by a careful nitration in acetic acid gave 2,5-dimethoxy-4-nitroacetanilide (**304**) as a mass of greenish-yellow crystals. To this point, all reactions had proceeded smoothly. The amide bond could also be cleaved successfully to give anilinum chloride derivative (**305**) (Scheme 13).

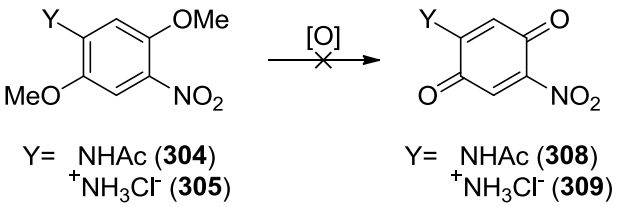


Scheme 13: Synthetic pathway towards asymmetric *t*-BBOs from 1,4-dimethoxy benzene

Unfortunately, when it came time to deprotect the phenolic oxygens, the methyl ether proved to be too robust. Indeed, all attempts to demethylate either acetanilide **4** or anilinium **305** to the hydroquinone derivatives **306** and **307** failed. Boron tribromide, hydroiodic and hydrobromic acids, and an aluminum trichloride melt were all tried (Scheme 14), and either had no effect, or resulted in the complete destruction of the molecule.

Scheme 14: Attempted removal of the methyl groups. BBr_3, HI, HBr, and $AlCl_3$ melts were all used.

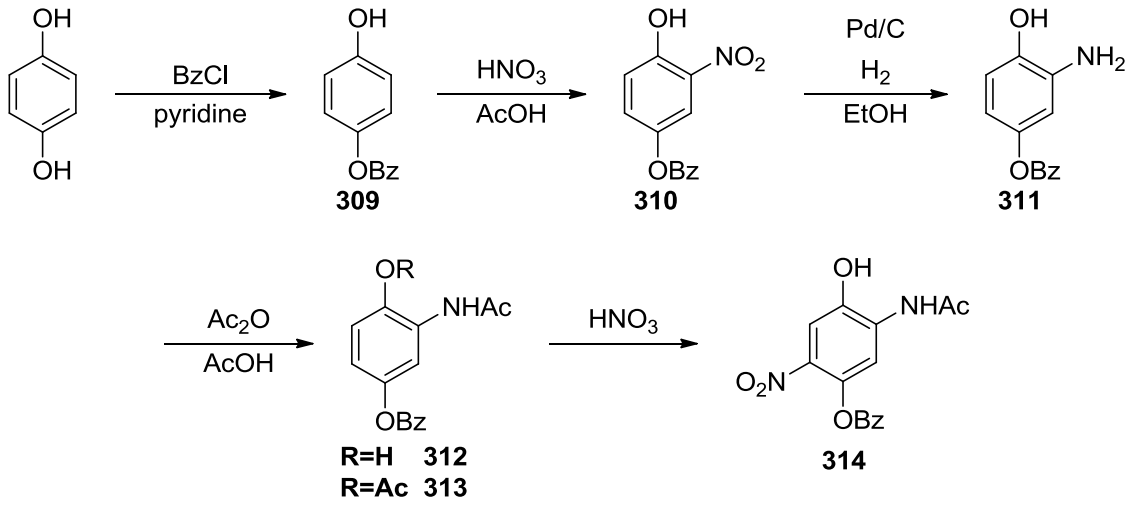
It is well known that 1,4-dimethoxybenzene can be oxidized to the *p*-benzoquinone using common oxidizers, such as chromium (VI) oxide,[12] cerium ammonium nitrate,[13] nitric acid,[14] and potassium permanganate[12] (Scheme 15); however, attempts to use these reagents on either starting material (**304** and **305**) resulted in either no reaction or decomposition, and it was thusly decided that a protecting group which is easier to remove should be chosen. It is speculated that due to the harshness of these reaction conditions, formation of other quinones accompanied the formation of desired quinones **308** and **309** when a reaction occurred,[15] and they were thus not isolated. It is also conceivable that oxidation of the amide nitrogen may take place under some oxidizing environments. [16]



Scheme 15: Attempted formation of a quinone from the 1,4-dimethoxy derivatives. CrO_3, CAN, HNO_3, and $KMnO_4$ all failed to produce the desired product.

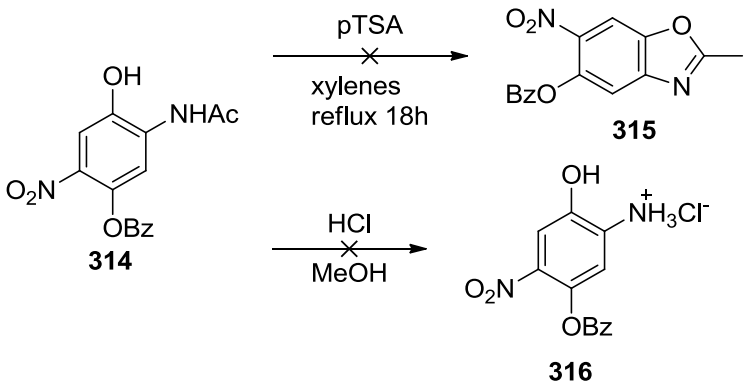
3.3.1.2. The Benzyol Protecting Group

The use of the benzoyloxy protecting group used a slightly different approach (Scheme 16), protecting only one phenolic oxygen on the ring via the synthesis of 4-hydroxyphenyl benzoate (**309**). It should be noted that the bisbenzoate is insoluble in nearly every common organic solvent, and is thus not useful. 4-Hydroxyphenyl benzoate nitrates preferentially *ortho* to the free hydroxyl to give compound **310**; this is likely due to the greater resonant electron-donating strength of the free hydroxy compare to the esterified oxygen. Catalytic hydrogenation produces the aniline compound **311**, which is acetylated instead of ring-closed because the former option allows for the proper directing of the other needed nitro group to position 5 on the ring. (The electron-donating ability of the amine/amide nitrogen is lost upon conversion to the imine-type nitrogen in the oxazole ring, thus necessitating nitration prior to ring closure.) The acylation step gives more the one product by NMR, producing mainly the acetoxyacetanilide derivative (**313**), but some hydroxyacetanilide (**330**) was also present, even when a large excess of acetic anhydride was used. However, a nitration reaction was performed on the mixture of compounds, and it proceeded smoothly with deprotection to the nitrated hydroxyacetanilide **314** (Scheme 16).



Scheme 16: Synthetic outline of using the benzoyl ester protecting group.

The 5-acetamido-4-hydroxy-2-nitrophenyl benzoate was then subjected to attempts to ring-close a benzoxazole (**315**) via acid-catalyzed dehydration concomitant with azeotropic removal of water, though the exceedingly poor solubility of the starting material in most organic solvents caused by strong intermolecular interactions precluded the success of this route. An attempt to cleave the amide and form the free aniline or anilinium compound (**316**) failed as the compound decomposed, though the mechanism behind this is unclear; it is possible that there was formation of an *o*- or *p*-benzoquinone upon deprotecting (Scheme 17).



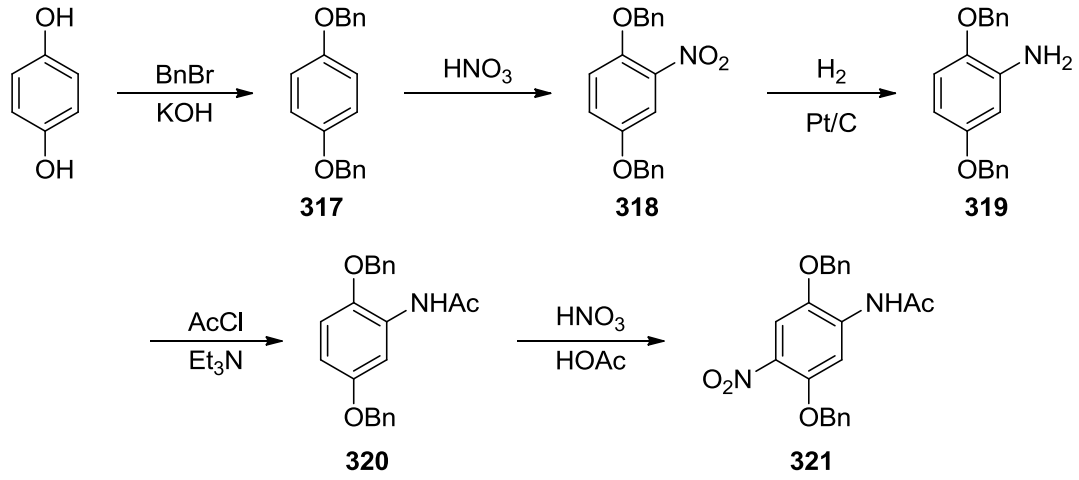
Scheme 17: Attempts to ring-close or cleave the amide bond were met with failure.

3.3.1.3. The Benzyl Protecting Group

An analogous route to the first attempt using benzyl instead of methyl ethers was devised (Scheme 18), as benzyloxy protection was seen as an attractive alternative to the persistent protecting group, and it can be easily removed by catalytic hydrogenation in the presence of palladium on carbon, forming toluene as a byproduct.

Hydroquinone was first protected by benzylation in a water/ethanol mix. The resultant diether was nitrated analogously to 1,4- dimethoxybenzene. Reduction of the nitro compound presented a minor hurdle, as catalytic hydrogenation of the nitro group would compete with the removal of the protecting groups if palladium is used. It is, however, known that using platinum instead of palladium as a hydrogenation catalyst results in reduction of the nitro group without debenzylation, and this was originally used to form 2,5-dibenzyloxyaniline, as shown below. Due to the high cost of platinum, several other methods were tried based on literature precedence on similar systems, including a reduction using zinc/acetic acid,[17] and a Béchamp reduction,[18] and sodium dithionite, all much cheaper alternatives. Earlier attempts at using sodium dithionite with

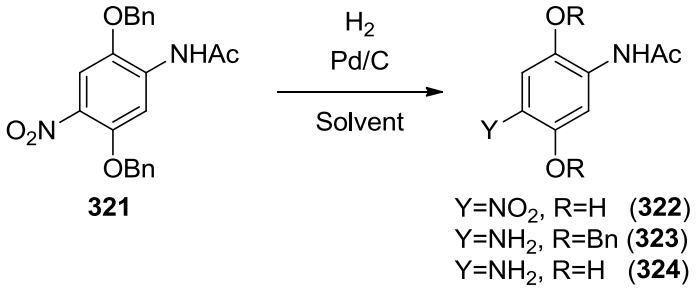
different ratios of water and ethanol all ended in failure, and the key to good resulted ended up being the use of 4:1 ethanol to concentrated aqueous ammonia as the solvent. The isolated 2,5-dibenzyloxyaniline produced with this method was isolated as a slightly off-while powder, which visually appeared to be of better quality than that produced by hydrogenation, perhaps due to less time spent in a suspension, in which it rather rapidly darkens. Acylation and nitration of this compound gave 2,5-dibenzyloxy-4-nitroacetanilide.



Scheme 18: The synthesis of benzyl-protected derivatives is analogous to that of the methyl-protected route.

Attempts to deprotect 2,5-dibenzyloxy-4-nitroacetanilide were met with mixed results. Caution had to be taken as deprotection of the phenolic oxygens competed with the reduction of the nitro group present on the molecule. It was discovered that this reaction was highly solvent dependent, with THF promoting debenzylation, and methanol inducing reduction of the nitro group (Scheme 19 and Table 3). A mixture of the two solvents was needed to effect both results simultaneously. Further research on this matter shows that, in general, nitro group reductions are performed in alcohols or

acetic acid, solvents in which proton transfer can occur,[19-21] while debenzylations can take place in various solvents, including THF,[22] or DMF,[23] as well as various alcohols.[24] It should be noted, though, that despite long reaction times in methanol, concomitant reduction of both the nitro group and debenzylation was not observed. This may be due to the slower kinetics of debenzylation in methanol than in THF,[25] as well potential poisoning of the palladium catalyst due to the formation of the aniline.



Scheme 19: The deprotection and reduction of 2,5-dibenzyloxy-4-nitroacetanilide.

Solvent	Pd/C loading (%)	Y	R	Time (hr)	Product
THF	2	Bn	NO_2	2	**321**
	5	H	NO_2	24	**322**
MeOH	2	Bn	NO_2/NH_2	2	**321/323***
	5	Bn	NH_2	18	**323**
1:1 MeOH:THF	5	Bn	NO_2	2	**323**
	5	H	NH_2	24	**324**

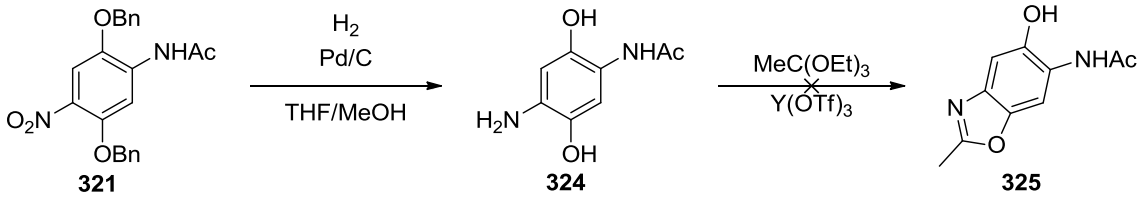
Table 3: The effect of solvent on the deprotection and reduction of **312** with hydrogen and palladium on carbon. *-both compounds were present in significant amounts.

2,5-Dihydroxy-4-nitroacetanilide (**320**) from the deprotection in THF could be isolated, but was insoluble in many organic solvents, likely due to strong hydrogen bonding in the solid state. 2,5-Dihydroxy-4-acetamidoaniline (**324**), produced in the mix

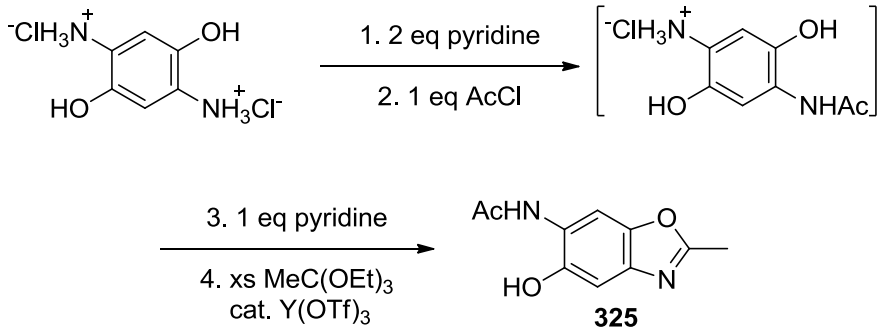
of THF and methanol, decomposed extremely rapidly when exposed to air due to the presence of four strongly electron-donating groups on the ring. To bypass this difficulty, a one-pot synthesis of the benzoxazole compound **325** was attempted, with a catalytic hydrogenation followed by addition of triethyl orthoacetate and yttrium triflate (Scheme 20); however, the ring failed to close, likely due to either the insolubility of yttrium triflate in these conditions or the presence of methanol as a polar protic solvent to act as a competing nucleophile.

3.3.1.4. Miscellaneous Attempts

Several other miscellaneous reactions were tried in an attempt to synthesize the desired 6-aminooxazol-6-ol derivatives, but these were ultimately unsuccessful. A one-pot synthesis starting from DAHQ was attempted (Scheme 21), with the premise being that, once neutralized, one equivalent of acetyl chloride would be able to form an acetanilide, and the hydrogen chloride produced would then form the ammonium salt with the other aniline nitrogen, suppressing diacetylation. Another equivalent of pyridine was used to deprotonate the anilinium compound, and an orthoester ring closure was attempted on the aminophenol.

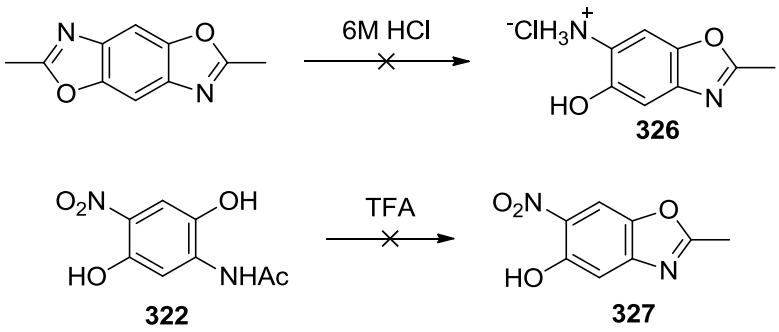


Scheme 20: Attempted synthesis of an oxazole ring from **321** in one pot.



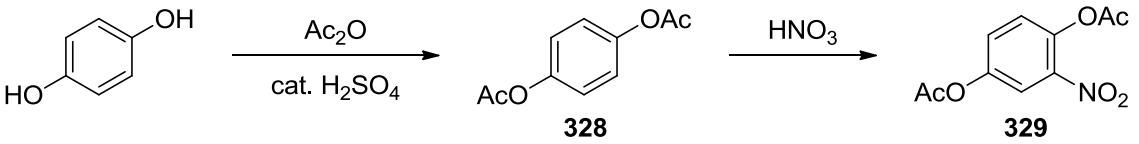
Scheme 21: An Attempted one-pot synthesis of 2-methyl-6-acetamidooxazol-6-ol (**323**) from DAHQ.

Additionally, as the BBO core is somewhat unstable to strong acids,[26] there was some precedence[27] for the ability for an acid-catalyzed ring-opening reaction to produce the benzoxazol-5-ol **326**. However, these results could not be replicated, presumably due to the insolubility of 2,6-dimethylBBO in 6 M hydrochloric acid as prescribed in the patent, even when ground into a fine powder. Another attempt was made to try to make a benzoxazole (**327**) from the previously made 2,5-dihydroxy-4-nitroacetanilide (**322**), but the solubility of this compound was not sufficient in THF, and no observable reaction occurred methanol or acetone despite some solubility.



Scheme 22: A Japanese patent suggested that an acid-catalyzed ring-opening should work, and a TFA-catalyzed ring-closure was also attempted. Both failed to produce any result.

The acetyl protecting group briefly garnered some attention as a potential protecting group, especially given the ease with which 1,4-diacetoxybenzene (**328**) was formed; however, this group was quickly abandoned due to the inability to effectively nitrate it to form 1,4-diacetoxy-2-nitrobenzene (**329**) (Scheme 23). Other products are formed, and purification is difficult.[28]

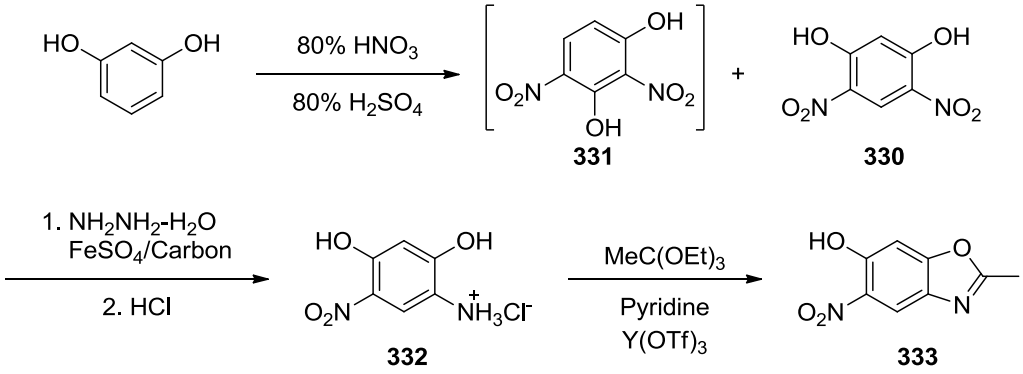


Scheme 23: While the synthesis of 1,4-diacetoxybenzene was exceedingly easy, this protected hydroquinone would not yield 1,4-diacetoxy-2-nitrobenzene.

3.3.2. Synthesis of asymmetric *c*-BBO

Due to the difficulties encountered in synthesizing the asymmetric *t*-BBO, it was decided that *c*-BBOs may provide a better chance of success due to known reactions that form the necessary precursors. Due to the substitution pattern of the precursor, resorcinol (1,3-dihydroxybenzene), obtaining the correct regioselectivity of the nitrogen atoms is a much simpler prospect as the presence of a nitro-group on the ring system in the 4-position helps improve the selectivity of nitration in the 6-posision, as shown in the synthesis of **330**. Additionally, resorcinol is much more tolerant to harsh nitration conditions than is hydroquinone, and is nitrated to **330** in 80% sulfuric acid by the addition of 80% nitric acid. Unfortunately, the synthesis of 4,6-dinitroresorcinol is accompanied by the production of a large amount of 2,4-dinitroresorcinol (**331**), as well as smaller amounts of 2-nitroresorcinol, 4-nitroresorcinol, and 2,4,6-trinitroresorcinol,

which must be separated out by recrystallization, giving the desired compound in yields below 50%.[29] **330** is capable of having a single nitro group reduced to the amine under carefully controlled conditions, such as the use of hydrazine and iron (II) on carbon, or the use of sodium sulfide, forming the aminophenol **332**, which can be subjected to an orthoester ring closure to form benzoxazole **333** (Scheme 24).

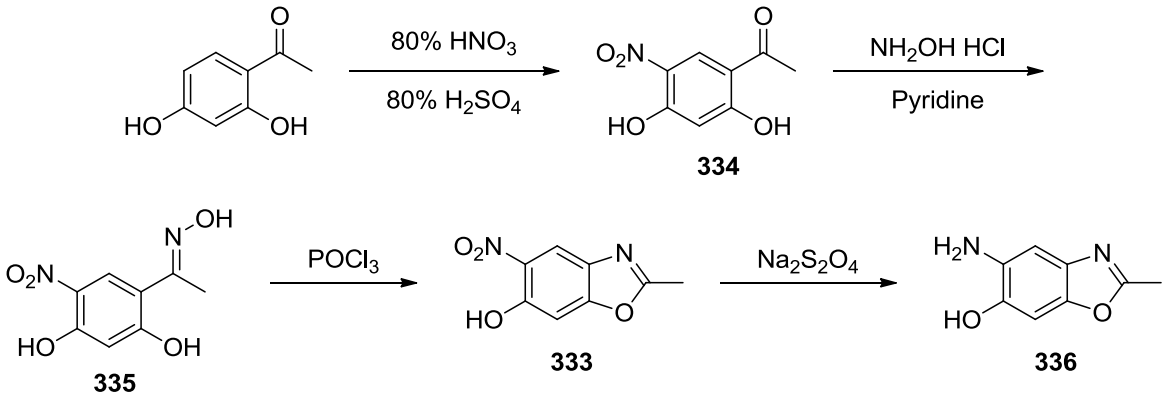


Scheme 24: Formation of an asymmetric *c*-BBO precursor, a benzoxazole-6-ol (**333**).

While this method has the benefit of using relatively cheap starting materials, the formation of large quantities of **331** is not ideal. Furthermore, the hydrazine reaction used to produce **332** from **330** produces some impurities of an unknown nature that are very difficult to remove from the final product. Additionally, some diamine is formed if the reaction is permitted to proceed for too long, and the anilinium salt **332** slowly decomposes in air. It was with such problems in mind that a new synthetic route was devised, avoiding the problems of air sensitivity altogether.

2',4'-Dihydroxyacetophenone is readily nitrated under conditions similar to resorcinol, and gives the desired nitro compound **334** in decent yields of around 65%.

The main impurity is 2',4'-dihydroxy-3'-nitroacetophenone, a compound analogous to 2,4-dinitroresorcinol in the aforementioned nitration. However, this impurity is readily removed from **334** by washing with tepid water due to its higher solubility, and the resultant product is usable in the following steps without recrystallization. The oxime **335** is formed by stirring with hydroxylamine in pyridine overnight. **335** is then subjected to a Beckmann rearrangement using phosphorus oxychloride in a mixture of DMAc and acetonitrile as solvents to produce a Vilsmeier-Haack–type reagent to give compound **333** (Figure 12), based on a procdure developed by Fujita et al.,[30] in high yield with no extra purification needed. The nitro group of this benzoxazol-6-ol is readily reduced with sodium dithionite to give 5-amino-2-methylbenzoxazol-6-ol (**336**), isolated as a neutral, air-stable solid (Scheme 25).



Scheme 25: The use of a Beckmann Rearrangement of an oxime to give an aminobenzoxazolol.

Compound **333** is capable of withstanding the harshly basic conditions of the Knoevenagal reaction, and was condensed in test reactions with both triphenylamine carboxaldehyde derivative **205** and *p*-anisaldehyde to give compounds **337** and **338**, respectively.

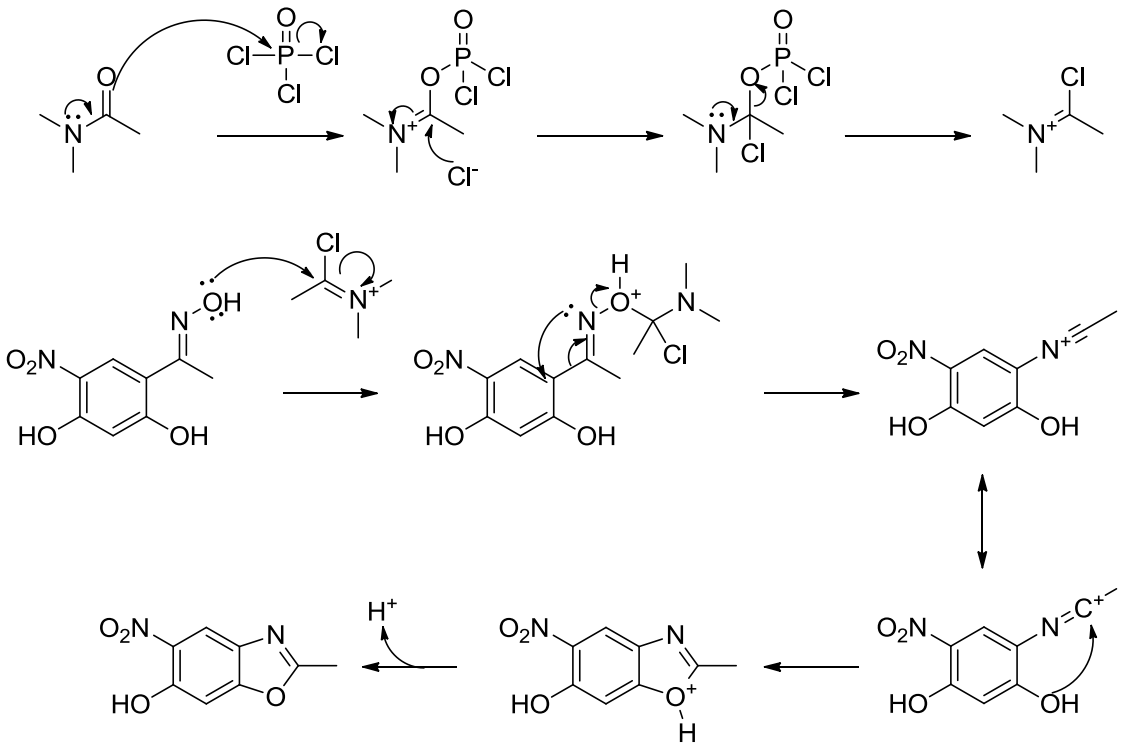
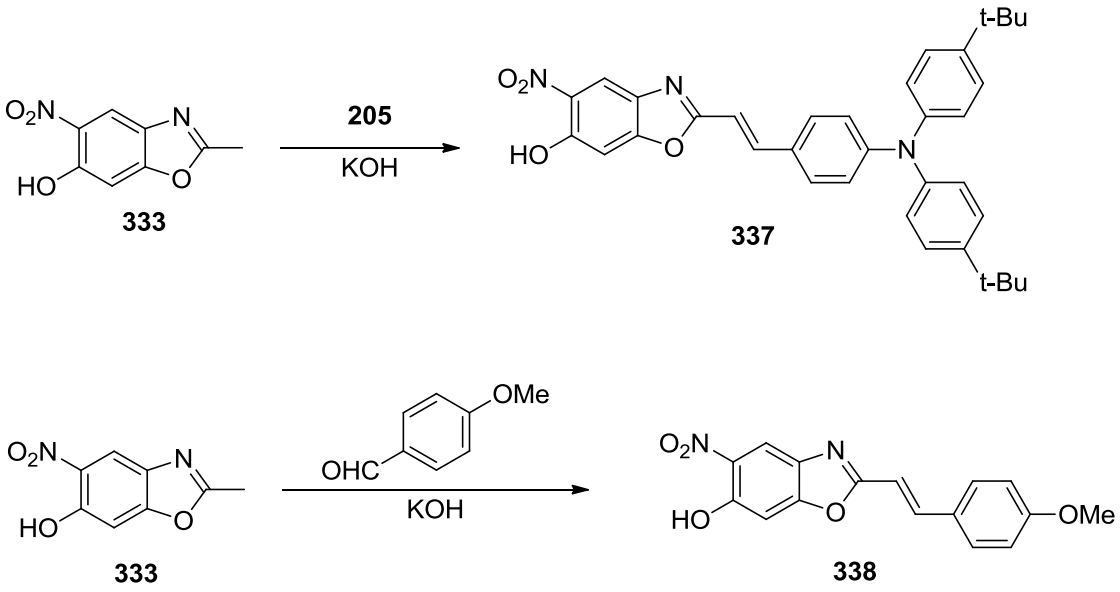
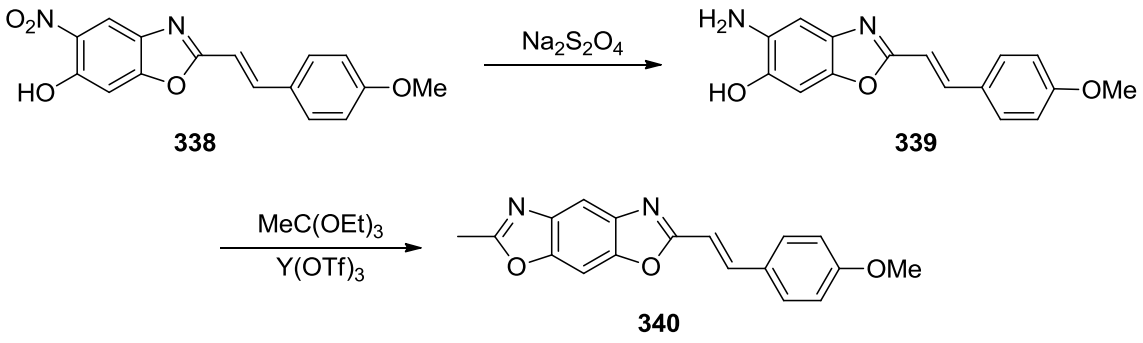


Figure 12: Proposed mechanism for the chloriminium reagent–mediated Beckmann rearrangement and subsequent oxazole ring formation.



Scheme 26: 2-Methyl-6-nitrobenzoxazol-5ol can be condensed with aromatic aldehydes in the presence of base as asymmetric dye precursors.

A sodium dithionite reduction of compound **338** gives the aminophenol **399**, which, while air-stable, was carried forward to the next reaction without additional purification. It is interesting to note that **339** showed a surprising amount of solvatochromism, fluorescing green in chloroform, but an orange-yellow in DMSO. An orthoester ring closure with triethyl orthoacetate gave the asymmetric *c*-BBO compound **340** (Scheme 27).



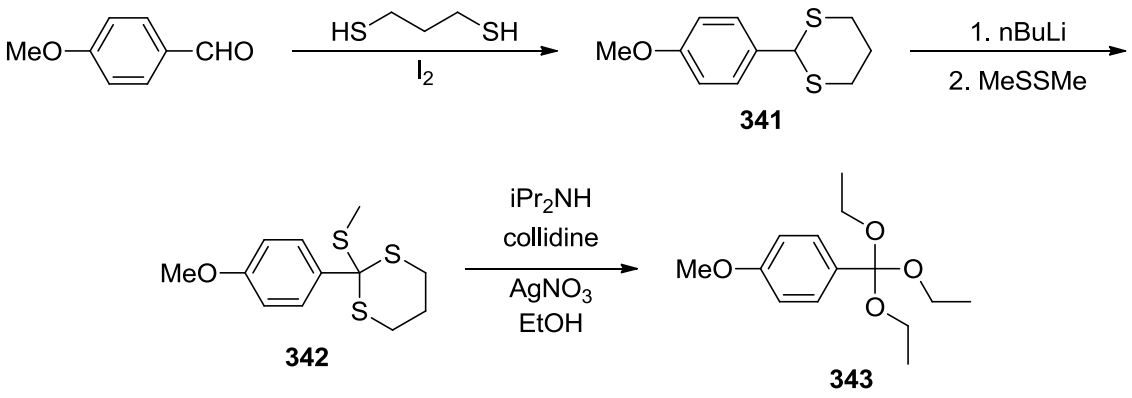
Scheme 27: The closure of the second oxazole ring in preparation of forming a final asymmetric dye.

3.3.3. Orthoester work

The majority of oxazole ring formations included in this thesis are based off the results of Dr. Jared Mike's work on the rare-earth metal-catalyzed ring-closure of benzobisazoles using orthoesters.[31] While Dr. Mike's research was crucial to the progress of the research within, the scope of this ring closure reaction was greatly limited in scope due to the limited selection of orthoesters available commercially. Furthermore, many other orthoesters known in literature involve complex syntheses and are often limited in the scope of potential substrates. A method developed by Dana Drochner of the Jeffries-EL Group to synthesize orthoesters from 2-substituted 1,3-dithianes proved effective and generated the desired compounds in a relatively pure form in yields much higher than generally observed in literature.[32-34] Several new orthoesters where made using minor modifications of Ms. Drochner's original method with the intent to eventually incorporate them into single-bonded asymmetric BBO dyes; however, due to the frustratingly slow progress on that front, the opportunity was never available to do so.

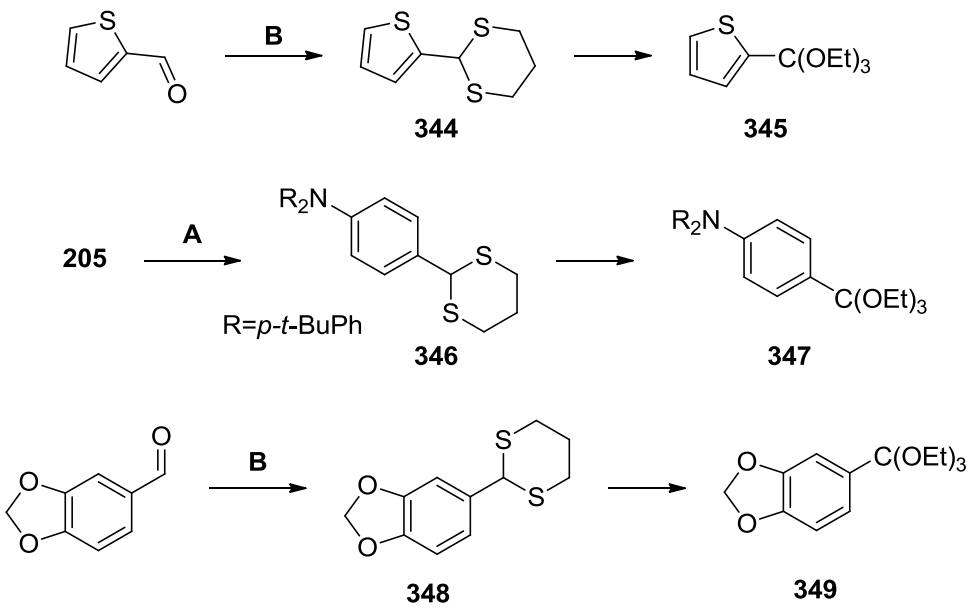
1,3-Dithianes are synthesized in generally high yields from aldehydes using either boron trifluoride diethyl etherate[35] or catalytic iodine[36] with 1,3-propanedithiol, as in the case of *p*-anisaldehyde forming **341** in Scheme 28. To form the orthoester in one pot, the dithianes are first deprotonated and reacted with dimethyl disulfide to form the trithioorthoester (**342**). Silver nitrate in acetonitrile is added in the presence of

diisopropyl amine and collidine, as well as ethanol, creating the orthoester (**343**). The collidine is required to form a more activated silver complex, capable sequestering thiol groups to of form a carbocation in which the charge is stabilized by resonance with the remaining sulfur atoms, which reacts with ethanol present in the reaction vessel.[37-38] It is by this route that the trithioorthoester undergoes solvolysis to the orthoester. The diisopropyl amine is responsible for neutralizing the protons formed during the solvolysis of ethanol. The Drochner method is beneficial in that the resultant orthoester is generally very pure, and can be used without additional purification. The main impurity generally present is the ester compound.



Scheme 28: The typical Drochner method of orthoester synthesis shown with *p*-anisaldehyde as the substrate.

This reaction could be used to form orthoesters of a variety of aromatic aldehydes, including thiophene-2-carboxaldehyde, aldehyde **205**, and piperonal via formation of dithianes **344**, **346**, and **348** to make the end products **345**, **347**, and **349** (Scheme 29).



Scheme 29: A variety of aryl aldehydes can be used to for dithianes and then orthoesters. A: 1,3-propanedithiol and BF_3OEt_2. B: 1,3-propanedithiol and catalytic iodine.

While the original Drochner methodology allowed for great variation in the aldehydes that could be used to make orthoesters, the orthoester moiety itself was limited to triethoxymethyl groups. Naturally occurring compounds with orthoesters, while rare, are much more complex, and it was with such knowledge that the orthoester group itself was varied as opposed to the R-group off of which the orthoester resided. Indeed, more often than not, the ether groups of the orthoester group are generally the more complex portion of the molecule, while the masked ester portion is usually relatively simple (Figure 13).

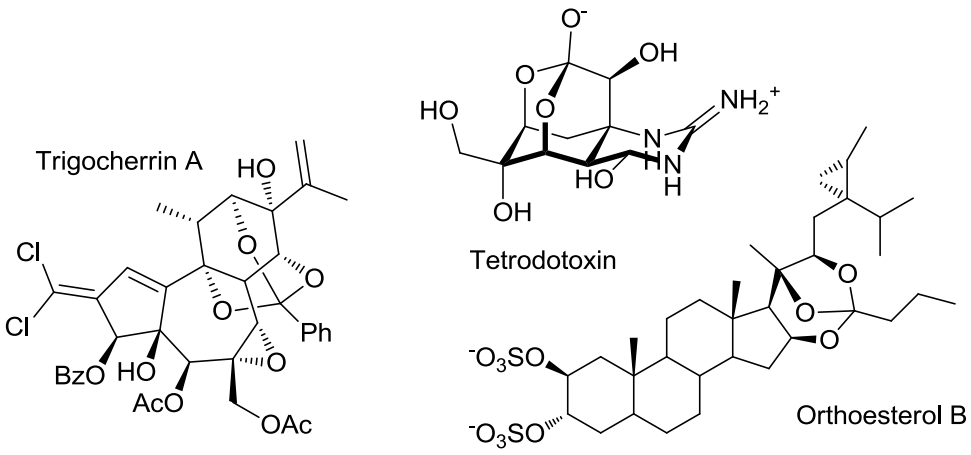
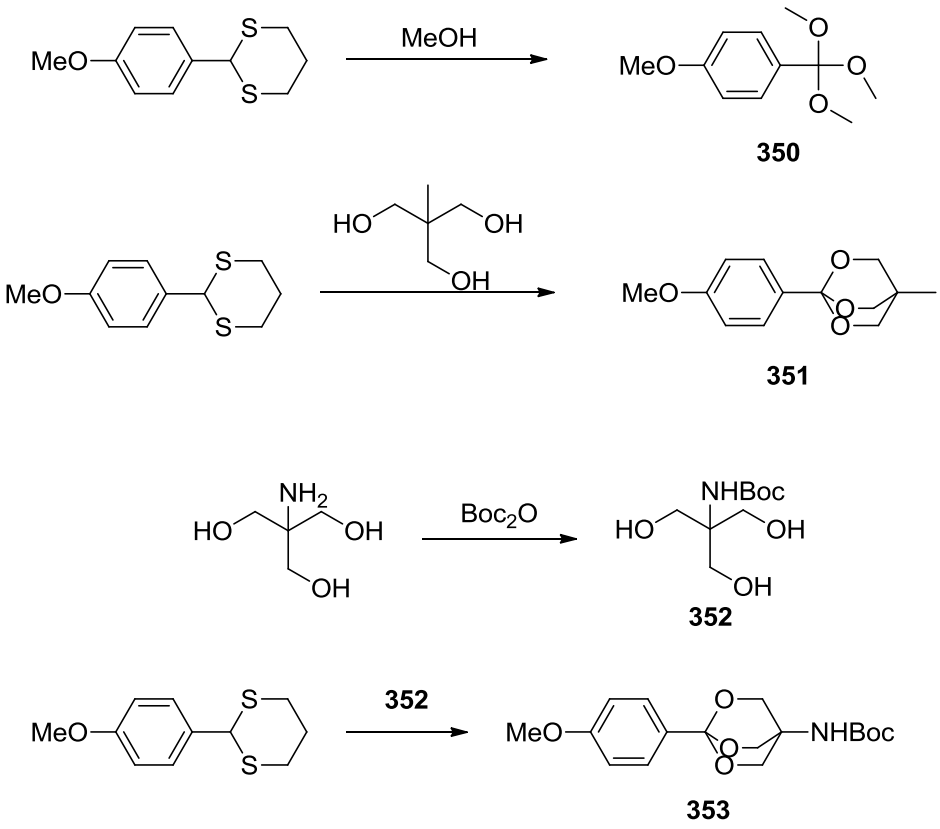


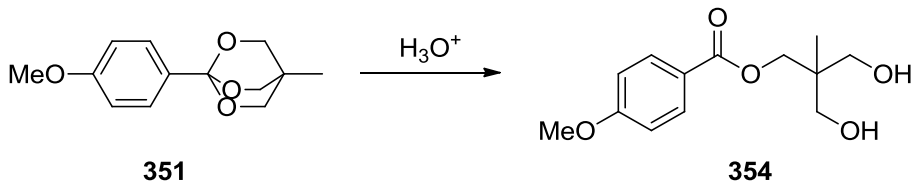
Figure 13: Naturally-occurring orthoesters generally have relatively simple ester portions, such as the orthobutyrate in orthoesterol B,[39] or the orthobenzoate in trigocherrin A.[40]

It was with such a premise in mind that the induction of new alcohol portions of the orthoester group was used to create novel orthoesters (Scheme 30). Anhydrous methanol was used to make the trimethoxymethyl derivative **350**, while the triol trimethylolethane was used to make the less labile bicyclic orthoester **351**, which was previously available only via a BF_3-OEt_2-mediated rearrangement of an oxetane ester.[41] More interestingly, after protecting tris(hydroxymethyl)aminomethane with the Boc group to form **352**, the heteroatom-rich orthoester **353** was formed. Orthoesters **351**and **353** hold additional value over the simple-alcohol–derived analogues in that they are solid at room temperature, allowing for recrystallization if high-purity orthoester is needed.



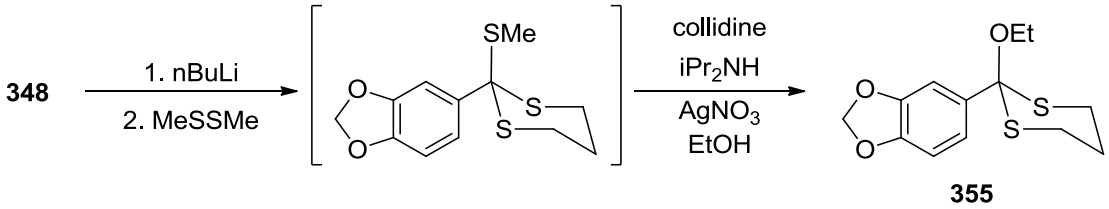
Scheme 30:Variation of the alcohol used allowed for a variety of orthoesters to be formed, including one with a Boc-protected amine group. The typical procedure from Scheme 28 was followed, changing only the alcohol.

Orthoesters can be hydrolyzed to the ester and eventually the free acid with mild aqueous acid.[42] While this is undesirable if the orthoester is the compound of interest, it does allow for the formation of more-complex molecules with more functionality, as seen in the dihydroxyester **354** in Scheme 31.



Scheme 31: As expected for an acid-sensitive group, the bicyclic orthoesters open in the presence of hydronium to form the ester. This also provides further evidence that the desired compound was synthesized.

Interestingly, when reacting piperonal dithiane **348** to form the orthoester under normal Drochner conditions, the 2-ethoxyl-1,3-dithiane derivative **355** was isolated during one reaction, as confirmed by HRMS and both 1D and 2DNMR. This provides some insight into the kinetics and mechanism of the reaction, showing that the less-sterically–bound methyl thioether is solvolyzed first. Additionally, this functional group appears to be relatively unstudied, returning very few hits in SciFinder©, and even fewer which actually have reliable methods of synthesis.



Scheme 32: The incomplete sulfur replacement from the trithioorthoester of **348** resulted in the peculiar compound 355, which has a dithioorthoester functionality.

3.4. Future Work

Unfortunately, despite the fact that an asymmetric *c*-BBO compound (**340**) was made, no studies were actually performed on it, and no electron-withdrawing derivatives were made with it to test the optical and electronic properties of a dye with both donating and accepting groups. As the methodology has now been developed, it should be relatively easy to create a series of asymmetric dyes. Furthermore, different orthoesters could be used in the ring-closing reaction of a 5-aminobenzoxazol-6-ol to produce single-bonded dyes as opposed to just vinylene-linked dyes. The novelty of a compound like **336** could be useful, as another ring-closure strep with an orthoester would allow for the development of asymmetric BBOs in only a few steps from a

commercially available material, and the more-sensitive amino and hydroxy groups are quickly protected.

3.5. Experimental Methods

Unless otherwise noted, all starting materials were purchased from commercial sources and used without further purification. All reactions were carried out under argon unless stated otherwise. Nuclear magnetic resonance spectra were obtained on a 400 MHz spectrometer (^{1}H at 400 MHz and ^{13}C at 100 MHz). ^{1}H NMR samples were referenced internally to residual protonated solvent ($CDCl_3$ at 7.26 and DMSO-d_6 at 2.49). ^{13}C NMR samples were referenced to the central carbon peak of $CDCl_3$ or DMSO-d_6. In both instances, chemical shifts are given in δ relative to solvent. Coupling constants are reported in Hz.

1,4-Dimethoxy-2-nitrobenzene (301): 1,4-dimethoxybenze (13.82 g, 100 mmol) was dissolved in acetic acid (100 mL) in a beaker. 70% Nitric acid (7.56 g, 120 mmol) was added drop-wise over five minutes. After stirring at room temperature for thirty minutes, the reaction was stopped by precipitating the product by pouring the reaction mix over ice (600 mL). The suspension was filtered to give a yellow solid which was washed copiously with water until the filtrate was neutral by pH paper. The resultant yellow solid was used without further purification. (17.66g, 96%) ^{1}H NMR ($CDCl_3$): 7.39 (s, 1H), 7.11 (d, 1H), 7.05 (d, 1H), 3.92 (s, 3H), 3.80 (s, 3H).

2,5-Dimethoxyaniline (302): *Catalytic Hydrogenation Method:* A two-neck, 500 mL RBF with a stirbar was charged with methanol (200 mL), 1,4-dimethoxy-2-nitrobenzene (9.16 g, 50 mmol), and 5% palladium on charcoal (1.06 g, 0.1 mmol). Oxygen was

removed by sparging with argon for fifteen minutes, after which hydrogen was bubbled through the mix for 24 hours. Hydrogen gas was removed by sparging with argon for five minutes, and the reaction mix was quickly filtered through diatomaceous earth to remove palladium/carbon. The solvent was removed by evaporation to yield the title product as a brown-tinted microcrystalline solid that was used in the next reaction without further purification (3.55g, 46%).

Sodium Dithionite Method: 1,4-dimethoxy-2-nitrobenzene nitrobenzene (9.16 g, 50 mmol) was dissolved in a boiling mix of 50:50 water and 95% ethanol (150 mL). Sodium dithionite (43.53 g, 250 mmol) was added in eight portions over tem minutes. After the completion of the addition, the solution turned from yellow to colorless, and the reaction was cooled to room temperature and poured into ice. The solid was filtered, and rinsed with water and then cold methanol, and dried under vacuum to give the product as a slightly off-white solid which was used without further purification (6.91g, 90%). ^{1}H NMR ($CDCl_3$): 6.67 (d, 1H), 6.29 (s, 1H), 6.25 (d, 1H), 3.78 (s, 3H), 3.72 (s, 3H).

2,5-Dimethoxyacetanilide (303):[43] 2,5-dimethoxyaniline (10.90 g, 71.2 mmol) was dissolved in dichloromethane (250 mL) containing diethylamine (6.25 g, 85.4 mmol) and the solution was cooled to 0 °C. Acetyl chloride (6.70 g, 85.4 mmol) was added slowly via syringe under the surface of the liquid with rapid stirring. After the addition was complete, the reaction was allowed to proceed for one hour at 0 °C. Water was then added, and the organic later was washed twice more with water (2x50mL), then with 1M HCl (50 mL), followed by saturated sodium bicarbonate solution (2x50mL), and

then saturated aqueous sodium chloride (50 mL), and dried over sodium sulfate. The solvent was removed under vacuum, and the product was recrystallized from isopropanol to give off-white, plumose crystals (13.24g, 95%). ^{1}H NMR ($CDCl_3$): 8.10 (s, 1H), 7.74(bs, 1H), 6.80 (d, 1H), 6.57 (d, 1H), 3.86(s, 3H), 3.79 (s, 3H), 2.20 (s, 3H). ^{13}C NMR ($CDCl_3$): 168.4, 154.1, 142.1, 128.5, 110.8, 106.6, 108.2, 56.2, 56.0, 25.2.

2,5-Dimethoxy-4-nitroacetanilide (304): 2,5-dimethoxyacetanilide (5.17 g, 26.5 mmol) was dissolved in acetic acid (100 mL) at 17 °C to give a yellow solution to which 70% nitric acid (2.00 g, 31.8 mmol) was added drop-wise, producing a deep red solution. After stirring at room temperature for 10 minutes, the reaction was quenched by pouring over ice (250 mL). The resultant suspension was filtered, and the solid was washed with large amounts of water. The product was recrystallized from methanol to give very fibrous, green-yellow crystals, resembling paper fibers (6.24 g, 98%).

2,5-Dimethoxy-4-nitroanilium chloride (305): 2,5-dimethoxy-4-nitroacetanilide (0.48 g, 2 mmol) was suspended in methanol (15mL), and concentrated hydrochloric acid (5 mL) was added, and the suspension was heated to reflux. After approximately one hour, most of the solid had dissolved, and the refluxing was permitted to continue for 17 more hours, after which the reaction was cooled to -20 °C, and the precipitate was filtered to give the product as a brown, granular solid (0.33 g, 67%). ^{1}H NMR (CD_3OD): 7.62 (s, 1H), 6.98 (s, 1H), 3.93 (s, 3H), 3.91 (s, 1H).

4-Hydroxyphenyl benzoate (309): Hydroquinone (17.34 g, 158 mmol) and pyridine (12.46 g, 158 mmol) were dissolved in methylene chloride (250 mL). Benzoyl chloride (21.09 g, 150 mmol) was added drop-wise over thirty minutes, and the reaction was then

stirred for two hours. The solvent was then removed, and the solid was suspended in water to remove residual hydroquinone and pyridinium chloride and filtered and dried, after which the solid was dissolved in hot diethyl ether and filtered to remove the undissolved dibenzoate compound. The solvent was removed and recrystallized from 75% ethanol. (24.16 g, 75%).

4-Hydroxy-3-nitrophenyl benzoate (310): 4-Hydroxyphenyl benzoate (10.71 g, 50 mmol) was dissolved in acetic acid (100 mL) and nitric acid (7.88 g, 125 mmol) was added drop-wise at 15 °C, and stirred for 30 minutes, during which rime it turned yellow, and then bright red. The reaction was then pour into ice water (700 mL) and stirred vigorously for one hour. Filtration and copious rinsing with cold water, followed by vacuum drying gave the desired compound as a yellow solid (9.87, 76%).

3-Amino-4-hydroxyphenyl benzoate (311): 4-Hydroxy-3-nitrophenyl benzoate (6.48 g, 25 mmol) was dissolved in methanol (100 mL), and 5% palladium on carbon (0.532 g, 0.25 mmol) was added. The reaction was sparged with argon, and then hydrogen was bubbled through for 48 hours. The catalyst was removed by vacuum filtration, and the solvent was removed to yield an off-white amorphous solid, which was used without further purification (4.53 g, 79%).

3-Acetamido-4-acetoxyphenyl benzoate (313): 3-Amino-4-hydroxyphenyl benzoate (6.88 g, 30 mmol) was dissolved in methylene chloride, and triethylamine (2.47 g, 31.5 mmol) was added, and cooled to 0 °C. Acetyl chloride (3.19, 31.5 mmol) was added dropwise with rapid stirring. The suspension was stirred at room temperature for one hour, and then water (50 mL) was added, and then the organic layer was rinsed twice

more with water, followed by 1 M HCl, then saturated $NaHCO_3$ solution, and finally brine before the organic layer was dried over magnesium sulfate. The solvent was removed to give a white solid (7.85 g, 84%).

5-Acetamido-4-acetoxy-2-nitrophenyl benzoate (314): 3-Acetamido-4-acetoxyphenyl benzoate (2.29 g, 10 mmol) was dissolved in 150 mL acetic acid, and acetic anhydride (2.04 g, 25 mmol) was added. After 30 minutes, nitric acid (0.63 g, 10 mmol) in acetic acid (20 mL) was added over twenty minutes. The reaction was allowed to stir for 45 minutes, and was then poured into ice water and filtered to give a yellow solide (2.57 g, 81%). ^{1}H NMR ($CDCl_3$): 10.98 (s, 1H), 8.65 (d, J = 2.8 Hz, 1H), 8.20 – 8.11 (m, 2H), 7.88 (s, 1H), 7.72 – 7.58 (m, 2H), 7.54 – 7.44 (m, 2H), 7.22 (s, 1H), 2.24 (s, 3H).

1,4-Dibenzyloxybenzene (317): Hydroquinone (22.02 g, 200 mmol) was dissolved in ethanol (270 mL), and benzyl bromide (76.97 g, 450 mmol) was added with stirring, giving a very slightly pink solution. Potassium hydroxide (23.00 g, 410 mmol) was dissolved in water (180 mL) and added in a steady stream to the hydroquinone solution, producing an orange, and then brown color. A precipitate started to form after five minutes, and the reaction was heated to reflux for four hours, and then cooled to room temperature and stirred for eight hours. The solids, which have been granular or ooids on different runs, were filtered and washed with water and cold methanol (50 mL). The solid was then triturated in hot methanol, cooled to 0 °C, and filtered again to give small, white prismatic crystals. (41.25 g, 71%)

1,4-Dibenzyloxy-2-nitrobenzene (318): 1,4-dibenzyloxybenzene (14.52 g, 50 mmol) was suspended in acetic acid (100 mL), and nitric acid (9.45 g, 150 mmol) was added.

The suspension was heated slowly to 45 °C, which was accompanied by the dissolution of the white solid and formation of a clear, yellow solution. After stirring at this temperature for 30 minutes, a yellow precipitate formed, and the reaction was poured over ice and filtered, washing with copious water. The yellow solid was triturated with boiling methanol, cooled to 0 °C, and filtered again, washing with methanol to give a microcrystalline yellow powder. (16.23 g, 97%).

2,5-Dibenzyloxyaniline (319): *Catalytic Hydrogenation Method:* A two-neck, 500 mL RBF with a stirbar was charged with isopropanol (200 mL), 1,4-dibenzyloxy-2-nitrobenzene (17.50 g, 52.18 mmol), and 10% platinum on charcoal (0.6 g). Oxygen was removed by sparging with argon for fifteen minutes, after which hydrogen was bubbled through the mix for 48 hours. Hydrogen gas was removed by sparging with argon for five minutes, and the reaction mix was quickly filtered through diatomaceous earth to remove platinum/carbon. The solvent was removed by evaporation to yield the title product as a brown-tinted microcrystalline solid that was used in the next reaction without further purification. (10.58 g, 66%).

Sodium Dithionite Method: 1,4-dibenzyloxy-2-nitrobenzene (8.38 g, 25 mmol) was added to boiling ethanol (100 mL), and then concentrated aqueous ammonia (25 mL) was added . Sodium dithionite (19.60 g, 112.5 mmol) was cautiously added in 8-10 portions to prevent overflowing due to frothing. After the completion of the addition, the solution turned from yellow to colorless, and the reaction was cooled to room temperature and poured over ice. The solid was filtered, and rinsed with water and then cold methanol, and dried under vacuum to give the product as a slightly off-white solid

which was used without further purification. (6.45 g, 85%) ^{1}H NMR ($CDCl_3$): 7.53 – 7.27 (m, 10H), 6.77 (d, J = 8.7 Hz, 1H), 6.45 (d, J = 2.9 Hz, 1H), 6.32 (dd, J = 8.7, 2.9 Hz, 1H), 5.03 (s, 2H), 4.99 (s, 2H), 3.97 (s, 2H). ^{13}C NMR ($CDCl_3$): 153.89, 141.20, 137.43, 137.36, 128.51, 127.93, 127.79, 127.63, 127.59, 127.55, 127.44, 127.39, 113.30, 103.47, 103.21, 71.26, 70.38.

2,5-Dibenzyloxyacetanilide (320): 2,5-dibenzyloxyaniline (9.16 g, 30 mmol) was dissolved in methylene chloride, and triethylamine (2.47 g, 31.5 mmol) was added, and cooled to 0 °C. Acetyl chloride (3.19, 31.5 mmol) was added by syringe beneath the surface of the solution while stirring rapidly. After the completion of the addition, a precipitate started to form due to the triethylammonium chloride. The suspension was stirred at room temperature for one hour, and then water (50 mL) was added, and then the organic layer was rinsed twice more with water, followed by 1 M HCl, then saturated $NaHCO_3$ solution, and finally brine before the organic layer was dried over magnesium sulfate, and the solvent was removed under vacuum to give a slightly brown, thick oil. Cold recrystallization from dichloromethane and hexane gave the product as a white, radially acicular solid. (10.09 g, 97%). ^{1}H NMR ($CDCl_3$): 8.28 (d, J = 3.0 Hz, 1H), 7.82 (s, 1H), 7.53 – 7.31 (m, 10H), 6.87 (d, J = 8.9 Hz, 1H), 6.64 (dd, J = 8.9, 3.0 Hz, 1H), 5.067 (s, 2H), 5.063 (s, 2H), 2.13 (s, 3H). ^{13}C NMR ($CDCl_3$): 168.25, 153.42, 141.37, 137.27, 136.73, 129.10, 128.83, 128.55, 128.41, 127.89, 127.72, 127.63, 113.09, 109.54, 107.10, 71.93, 70.50, 25.01.

2,5-Dibenzyloxy-4-nitroacetanilide: (321) 2,5-dibenzyloxyacetanilide (3.47 g, 10 mmol) was suspended in acetic acid and cooled to 17 °C. Nitric acid (1.89 g, 10 mmol)

was diluted with acetic acid (20 mL), and was added drop-wise to the reaction. The solution was allowed warm to 30 °C for 15 minutes, after which ice was added. The solid was filtered and rinsed with water to give a yellow-orange solid which was recrystallized from isopropanol to give orange-yellow, acicular crystals (3.72 g, 95%). ^{1}H NMR ($CDCl_3$): 8.51 (s, 1H), 7.94 (s, 1H), 7.64 (s, 1H), 7.54 – 7.49 (m, 2H), 7.46 – 7.36 (m, 7H), 7.34 – 7.28 (m, 1H), 5.23 (s, 2H), 5.11 (s, 2H), 2.17 (s, 3H). ^{13}C NMR ($CDCl_3$): 168.86, 148.71, 139.63, 135.74, 135.23, 134.24, 132.80, 128.96, 128.87, 128.58, 128.08, 128.00, 127.28, 109.29, 105.95, 77.35, 77.04, 76.72, 71.99, 71.49, 25.14.

2,5-Dihydroxy-4-nitroacetanilide (322): 2,5-Dibenzyloxy-4-nitroacetanilide (0.392 g, 1 mmol) was dissolved in THF (50 mL) and palladium on carbon (22 mg, 0.01 mmol) was added. The suspension was sparged with argon, and an atmosphere of hydrogen was established with a balloon. The reaction was allowed to proceed for 18 hours, after which the solution was sparged with argon again to remove hydrogen, and the solid was filtered and rinsed with acetone. The solvent was removed from the filtrate to give the desired compound as a brick-red, lustrous solid (0.21 g, 95%). ^{1}H NMR (DMSO-d_6): 9.55 (s, 1H), 7.7 (bs, 1H), 7.15 (s, 1H), 7.1 (bs, 1H), 5.48 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (DMSO-d_6): 184.6, 178.8, 171.6, 150.6, 142.4, 109.3, 96.3, 25.0.

4,6-Dinitroresorcinol (330):[44] To 80% sulfuric acid (1000 mL) was added 80% nitric acid (46.5 ml) which had traces of nitrous acid removed with urea, and the solution was cooled to 0 °C. 1,3-diacetoxybenzene (47.53 g, 245 mmol) was added drop-was over 30 minutes, ensure that the temperature never increased above 10 °C. Stir at 0 °C for three

hours, and then filter the strongly acidic suspension carefully through glass filter paper. Rinse the solid with water until neutral. The yellow solid was recrystallized with ethyl acetate to give the desired compound as yellow prisms (21.70 g, 44%).[1]H NMR (DMSO-d_6): 12.00 (bs, 2H), 8.60 (d, J = 1.1 Hz, 2H), 6.71 (d, J = 1.1 Hz, 2H). [13]C NMR (DMSO-d_6): 158.27, 128.97, 125.72, 106.01.

2',4'-Dihydroxy-5-nitroacetophenone (334): 2',4'-Dihydoxyacetophenone (15.22 g, 100 mmol) was ground finely in a mortar and pestle, added slowly to 80 w% sulfuric acid (300 mL), and stirred at room temperature for one hour to ensure complete dissolution. The solution was cooled to 0 °C, and 70% nitric acid (9.51 mL, 150 mmol) was added drop-wise over ten minutes to produce a deep yellow-brown solution, which is allowed to stir for an hour while cooling in ice water. The reaction is then poured over ice (600 g), and then filtered via vacuum filtration. The solid is rinsed twice with cold water (2 X 100 mL), and the filter cake is then suspended and stirred in warm water (300 mL, 50 °C) to dissolve the 2,4-dihydroxy-3-nitroacetophenone impurity. The suspension is filtered while warm, and rinsed once with warm water (100 mL, 50 °C), and allowed to dry under vacuum to give a crème-colored solid (13.14 g, 67%). [1]H NMR (DMSO-d_6): 12.5 (bs, 1H), 11.9 (bs, 1H), 8.47 (s, 1H), 6.54 (s, 1H), 2.59 (s, 3H). [13]C NMR (DMSO-d_6): 201.4, 165.8, 158.8, 131.1, 130.4, 114.5, 105.1, 28.5.

(*E*)- 2',4'-Dihydroxy-5-nitroacetophenone oxime (335): 2',4'-Dihydroxy-5-nitroacetophenone (7.89 g, 40 mmol) was added to pyridine (100 mL) with stirring to give a bright yellow suspension. Granular hydroxylamine hydrochloride (2.92 g, 42 mmol) was added in three portions three minutes apart. After fifteen minutes, all the

solids had dissolved to give a bright yellow-orange solution, and product precipitates out within an hour. The suspension is permitted to stir for 12 hours, after which pyridine is removed by rotary evaporation. The remaining solid was dissolved in ethyl acetate, and rinsed with water, 1 M HCl, and brine. The organic layer was dried over sodium sulfate and the solvent was removed by rotary evaporation to give a bright yellow, acicular solid. (7.96 g, 94%); mp: slow decomposition above 130 °C. ^{1}H NMR (DMSO-d_6): 12.55 (s, 1H), 11.65 (s, 1H), 11.14 (s, 1H), 8.06 (s, 1H), 6.52 (s, 1H), 2.55 (s, 3H). ^{13}C NMR (DMSO-d_6): 164.0, 156.3, 155.7, 129.1, 126.6, 113.8, 105.1, 11.7.

2-Methyl-5-nitrobenzo[d]oxazol-6-ol (333): (*E*)- 2,4-Dihydroxy-5-nitroacetophenone oxime was dissolved in a 3:1 mixture of acetonitrile and *N*,*N*-dimethylacetamide and cooled to 0 °C. Phosphorus oxychloride was added as rapidly as possible without increasing the temperature above 5 °C, and the reaction was allowed to proceed at room temperature for one hour, after which the yellow suspension was poured into a beaker containing sodium acetate and ice. This mixture was stirred for two hours, and the product was isolated by vacuum filtration as an amorphous yellow powder which could be purified by sublimation under vacuum.

5-Amino-2-methylbenzo[d]oxazol-6-ol (336): 2-Methyl-5-nitrobenzo[d]oxazol-6-ol was dissolved in a 4:1 mixture of ethanol and concentrated aqueous ammonia and heated to boiling to give a deep red solution. Sodium dithionite was added in approximately ten portions over a five-minute period to reduce the risk of severe foaming. The solution changes from red to bright yellow, after which the reaction is cooled to room temperature and diluted with ice water (500 mL) and 0.5 M pH 7 phosphate buffer (100

mL), and filtered under vacuum, washing with cold water to give an amorphous yellow-orange powder. %). ^{1}H NMR (DMSO-d_6): 9.4 (bs, 1H), 6.87 (s, 1H), 6.79 (s, 1H), 4.7 (bs, 2H), 2.44 (s, 3H). ^{13}C NMR (DMSO-d_6): 161.3, 143.2, 143.1, 134.6, 134.0, 103.1, 96.5, 14.4.

(*E*)-2-(4-(Bis(4-(tert-butyl)phenyl)amino)styryl)-5-nitrobenzo[d]oxazol-6-ol (337): ^{1}H NMR ($CDCl_3$): 10.97 (s, 1H), 8.36 (s, 1H), 7.68 (d, *J*=16.0 Hz, 1H), 7.38 (d, 2H), 7.29 (d, 4H), 7.23 (s, 1H), 7.16 (s, 1H), 7.05 (d, 4H), 6.97 (d, 2H), 6.79 (d, *J*=16 Hz, 1H), 1.30 (s, 18H). ^{13}C NMR ($CDCl_3$): 166.1, 156.4, 154.7, 150.7, 147.5, 144.1, 141.7, 136.5, 131.7, 129.2, 126.8, 126.6, 125.5, 120.6, 115.6, 109.1, 100.1, 34.6, 31.6.

(*E*)-2-(4-Methoxystyryl)-5-nitrobenzo[d]oxazol-6-ol (338): 2-Methyl-5-nitrobenzo[d]oxazol-6-ol (0.971 g, 5 mmol) was dissolved in DMF (20 mL), and powdered potassium hydroxide (2.81 g, 25 mmol) was added in one portion and allowed to stir for five minutes to produce a deep red solution. 4-Anisealdehyde (1.36 g, 10 mmol) was added, and the reaction was allowed to proceed for one hour, after which the mixture was poured into a beaker containing chilled 0.2 M HCl (200 mL). The solid was isolated by vacuum filtration and was with water. Recrystallization from isopropanol yielded fluffy, small, acicular, orange-yellow crystals.

(*E*)-5-Amino-2-(4-methoxystyryl)benzo[d]oxazol-6-ol (339): (*E*)-2-(4-Methoxystyryl)-5-nitrobenzo[d]oxazol-6-ol (.468 g, 1.5 mmol) was dissolved in boiling 4:1 ethanol:concentrated ammonia. Sodium dithionite (1.6 g, 7 mmol) was added in portions, and the solution turned from deep red to yellow. The reaction is cooled to room temperature, neutralized with 1 M HCl, and pH 7 phosphate buffer, and then filtered and

washed with water to yield a salmon-colored solid that was used in the next step without purification.

(*E*)-2-(4-Methoxystyryl)-6-methylbenzo[1,2-d:5,4-d']bis(oxazole) (340): Crude (*E*)-5-amino-2-(4-methoxystyryl)benzo[d]oxazol-6-ol from the previous step was dissolved in DMSO (20 ml), andyttrium triflate (40.2 mg, 0.075 mmol) and triethyl orthoacetate (0.730 g, 3 mmol) were added. The reaction was heated to 50 °C for two days, and the product was precipitated from solution by pouring the reaction into water (200 mL) to yield a brown powder (0.401 g, 87% over two steps). ^{1}H NMR ($CDCl_3$): 7.90 (s, 1H), 7.74 (d, J = 16.2 Hz, 1H), 7.60 (s, 1H), 7.55 (d, 2H), 6.95 (d, 2H), 6.93 (d, J = 16.2 Hz, 1H), 3.86 (s, 3H), 2.66 (s, 3H). ^{13}C NMR ($CDCl_3$): 164.7, 164.1, 161.3, 149.1, 148.3, 139.5, 139.3, 129.4, 128.1, 114.7, 111.5, 109.1, 92.9, 55.6, 14.9.

2-(4-Methoxyphenyl)-1,3-dithiane (341): *p*-Anisaldehyde (6.81 g, 50 mmol) and 1,3-propanedithiol (5.59 g, 55 mmol) were dissolved in ethyl acetate (50 mL) at room temperature, and iodine (6.35 g, 2.5 mmol) was added. After 30 minutes, the reaction was quenched by the addition of 1 M sodium dithionite (30 mL) and 6 M sodium hydroxide (20 mL). The organic layer was washed with water, and then bring, the solvent was dried and removed under vacuum, and the product was recrystallized from ethanol to give white, acicular crystals. ^{1}H NMR ($CDCl_3$): 7.51 – 7.31 (m, 2H), 6.97 – 6.79 (m, 2H), 5.13 (s, 1H), 3.76 (s, 3H), 3.01 (tdd, J = 12.3, 2.5, 1.1 Hz, 2H), 2.90 – 2.82 (m, 2H), 2.11 (dtt, J = 11.3, 4.6, 2.3 Hz, 1H), 1.95 – 1.81 (m, 1H). ^{13}C NMR ($CDCl_3$): 159.54, 131.35, 128.94, 114.07, 55.31, 50.72, 32.18, 25.08.

Triethyl 4-methoxyorthobenzoate (343): 2-(4-Methoxyphenyl)-1,3-dithiane (1.13 g, 5 mmol) was dissolved in dry THF (20 ml) and cooled to -78 °C under argon. Freshly titrated *n*-BuLi (1.68 M, 5.5 mmol) was added drop-wise over ten minutes, and the deprotonation of the dithiane was allowed to proceed for three hours, during which time the solution turned deep yellow. Dimethyl disulfide (0.467 g, 5.25 mmol) was added, and the reaction was warmed to room temperature and stirred for one hour, forming a cloudy yellowish mix. Anhydrous ethanol (40 mL) was added, clearing up the precipitate, followed by the addition of collidine (1.82 g, 15 mmol) and diisopropylamine (1.52 g, 15 mmol). 2 M Silver nitrate in acetonitrile (10 mL, 20 mmol) was added by syringe. After stirring overnight, the reaction was diluted with hexane, filtered, and thfiltrate was collected and washed with water several times, followed by 0.25 M copper (II) nitrate solution to remove collidine, and then with brine. The organic layer was dried over sodium sulfate, and the solvent was removed to yield a colorless oil (1.112 g, 82%). ^{1}H NMR ($CDCl_3$): 7.54-7.50 (m, 2H), 6.88-6.84 (m, 2H), 3.81 (s, 3H), 3.33 (q, 6H), 1.16 (t, 9H). ^{13}C NMR ($CDCl_3$): 159.8, 130.6, 128.9, 114.0, 113.2, 57.6, 55.3, 15.1. HRMS (+ESI): m/z calcd for $C_{14}H_{22}NaO_3$ $[M+Na]^+$, 277.1410; found 277.1411.

2-(4-methoxyphenyl)-2-(methylthio)-1,3-dithiane (342): 2-(4-Methoxyphenyl)-1,3-dithiane (2.26 g, 10 mmol) was dissolved in dry THF (20 ml) and cooled to -78 °C under argon. Freshly titrated *n*-BuLi (1.68 M, 11 mmol) was added drop-wise over ten minutes, and the deprotonation of the dithiane was allowed to proceed for three hours, during which time the solution turned deep yellow. Dimethyl disulfide (0.99 g, 10.5

mmol) was added, and the reaction was warmed to room temperature and stirred for one hour, forming a cloudy yellowish mix. The reaction is quenched by careful addition of ethanol, and then water, and the product is extracted with hexane. The organic layer is washed with brine, and then dried over sodium sulfate, and the solvent was removed to give a thick, yellow oil. ^{1}H NMR ($CDCl_3$): 7.87 – 7.83 (m, 2H), 6.90 – 6.85 (m, 2H), 3.79 (s, 3H), 3.34 (ddd, *J* = 14.2, 11.3, 2.8 Hz, 2H), 2.70 (ddd, *J* = 13.4, 5.7, 3.1 Hz, 2H), 2.11 (dtt, *J* = 14.2, 5.7, 2.8 Hz, 1H), 1.95 (s, 3H), 1.88 (dtt, *J* = 13.4, 11.3, 3.1 Hz, 1H). ^{13}C NMR ($CDCl_3$): 159.47, 132.89, 129.28, 113.74, 55.37, 29.05, 24.46, 16.35.

2-(Thiophen-2-yl)-1,3-dithiane (344): A procedure analogous to the synthesis of **341** was used, using thiophene-2-carboxaldehyde (5.71 g, 10.17 mmol). Recrystallization from ethanol gave large, colorless lamellar crystals (9.71 g, 94%). ^{1}H NMR ($CDCl_3$): 7.18 (dd, J = 5.1, 1.3 Hz, 1H), 7.08 (dt, J = 3.6, 1.1 Hz, 1H), 6.88 (dd, J = 5.1, 3.6 Hz, 1H), 5.33 (d, J = 0.9 Hz, 1H), 2.97 – 2.78 (m, 4H), 2.05 (dtt, J = 14.2, 5.7, 2.9 Hz, 1H), 1.87 (dtt, J = 13.9, 10.2, 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): 142.58, 126.80, 126.22, 125.70, 44.74, 31.04, 25.05.

2-(Triethoxymethyl)thiophene (345): The procedure used for 343 was used here, using 2-(thiophen-2-yl)-1,3-dithiane as the starting material to yield a reddish oil (.955 g, 83%). ^{1}H NMR ($CDCl_3$): 7.27 (dd, J = 5.0, 1.3 Hz, 1H), 7.17 (dd, J = 3.6, 1.3 Hz, 1H), 6.97 (dd, J = 5.0, 3.6 Hz, 1H), 3.43 (q, J = 7.1 Hz, 6H), 1.18 (t, J = 7.1 Hz, 9H). ^{13}C NMR ($CDCl_3$):142.2, 126.9, 126.6, 126.2, 113.2, 58.2, 15.0.

***N*-(4-(1,3-Dithian-2-yl)phenyl)-4-(*tert*-butyl)-*N*-(4-(*tert*-butyl)phenyl)aniline (346):** 4-(bis(4-(*tert*-butyl)phenyl)amino)benzaldehyde (3.56 g, 10 mmol) and 1,3-

propanedithiol (1.62 g, 15 mmol) were dissolved in dry methylene chloride under argon, and cooled to -78 °C. Boron trifluoride diethyl etherate (2.13 g, 1.5 eq) was added, and the color changes from green to yellow to red within three minutes. While stirring at -78 °C for one hour, the color became deep purple, and then ink-blue. The reaction was quenched by adding 1 M potassium hydroxide, producing a teal color that became green, and then beige. The organic compound was extracted with methylene chloride, and washed with more 1 M potassium hydroxide, and then brine. The organic layer was dried with sodium sulfate, and the solvent was removed under vacuum to give a beige solid. (4.56 g, 96%). mp: 213-216 °C. ^{1}H NMR ($CDCl_3$): 7.32 – 7.21 (m, 6H), 7.05 – 6.95 (m, 6H), 5.13 (s, 1H), 3.06 (ddd, J = 13.5, 12.4, 2.4 Hz, 2H), 2.91 (ddd, J = 14.4, 4.3, 3.0 Hz, 2H), 2.16 (dtt, J = 13.5, 4.3, 2.4 Hz, 1H), 1.92 (dtt, J = 14.4, 12.4, 3.0 Hz, 1H), 1.31 (s, 18H). HRMS (+ESI): m/z calcd for $C_{30}H_{37}NS_2$ $[M+H]^+$, 475.2362; found 474.2351.

Triethyl 4-(bis(4-(*tert*-butyl)phenyl)amino)orthobenzoate (347): *N*-(4-(1,3-Dithian-2-yl)phenyl)-4-(*tert*-butyl)-N-(4-(*tert*-butyl)phenyl)aniline (0.952 g, 2 mmol) was dissolved in dry THF and cooled to -78 °C under argon. Freshly titrated *n*-BuLi (2.5 M, 0.96 mL, 2.4 mmol) was added drop-wise over ten minutes, and the deprotonation of the dithiane was allowed to proceed for two hours, during which time the solution turned deep yellow. Dimethyl disulfide (0.153 g, 2.2 mmol) was added, and the reaction was warmed to room temperature and stirred for one hour, forming a cloudy yellowish mix. Anhydrous ethanol (40 mL) was added, clearing up the precipitate, followed by the addition of collidine (.721 g, 6 mmol) and diisopropylamine (.202 g, 2 mmol). Silver

nitrate (1.02 g, 6 mmol) was dissolved in dry acetonitrile (10 mL) and added by syringe to the reaction mixture, changing the color to purple, then mauve, and then beige. After stirring for two hours, hexane (30 mL) was added, and the suspension was filtered. The filtrate was collected and washed with water several times and then brine. The organic layer was dried over sodium sulfate, and the solvent was removed to give a thick, orange oil. (.84 g, 83%) . ^{1}H NMR ($CDCl_3$): 7.38 – 7.31 (m, 2H), 7.20 – 7.16 (m, 4H), 6.97 – 6.90 (m, 6H), 3.30 (q, J = 7.0 Hz, 6H), 1.24 (s, 18H), 1.11 (t, J = 7.1 Hz, 9H). ^{13}C NMR ($CDCl_3$): 145.99, 145.12, 128.30, 126.29, 126.22, 124.70, 124.35, 121.79, 121.66, 57.66, 34.50, 31.65, 15.16. HRMS (+ESI): m/z calcd for $C_{33}H_{45}NO_3$ $[M+H]^+$, 503.3394; found 503.3385.

5-(1,3-Dithian-2-yl)benzo[d][1,3]dioxole (348): Piperanal (7.50 g, 50 mmol) and 1,3-propanedithiol (5.95 g, 55 mmol) were dissolved in ethyl acetate (50 mL) at room temperature, and iodine (0.634 g, 55 mmol) was added. After 30 minutes, the reaction was quenched by adding 1M sodium thiosulfate (30 mL) and 6 M sodium hydroxide (30 mL). The organic layer was then washed with brine and dried over sodium sulfate. The product was isolated as white, acicular crystals after recrystallization from ethanol. (11.25 g, 94%). mp: 86.5-88 °C. ^{1}H NMR ($CDCl_3$): 6.99 (d, J = 1.8 Hz, 1H), 6.95 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.96 (s, 2H), 5.10 (s, 1H), 3.05 (ddd, *J* = 13.9, 12.5, 3.1 Hz 2H), 2.89 (ddd, 2H), 2.16 (dtt, *J* = 13.8, 4.5, 2.0 Hz, 1H), 1.91 (dtt, *J* = 14.3, 12.5, 3.1 Hz, 1H). ^{13}C NMR ($CDCl_3$): 147.9, 147.8, 133.1, 121.4, 108.534, 108.531, 51.3, 32.4, 25.2.

5-(Triethoxymethyl)benzo[d][1,3]dioxole (348): The same procedure was used as for 343, but with 5-(1,3-Dithian-2-yl)benzo[d][1,3]dioxole (1.20 g, 5 mmol) as the starting material to yield a yellowish oil (1.04 g, 77%). ^{1}H NMR ($CDCl_3$): 7.11 (dd, J = 8.1, 1.7 Hz, 1H), 7.07 (dd, J = 1.7, 0.4 Hz, 1H), 6.76 (dd, J = 8.1, 0.4 Hz, 1H), 5.95 (s, 2H), 3.33 (q, J = 7.1 Hz, 6H), 1.15 (t, J = 7.1 Hz, 9H). ^{13}C NMR: 147.77, 147.61, 132.51, 121.42, 113.79, 108.11, 107.58, 101.24, 57.66, 15.06. $C_{14}H_{20}NaO_5$ $[M+Na]^+$, 291.1203; found 291.1205.

3-(1,3-dithian-2-yl)-9-hexyl-9*H*-carbazole: 9-hexylcarbazole-3-carboxaldehyde (4.19 g, 15 mmol) was dissolved in ethyl acetate (40 mL), and 1,3-propanedithiol (1.79 g, 16.5 mmol) was added. Iodine (.381 g, 1.5 mmol) was added, and the reaction was stirred at room temperature for one hour. The reaction was quenched by the addition of 1 M aqueous sodium thiosulfate (20 mL), and the organic layer was washed with 1 M potassium hydroxide to remove the dithiol, and then brine, and the dried over sodium carbonate. The organic solvent was removed under vacuum and the solid was recrystallized from hexane to give white, fibrous, fluffy crystals. ^{1}H NMR ($CDCl_3$): 8.26 (d, *J* = 1.8 Hz, 1H), 8.12 (d, *J* = 7.7 Hz, 1H), 7.60 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.48 (td, *J* = 7.6, 7.0, 1.3 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.25 (t, *J* = 7.4 Hz, 1H), 5.41 (s, 1H), 4.26 (t, *J* = 7.3 Hz, 2H), 3.14 (ddd, *J* = 13.9, 12.6, 2.5 Hz, 2H), 2.97 (ddd, *J* = 14.1, 13.9, 3.7 Hz, 2H), 2.21 (dtt, *J* = 13.9, 4.6, 2.5 Hz, 1H), 2.02 (dtt, 14.1, 12.6, 3.7, 1H), 1.85 (p, *J* = 7.2 Hz, 2H), 1.46 – 1.23 (m, 6H), 0.89 (t, 3H). ^{13}C NMR ($CDCl_3$): 141.0, 140.5, 129.7, 125.9, 125.5, 123.1, 122.8, 120.7, 119.9, 119.1,

108.9, 52.1, 43.3, 32.7, 31.7, 29.1, 25.4, 22.7, 14.2. HRMS (+ESI): m/z calcd for $C_{22}H_{28}NS_2$ $[M+H]^+$, 370.1647; found 370.1658.

Trimethyl 4-methoxyorthobenzoate (352): Performed analogously to **341**, only on a 2 mmol scale, with methanol used instead of ethanol. Product was isolated as a yellowish oil (0.361 g, 85^{1}H NMR ($CDCl_3$): 7.47 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 3.10 (s, 9H). ^{13}C NMR ($CDCl_3$):160.00, 129.12, 128.87, 115.17, 113.41, 55.38, 49.78.

3-hydroxy-2-(hydroxymethyl)-2-methylpropyl 4-methoxybenzoate (354): 1-(4-Methoxyphenyl)-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane was allowed to decompose in the presence of moist air with trace amounts of hydrogen chloride vapors to yield a solid white compound which looked identical to the starting material. ^{1}H NMR ($CDCl_3$): 8.11 – 7.94 (m, 2H), 6.99 – 6.88 (m, 2H), 4.41 (s, 2H), 3.86 (s, 3H), 3.63 (m, 2H), 3.58 (m, 2H), 2.83 (s, 3H), 0.92 (s, 3H). ^{13}C NMR ($CDCl_3$):167.5, 163.9, 132.0, 122.2, 113.9, 68.0, 66.8, 55.7, 41.3, 17.2.

***tert*-Butyl (1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)carbamate (352):**[45] 2-amino-2-(hydroxymethyl)propane-1,3-diol (6.06 g, 50 mmol) was suspended in 1:1 methanol:*t*-butanol (90 mL). Boc anhydride (14.19 g, 65 mmol) was dissolved in *t*-butanol, and added in one portion. The reaction was allowed to stir for 18 hours. The solvent was removed under vacuum, and the solid was recrystallized form ethyl acetate to give large, fibrous, white crystals (10.04 g, 91%).

***tert*-Butyl (1-(4-methoxyphenyl)-2,6,7-trioxabicyclo[2.2.2]octan-4-yl)carbamate (353):** Performed on a 2 mmol scale following the procedure for 341. *tert*-Butyl (1,3-

dihydroxy-2-(hydroxymethyl)propan-2-yl)carbamate (.664 g, 3 mmol) was used instead of ethanol, and was added as a suspension in THF. The product was recrystallized from methanol to give a white powder (0.567 g, 84%). ^{1}H NMR ($CDCl_3$): 7.65 – 7.46 (m, 2H), 6.90 – 6.78 (m, 2H), 4.39 (s, 1H), 4.31 (s, 6H), 3.79 (s, 3H), 1.45 (s, 10H). ^{13}C NMR ($CDCl_3$): 160.51, 132.18, 127.28, 113.55, 113.54, 110.21, 108.42, 70.16, 55.51, 47.09, 28.47, 1.24.

1-(4-Methoxyphenyl)-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (352): The standard procedure from **341** was followed, only instead of adding ethanol, 2-(hydroxymethyl)-2-methylpropane-1,3-diol (1.80 g, 15 mmol) was added as a suspension in THF. The product was isolated as a solid which was recrystallized from hexane to give beige prisms (0.909 g, 77%). ^{1}H NMR ($CDCl_3$): 7.55 (d, 2H), 6.86 (d, 2H), 4.07 (s, 6H), 3.78 (s, 3H), 0.86 (s, 3H). ^{13}C NMR ($CDCl_3$):160.2, 130.2, 127.2, 113.4, 107.6, 73.3, 55.4, 30.5, 14.6.

5-(2-ethoxy-1,3-dithian-2-yl)benzo[d][1,3]dioxole (355): On one run of **348**, the reaction with silver nitrate was only permitted to take place for 30 minutes. A solid was isolated upon work-up, which was recrystallized from toluene/hexan to give off-white prisms (2.84 g, 54%); mp: 111-112 °C; ^{1}H NMR ($CDCl_3$): 7.14 – 7.10 (m; overlap, 2H), 6.77 (d, J = 8.6 Hz, 1H), 5.95 (s, 2H), 3.42 (q, J = 7.1 Hz, 2H), 3.33 (ddd, J = 13.9, 12.7, 2.5 Hz, 2H), 2.70 (dtd, J = 13.2, 3.0, 1.3 Hz, 2H), 2.13(dtt, J = 13.2, 12.7, 2.5 Hz ,1H), 1.96 (dtt, J = 13.9, 3.0, 1.3 Hz ,1H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR: 148.04, 147.97, 134.9, 120.2, 108.2, 107.0, 101.5, 90.9, 61.0, 28.3, 24.6, 15.2. HRMS (+ESI): m/z calcd for $C_{13}H_{17}O_3S_2$ $[M+H]^+$, 285.0614; found 285.0608.

3.6. References

1. Beaujuge, P. M.; Vasilyeva, S. V.; Ellinger, S.; McCarley, T. D.; Reynolds, J. R., *Macromolecules* **2009,** *42* (11), 3694-3706.

2. Schafer, F. P.; Schmidt, W.; Volze, J., *Appl. Phys. Lett.* **1966,** *9* (8), 306-309.

3. Ajayaghosh, A., *Acc. Chem. Res.* **2005,** *38* (6), 449-459.

4. Kolotuchin, S. V.; Zimmerman, S. C., *J. Am. Chem. Soc.* **1998,** *120* (35), 9092-9093.

5. Yamamoto, Y.; Fukushima, T.; Suna, Y.; Ishii, N.; Saeki, A.; Seki, S.; Tagawa, S.; Taniguchi, M.; Kawai, T.; Aida, T., *Sci* **2006,** *314* (5806), 1761-1764.

6. Percec, V.; Glodde, M.; Bera, T.; Miura, Y.; Shiyanovskaya, I.; Singer, K.; Balagurusamy, V.; Heiney, P.; Schnell, I.; Rapp, A., *Nature* **2002,** *419* (6905), 384-387.

7. Karna, S. P.; Yeates, A. T., *Nonlinear Optical Materials: Theory and Modeling*. ACS Publications: 1996.

8. Wasielewski, M. R., *Acc. Chem. Res.* **2009,** *42* (12), 1910-1921.

9. Geissman, T. A., The Cannizzaro Reaction. In *Organic Reactions*, John Wiley & Sons, Inc.: 2004.

10. Devlin, H. R.; Harris, I. J., *Ind. Eng. Chem. Fundamen.* **1984,** *23* (4), 387-392.

11. Oliviero, L.; Barbier Jr, J.; Duprez, D., *Applied Catalysis B: Environmental* **2003,** *40* (3), 163-184.

12. Howell, F. H. Benzo-1,4-quinones. U.S. Patent 4,608,435, 1986.

13. Jacob, P.; Callery, P. S.; Shulgin, A. T.; Castagnoli, N., *J. Org. Chem.* **1976,** *41* (22), 3627-3629.

14. Suzuki, H., *Synthesis* **1977,** *1977* (04), 217-238.

15. Musgrave, O. C., *Chem. Rev.* **1969,** *69* (4), 499-531.

16. Leyva, S.; Castanedo, V. c.; Leyva, E., *J. Fluorine Chem.* **2003,** *121* (2), 171-175.

17. Zambito, A. J.; Howe, E. E., *Org. Syntheses* **1960,** *40*, 21.

18. Béchamp, A., *Anal. Chim. Phys.* **1854,** *42*, 186.

19. Entwistle, I. D.; Jackson, A. E.; Johnstone, R. A. W.; Telford, R. P., *J. Chem. Soc., Perkin Trans. 1* **1977,** *0* (4), 443-444.

20. Entwistle, I. D.; Johnstone, R. A. W.; Povall, T. J., *J. Chem. Soc., Perkin Trans. 1* **1975,** *0* (13), 1300-1301.

21. Nishimura, S., *Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis*. John Wiley & Sons: 2001.

22. Buechi, G.; Weinreb, S. M., *J. Am. Chem. Soc.* **1971,** *93* (3), 746-752.

23. Sajiki, H.; Kuno, H.; Hirota, K., *Tetrahedron Lett.* **1997,** *38* (3), 399-402.

24. Heathcock, C. H.; Ratcliffe, R., *J. Am. Chem. Soc.* **1971,** *93* (7), 1746-1757.

25. Hawker, S.; Bhatti, M. A.; Griffin, K. G., **1992,** *10* (1-2), 49.

26. So, Y. H.; Heeschen, J. P., *J. Org. Chem* **1997,** *62*, 3552-3561.

27. Junji, K.; Hiromoto, M. Benzoxazole Derivative and its Production. Japanene Patent 198,777, 2000.

28. Rao, M. M.; Lavie, D., *Tetrahedron* **1974,** *30* (18), 3309-3313.

29. Schmitt, R. J.; Ross, D. S.; Hardee, J. R.; Wolfe, J. F., *J. Org. Chem.* **1988,** *53*, 5568-5569.

30. Fujita, S.; Koyama, K.; Inagaki, Y., *Synthesis* **1982,** *1982* (01), 68-69.

31. Mike, J. F.; Makowski, A. J.; Jeffries-EL, M., *Org. Lett.* **2008,** *10* (21), 4915-4918.

32. McElvain, S. M.; Nelson, J. W., *J. Am. Chem. Soc.* **1942,** *64*, 1825-7.

33. McElvain, S. M.; Stevens, C. L., *J. Am. Chem. Soc.* **1947,** *69*, 2663-6.

34. DeWolfe, R. H., *Synthesis* **1974,** *1974* (03), 153-172.

35. Marshall, J. A.; Belletire, J. L., *Tetrahedron Lett.* **1971,** *12* (13), 871-874.

36. Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H., *J. Org. Chem.* **2001,** *66* (22), 7527-7529.

37. Reece, C. A.; Rodin, J. O.; Brownlee, R. G.; Duncan, W. G.; Silverstein, R. M., *Tetrahedron* **1968,** *24* (11), 4249-4256.

38. Corey, E. J.; Erickson, B. W., *J. Org. Chem.* **1971,** *36* (23), 3553-3560.

39. Giner, J.-L.; Faraldos, J. A., *J. Org. Chem.* **2002,** *67* (8), 2717-2720.

40. Allard, P.-M.; Martin, M.-T.; Tran Huu Dau, M.-E.; Leyssen, P.; Guéritte, F.; Litaudon, M., *Org. Lett.* **2011,** *14* (1), 342-345.

41. Corey, E. J.; Raju, N., *Tetrahedron Lett.* **1983,** *24* (50), 5571-5574.

42. Giner, J.-L., *Org. Lett.* **2005,** *7* (3), 499-501.

43. Nawrat, C. C.; Lewis, W.; Moody, C. J., *J. Org. Chem.* **2011,** *76* (19), 7872-7881.

44. Schmitt, R. J.; Ross, D. S.; Hardee, J. R.; Wolfe, J. F., *J. Org. Chem.* **1988,** *53* (23), 5568-5569.

45. Chabre, Y. M.; Contino-Pépin, C.; Placide, V.; Shiao, T. C.; Roy, R., *J. Org. Chem.* **2008,** *73* (14), 5602-5605.