TETRAZINE USAGE IN THE SYNTHESIS AND POST-FUNCTIONALIZATION OF POLYMERS TOWARDS GENERATING FOAMS, ANTIOXIDANT-RICH MATERIALS, AND OPTICAL WAVEGUIDES

by

Robb Eben Bagge

Copyright © Robb Eben Bagge 2017

A Dissertation Submitted to the Faculty of the
DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY
In Partial Fulfillment of the Requirements
For the Degree of
DOCTOR OF PHILOSOPHY
WITH A MAJOR IN CHEMISTRY
In the Graduate College
THE UNIVERSITY OF ARIZONA

2017
As members of the Dissertation Committee, we certify that we have read the dissertation prepared by Robb Eben Bagge, titled “Tetrazine Usage in the Synthesis and Post-functionalization of Polymers Towards Generating Foams, Antioxidant-rich Materials, and Optical Waveguides” and recommend that it be accepted as fulfilling the dissertation requirement for the Degree of Doctor of Philosophy.

Prof. Douglas Loy
Date: 07/14/2017

Prof. Erica Corral
Date: 07/14/2017

Prof. John Jewett
Date: 07/14/2017

Prof. Jon Njarðarson
Date: 07/14/2017

Final approval and acceptance of this dissertation is contingent upon the candidate’s submission of the final copies of the dissertation to the Graduate College.

I hereby certify that I have read this dissertation prepared under my direction and recommend that it be accepted as fulfilling the dissertation requirement.

Date: 07/14/2017

Dissertation Director: Prof. Douglas A. Loy
STATEMENT BY AUTHOR

This dissertation has been submitted in partial fulfillment of the requirements for an advanced degree at the University of Arizona and is deposited in the University Library to be made available to borrowers under rules of the Library.

Brief quotations from this dissertation are allowable without special permission, provided that an accurate acknowledgement of the source is made. Requests for permission for extended quotation from or reproduction of this manuscript in whole or in part may be granted by the head of the Chemistry & Biochemistry department or the Dean of the Graduate College when in his or her judgement the proposed use of the materials is in the interests of scholarship. In all other instances, however, permission must be obtained from the author.

SIGNED: Robb Eben Bagge
It’s been a tortuous route that I’ve found myself on while reaching this point, but I’m overjoyed and awestruck to finally be here. There are so many people who have inspired me throughout my life and have provided insight which has helped me to achieve this accomplishment. I cannot thank you enough.

I would like to thank my family for the unconditional love and support throughout my life and especially through the very many difficult & often frustrating experiences over the last six years of working with tetrazines. I owe my inquisitiveness and creativity to my parents. The many trips to science & art museums as well as concerts, plays, and trips to new locations helped to provide me with a cultural and creative advantage over that of many of my peers, and helped me to create other avenues to pursue when research projects & life in general reached dead-ends. You’ve both inspired me to strive for something better in life, thank you for everything you’ve given me. To my brothers, Chad, Sean, Ross, and Lance, I’ve missed out on so many experiences with you and your families over these last six years, but I hope it makes you feel proud to know that your little brother has finally finished school after all these years. I’m looking forward to making up on lost time, and it will be a wonderful experience to see my nephews again.

To Barb and Bill, you are the best godparents someone like me could have ever hoped for, thank you for your support throughout my life. It’s meant so much to me.

To all my friends, I’m lucky to have met you and I’m sorry I won’t be able to do this section justice by thanking you all personally. Dustin, you’ve been my friend for
most of my life, thanks for being diligent with keeping in touch throughout the years, I am incredibly grateful for it. Phil & Bereketab you both helped me survive the first year of graduate school and onward. I’m looking forward to maintaining close friendships after this. Evan and Stephanie, you helped me enjoy my time here in Tucson and I wouldn’t sacrifice that for anything. Evan, thanks for dragging me out hiking, and the views of the Tucson area from the tops of Mts. Kimball, Wrightson, Wasson, will be something I remember fondly from Tucson. Jared, Lawrence, Edon, and Tristan thanks for your friendship and expert advice through my time here. It would have been a much more difficult road without you all. To my labmates, Stephanie, Niharika, Yani, Peter, Wenmo, Alyssa, and Kevin thanks for your support and making time in lab enjoyable during my time here. Thanks for everything over these years. To Ryan, Chris, Zach, Cody, and Mike, thanks for your friendship and for humbling me during our Tuesday night game sessions. It was a great escape from the excitement of grad school, and I’ll definitely miss the experience when I leave Tucson.

Prof. Loy, thank you for your patience and guidance over the years. It took a while to get things going with tetrazines, and I’m grateful that you were supportive throughout the process. You’ve helped me to develop into a capable, confident and ethical scientist, and I’m grateful for it. Thank you for your mentorship these last 6 years, and for believing in my abilities.

Finally to Calley, thank you for your love and support during these final two years of graduate school and throughout the experience of writing this dissertation. Over the last two years you’ve inspired me to be a better scientist, and filled my life with joy. I’m extremely lucky and eternally grateful to you for everything.
DEDICATION

To Larry and Susan Bagge,

You’ve provided me with love, support, and inspiration throughout my life, as well as a 5-letter last name which no one can pronounce correctly.

For clarification, phonetically it’s pronounced “bah – ghee”
Contents

List of Figures........................................................................................................................................12
List of Schemes........................................................................................................................................20
List of Tables ...........................................................................................................................................21
List of Abbreviations ..............................................................................................................................22
Abstract..................................................................................................................................................24

Chapter 1: History of Tetrazines in Polymer Synthesis & Modification .................27

1.1 Introduction .......................................................................................................................................27
1.2 Tetrazines in polymer chemistry ....................................................................................................31
   1.2.1 Polymers with Backbone Tetrazine Units Through Cycloaddition and Step-Growth Reactions ..................................................................................................................31
   1.2.2 Conjugated Tetrazine Polymers Through Electropolymerization and Stille Coupling .................................................................................................................................38
   1.2.3 Nanoparticle Functionalization .................................................................................................50
   1.2.4 Verdazyl-Controlled Living polymerizations .........................................................................55
   1.2.5 Tetrazine IEDDA Polymer Post-Modification .........................................................................60
1.3 Conclusion .........................................................................................................................................79

Chapter 2: Transforming polybutadiene with tetrazine click chemistry into self-indicating, antioxidant foams .................................................................80

2.1 Introduction .......................................................................................................................................80
Chapter 3: Fluorescent anti-oxidant macromolecules through click modification of polybutadiene with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate

3.1 Introduction

3.2 Results & Discussion

3.2.1 Click modification of polybutadienes

3.2.2 Structure of click modified polymers

3.2.3 Thermal Properties

3.2.4 Optical and Electrochemical Properties

3.3 Conclusion

3.4 Experimental Section

Chapter 4: Bleaching of copolymers containing photodegradable pendant chloroalkoxy tetrazines groups: a potential approach towards preparing low-cost photoresists and optical waveguides

4.1 Introduction

4.2 Results & Discussion

4.2.1 Click modification of copolymers

4.2.2 Structure of click modified copolymers

4.2.3 Thermal Properties

4.2.4 Optical and Electrochemical Properties

4.3 Conclusion

4.4 Experimental Section

Chapter 5: Photodegradation of copolymers containing tetrazine-functionalized pendant chloroalkoxy groups

5.1 Introduction

5.2 Results & Discussion

5.2.1 Photodegradation of copolymers

5.2.2 Structure of photodegraded copolymers

5.2.3 Thermal Properties

5.2.4 Optical and Electrochemical Properties

5.3 Conclusion

5.4 Experimental Section
Chapter 4: Results & Discussion

4.1 Introduction .................................................................................................................................................. 126

4.2 Results & Discussion ................................................................................................................................... 128

4.2.1 Synthesis of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) and the development of a pendant tetrazine copolymer ........................................................................................................... 128

4.2.2 Structure of copolymers and 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) ........................................................................................................................................................................................................................................... 129

4.2.3 Thermal and photochemical properties .................................................................................................. 131

4.3 Conclusion .................................................................................................................................................... 135

4.4 Experimental Section .................................................................................................................................. 136

Chapter 5: Conclusions and future work ........................................................................................................... 140

5.1 Conclusion ................................................................................................................................................... 140

5.2 Future Work ............................................................................................................................................... 144

5.2.1 Tetrazines as chemical blowing agents (Organosilicon foams) ......................................................... 144

5.2.2 Tetrazines as chemical blowing agents (1,2,4,5-tetrazine blowing agent) ........................................ 145

5.2.3 Poly(MMA-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) photoresists ..................... 146

Appendix A: Chapter 2 Supporting Information ............................................................................................. 148

A.1 Materials ...................................................................................................................................................... 148

A.2 Instrumentation .......................................................................................................................................... 149

A.3 Experimentals .......................................................................................................................................... 150
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.4</td>
<td>SEM of Foams</td>
<td>155</td>
</tr>
<tr>
<td>A.5</td>
<td>NMR Spectra</td>
<td>155</td>
</tr>
<tr>
<td>A.6</td>
<td>IR Spectra</td>
<td>162</td>
</tr>
<tr>
<td>A.7</td>
<td>TGA</td>
<td>168</td>
</tr>
<tr>
<td>Appendix B: Chapter 3 Supporting Information</td>
<td></td>
<td>169</td>
</tr>
<tr>
<td>B.1</td>
<td>Instrumentation</td>
<td>169</td>
</tr>
<tr>
<td>B.2</td>
<td>Materials</td>
<td>170</td>
</tr>
<tr>
<td>B.3</td>
<td>Experimentals</td>
<td>171</td>
</tr>
<tr>
<td>B.4</td>
<td>NMR Spectra</td>
<td>176</td>
</tr>
<tr>
<td>B.5</td>
<td>Comparison NMR Spectra</td>
<td>184</td>
</tr>
<tr>
<td>B.6</td>
<td>IR Spectra</td>
<td>188</td>
</tr>
<tr>
<td>B.7</td>
<td>GPC Data</td>
<td>190</td>
</tr>
<tr>
<td>B.9</td>
<td>UV-Vis Spectra (all samples were dissolved in CHCl₃)</td>
<td>193</td>
</tr>
<tr>
<td>B.10</td>
<td>Fluorimeter (all samples were dissolved in CHCl₃)</td>
<td>197</td>
</tr>
<tr>
<td>B.11</td>
<td>Quantum Yield Data</td>
<td>198</td>
</tr>
<tr>
<td>Appendix C: Chapter 4 Supporting Information</td>
<td></td>
<td>200</td>
</tr>
<tr>
<td>C.1</td>
<td>Materials</td>
<td>200</td>
</tr>
<tr>
<td>C.2</td>
<td>Instrumentation</td>
<td>201</td>
</tr>
<tr>
<td>C.3</td>
<td>Experimentals</td>
<td>202</td>
</tr>
<tr>
<td>C.4</td>
<td>NMR Spectra</td>
<td>202</td>
</tr>
</tbody>
</table>
C.5 IR Spectra ........................................................................................................205

C.6 Absorbance & Emission Spectra ........................................................................207

C.7 TGA Data ...........................................................................................................208

Permissions ..............................................................................................................208

References ...............................................................................................................215
List of Figures

Figure 1: Representative 1,2,4,5-tetrazine structure, numbered per convention. ..............27

Figure 2: Representative IEDDA reaction of 1,2,4,5-tetrazine. The initial cycloaddition results in a bicyclic intermediate, which undergoes a retro-cycloaddition releasing nitrogen gas and forming a dihydropyridazine ring. Subsequent tautomerization yields the 1,4-dihydropyridazine isomer. ...........................................................................................................28

Figure 3: Qualitative frontier molecular orbital (FMO) energy diagram showing the shift in FMO energies going from benzene to 1,2,4,5-tetrazine and the effect that electron donating groups at the 3 & 6 positions have on FMO energy levels of 1,2,4,5-tetrazines.30

Figure 4: (A, B) First tetrazine polymers, formed through 1,3-dipolar cycloaddition to form linear poly(1,3,4-triphenyl-1λ4,2,4λ4,5-tetrazine (2,4). (C) Synthesis of poly(1,4-diphenyl-1λ4,2,4λ4,5-tetrazine) (5) and through 1,3-dipolarophile cycloaddition poly(1,4-diphenyl-3-(pyridin-2-yl)-1λ4,2,4λ4,5-tetrazine) (6). (D) Polymerization of N,N'-diphenyl-2,6-pyridindioic (bis-hydrazonoyl dichloride) (7) through 1,3-dipolar cycloaddition..................................................................................................................................................32

Figure 5: Synthesis of Poly(2,6-pyridinediyl-s-tetrazinylene) (11) through microwave irradiation of pyridine2,6-diamidrazone (9) and NO gas oxidation of the dihydro intermediate (10) Polycondensation of 1,3,5-triazine-2,4,6-tris(carboximidhydrazide) (12) to form a high nitrogen content hyperbranched triazine/s-tetrazine network (13). Oxidation methods proved unable to fully convert all dihydro tetrazine units to their aromatic counterparts (14). ..................................................................................................................................................34
**Figure 6:** Formation of high nitrogen content linear polyurethanes through reaction of 3,6-dihydrazinyl-1,2,4,5-tetrazine with diisocyanates..................................................37

**Figure 7:** (A) Synthesis of 3,6-bis-(4-phenyl-4-thiophene)-1,2,4,5-tetrazine and 3,6-bis(4-[3,4-ethylenedioxythiophene])-4,40-bis(phenyl)-1,2,4,5-tetrazine through Stille coupling. Through DFT analysis, both structures showed potential for electropolymerization. (B) A series of heterocyclic substituted tetrazines studied for their potential to undergo electropolymerization, only 34 was found to polymerize. (C) Structure of bis[5-(2-2’-bithienyl)]-s-tetrazine, the first thiophene-substituted tetrazine monomer discovered to undergo electropolymerization.................................................................39

**Figure 8:** (A) Structure of poly[2,6-(4,4-dihexyl-4H-cyclepenta[2,1-b:3,4-b’]dithiophene)-alt-5,5’-(3,6-bis(4-hexylthienyl-2-yl)-s-tetrazine)]. (B & C) Derivatives of poly[2,6-(4,4-dihexyl-4H-cyclepenta[2,1-b:3,4-b’]dithiophene)-alt-5,5’-(3,6-bis(4-hexylthienyl-2-yl)-s-tetrazine)] used for comparison studies of alkyl substituent effects on the properties of the polymer..................................................................................................................42

**Figure 9:** Synthesis 3,6-bis(5-bromofuran-2-yl)-s-tetrazine 46 and structures of benzo[1,2-b:4,5-b’]dithiophene & cyclopenta[2,1-b:3,4-b’]dithiophene tetrazine copolymers..................................................................................................................44

**Figure 10:** Synthesis of (D – A) copolymers containing an indacenodithiophene repeat unit and four alternate acceptor groups including bis(thiophen-2-yl)-tetrazine ..............45

**Figure 11:** (A) Synthesis of a (D – A) copolymer containing alternating benzo[1,2-b:4,5-b’]dithiophene & bisthienyl-s-tetrazine units. (B) Synthesis of benzo[1,2-b:4,5-b’]dithiophene copolymers 61 & 63 with alternating donor units of either 3,6-Bis(3,4'
dihexyl-2,2’-bithiophen-5-yl)-1,2,4,5-Tetrazine (60) or 3,6-Bis(3,4'-dihexyl-2,2’-bithiophen-5-yl)-1,2,4,5-tetrazine (62) acceptor units..........................................................47

Figure 12: (A) Structures of tetrazine-based D-A copolymers used in DFT analysis to understand aryl substituent effect of the polymers’ properties (B) Synthesis of copolymers containing 4,8-bis(5,5”-didodecyl-[2,2’:3’,2”-terthiophen]-5’-yl)benzo[1,2-b:4,5-b’]di-thiophene alternate co-units, one being 3,6-di(thiophen-2-yl)-1,2,4,5-tetrazine (75)..................................................................................................................................................49

Figure 13: (A) Using copper nanoparticle “click” chemistry to attach polystyrene functionalities to β-cyclodextrin, and prepare tetrazine encapsulated nanoparticles through a method of solvent/water initiated self-assembly and nanoprecipitation. (B) Redox active fluorescent tetrazine-grafted silica particles which quench upon exposure to amines. (C) Single chain polymer nanoparticle formation through telechelic tetrazine IEDDA polymer chain collapse. (D) White light emitting fluorescent silica nanoparticles through surface-functionalization with chloroalkoxytetrazine and naphthalimide species.53

Figure 14: Functionalization of polystyrene nanoparticles through nucleophilic aromatic substitution of 3-bromo-6-phenyl-1,2,4,5,-tetrazine..................................................................................................55

Figure 15: (A) Linear polystyrene prepared through verdazyl mediated radical polymerization. (B) Styrene-verdazyl unimers used in the controlled polymerization of styrene. (C) Styrene-verdazyl unimers utilized in the controlled polymerization of styrene and n-butyl acrylate. (D) Structures of verdazyls used to compare steric and electronic effect on the living polymerization quality of verdazyl unimers with styrene and n-butyl acrylate..........................................................................................................................59
Figure 16: (A) Tetrazine IEDDA functionalization of degradable PLA containing end or repeating norbornene units. (B) Reaction scheme for the synthesis of PEG-Tz through amide coupling (left), and ring opening polymerization of δ-valerolactone using 2-(6-(pyridine-2-yl)-1,2,4,5-etrazin-3-yl)ethan-1-ol as initiator to form PVL-Tz (bottom left), SEC diagrams showing the formation of PS-b-PEG diblock copolymers through tetrazine-norbornene IEDDA click chemistry (right). (C) Orthogonal modification of the core and shell of micellar structures using tetrazine-norbornene IEDDA and copper-azide click chemistries, respectively .................................................................63

Figure 17: Modification of CNTs through IEDDA with 3,6-diaminotetrazine provides surface amines which can react with epoxies, and leads to a more uniform dispersion of CNTs in epoxy films and enhanced conductivity ..........................................................65

Figure 18: (A) Surface functionalized of aminopropylsilanilized glass slides with 2,5-dioxopyrrolidin-1-yl 4-(6-(pyrimidin-2-yl)-1,2,4,5-tetrazin-3-yl)benzoate to function as click anchors for making carbohydrate microarrays. (B) Surface modification of glass slides with tetrazine for micropatterning through tetrazine IEDDA and attachment of an ATRP initiator for growing graft PMA brushes ..........................................................67

Figure 19: Functionalization of polymers with repeating norbornene units through thiolene and tetrazine IEDDA click chemistries ...........................................................................................................69

Figure 20: (A) Synthesis of poly(allyl glycidyl ether) and its modification with 1,2,4,5-tetrazines. (B) Structures of tetrazines used to modify poly(allyl glycidal ether) and conduct kinetic rate experiments. ...........................................................................................................71

Figure 21: Ideal hydrogel structure prepared from reacting telechelic norbornene monomer (168) with tris-tetrazine linker (169) ...........................................................................................................73
**Figure 22:** (A & B) Tetrazine IEDDA reaction between a bis-cyclooctene linker (172) and tetrazine modified hyaluronic acid to form a networked hydrogel. (C & D) Structures and reaction of bis-transcylooctene crosslinker, and tetrazine end-capped PEG used in interfacial polymerization ........................................................................................................................................75

**Figure 23:** The synthesis of supramolecular metallo-hydrogels through tetrazine-norbornene IEDDA crosslinking followed by metal complexation ................................................76

**Figure 24:** (A) Combining alginite biopolymers functionalized with pendant norbornene and tetrazine moieties results in the formation of hydrogel matrix. (B) Applying this same chemistry to gelatin biopolymers results in the rapid formation of biocompatible gelatin hydrogels...............................................................................................................................................78

**Figure 25:** (A) Carboni-Lindsey reaction of polybutadiene with tetrazines as reactive modifiers and chemical blowing agents for the production of poly(dihydropyridazine) foams, shown completely converted. (B) The dihydropyridazine acts as a two H atom donor antioxidant oxidizing to the heteroaromatic polypyridazines...............................82

**Figure 26:** Liquid PBD (A) is blended neat with DCT and nitrogen release from the TzIEDDA reaction results in foaming (B, C). Dependent on the type of PBD used, different product results are observed. Foams produced from lower viscosity PBD14 will collapse over 72-120 hours (D) and an intractable material forms through interchain crosslinking (188). Using higher viscosity PBD12 produces a brittle foam that retains its shape indefinitely and is soluble in halogenated solvents (E). Thermoset soft foams (F) are generated from PBDOH (193). Polymers synthesized in solution (191, 192) must be accompanied with in-situ oxidation (189) otherwise cross-linking upon precipitation results in intractable products. ........................................................................................................................................83
**Figure 27:** Solution 1H NMR of (A) 191, (B) 192, and (C) 187 and solid state 13C NMR spectra of (D) 191, (E) 192, and (F) 190. .................................................................................................................89

**Figure 28:** (A) Evaluation of antioxidant properties of BHT (195), dichloro-dihydropyridazine (196) and dimethyl dihydropyridazine dicarboxylate (197) by inhibition of free radical polymerization and gelation of styrene/divinylbenzene solutions. (B) Chemical structures of each inhibitor are provided above their respective gels, and gelation times are listed showing the improved inhibition of dihydropyridazines over the commercial antioxidant BHT. .................................................................................................................94

**Figure 29:** (left) DCP fluoresces white light upon Long-Wave UV excitation. (middle) The outside layer of a 6-month aged sample of 193B emits white fluorescence under the same conditions indicating that 1,4-dihydroxyridazine units on the foam surface have undergone air oxidation. (right) Slow diffusion of air into the foam leads to a more gradual oxidation in the foam interior, evident when observing a freshly-cut cross-section of 6-month aged 193B. .................................................................................................................95

**Figure 30:** (A) Scheme for the synthesis of poly(dimethyl 4,5-dimethylene-1,4-dihydropyridazine-3,6-dicarboxylate) from the IEDDA reaction between PBD14 and DMDT (197) (B) Reaction progress can be monitored visually as the dark red color of DMDT gradually fades to a light yellow solution as the rxn proceeds indicating the complete conversion of DMDT to dihydro pyridazine..................................................................................110

**Figure 31:** (A) 1H NMR PBD12 (B) 1H NMR of 199, both NH and C=C-H peaks can be observed at 8-9 ppm and 5.74 ppm, respectively (C) 1H NMR of 200 showing the disappearance of the dihydro NH and C=C-H peaks, and a new peak at 7.97 ppm from the pyridazine ring hydrogen. (D) 13C NMR of PBD14 (E) 13C NMR of 197 showing no
peaks from residual PBD14 (F) $^{13}$C NMR of 198 showing more defined peaks as the oxidized pyridazine ring is now symmetric. CDCl$_3$ used for both proton and carbon NMR. ..........................................................................................................................112

**Figure 32:** Thermal degradation of polymers synthesized through DMDT click reactions with PBD14 (left), and PBD12 (right)...........................................................................................................113

**Figure 33:** Image of dihydropyridazine polymers 197 & 199 and their oxidized form 198 & 200 (left). Quenching of fluorescence is observed in the polymers after oxidation (right). ........................................................................................................................................115

**Figure 34:** (A) Anodic sweep of 201 and 203 showing an irreversible 1-electron oxidation for both dihydropyridazine species. (B) Cathodic sweep of 202 and 204 showing 3 distinct reduction peaks. The first peak is quasi-reversible, but the second and third are irreversible indicating either a geometric or chemical change is occurring upon reduction. Both scans conducted with a sweep rate of 100 mV/s. Counter electrode: platinum wire; reference electrode: Ag/AgNO$_3$ ........................................................................................................116

**Figure 35:** $^1$H NMR of (A) 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) (205), (B) poly(MMA-co-HEMA) (207), and (C) poly(MMA-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (208). $^{13}$C NMR of (D) 205, (E), 207, and (F) 208

**Figure 36:** (A) Tuning the extent of post-functionalization with tetrazine provides polymers that display both thermoplastic and thermoset properties. (B & C) A solvent cast film can be readily dissolved in chloroform. (D & E) Melt processing of copolymers with residual hydroxyl groups results in crosslinking, and swelling is observed when the film is exposed to chloroform. ........................................................................................................133
**Figure 37:** (A) An image of a film of 207 cast from CHCl$_3$ (B) Two films sandwiched above a UV light source, a black halo on the top film shows that the polymer underneath it is absorbing the incoming light (C) A film cast from THF that has been exposed to ambient light for 2 years, followed by further bleaching with 365 nm light for 7 days..134

**Figure 38:** Organosilicon foams from DCT IEDDA reaction with poly(allylsiloxane).144

**Figure 39:** (A) Images of soft foams prepared from the IEDDA reaction between 1,2,4,5-tetrazine and PBD (B) SEM image of the soft-foam, showing a much more uniform open cell network than SEMs of DCT based foams..........................................................146
List of Schemes

**Scheme 1:** Incorporation of DAT into linear polyurethane elastomers. A one-pot 3-step synthesis is required due to the poor nucleophilicity of DAT. Initially, (15) is prepared by reacting DAT with excess H$_2$MDI. Following that, the hard-block PU segments can be grown by reacting 15 with additional H$_2$MDI and 1,4-butanediol. Finally, soft-block segments are incorporated by reacting the TPU chain with adipate diol and additional (15).........................................................................................................................36

**Scheme 2:** (right) Reaction scheme showing the synthesis of poly(dimethyl 1,4-dihydropyridazine-3,6-dicarboxylates) (197, 198) from polybutadienes and their oxidation with DDQ to poly(dimethyl pyridazine-3,6-dicarboxylates) (198, 200). (left) Synthesis of small molecule dimethyl 1,4-dihydropyridazine-3,6-dicarboxylates (201, 203) by reacting DMDT with either cyclohexene or 1-hexene and their subsequent reaction with DDQ.................................................................................................................108

**Scheme 3:** (A) Synthesis of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (206) from reaction of DCT with 2-hydroxyethyl methacrylate (HEMA). No poly(2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) homopolymer (207) resulted from attempts at radical polymerization with AIBN, presumably due to radical inhibition by the tetrazine species. (B) Synthesis of poly(methyl methacrylate-co-2-hydroxyethyl methacrylate) (209) from AIBN initiated polymerization of methyl methacrylate (MMA) and HEMA. Post-modification of 207 with DCT produced poly(methyl methacrylate-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) in near quantitative conversions. ........................................................................................................................................127
List of Tables

Table 1: Extent of conversion and thermal properties of copolymers produced from the modification of polybutadienes with DCT. .................................................................86

Table 2: Absorption and emission data for dihydropyridazine/pyridazine polymers and small molecules prepared from DMDT click .................................................................114

Table 3: Thermal properties of 207 & 208, and photochemical properties of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (205) and 208.................................................131

Table 4: Refractive index change of poly(methyl methacrylate-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) .........................................................................................135
# List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFM</td>
<td>atomic-force microscopy</td>
</tr>
<tr>
<td>AIBN</td>
<td>azobisisobutyronitrile</td>
</tr>
<tr>
<td>BD</td>
<td>1,4-butanediol</td>
</tr>
<tr>
<td>BHJ</td>
<td>bulk heterojunction</td>
</tr>
<tr>
<td>BPO</td>
<td>benzoyl peroxide</td>
</tr>
<tr>
<td>CHCl₃</td>
<td>chloroform</td>
</tr>
<tr>
<td>CNT</td>
<td>carbon nanotube</td>
</tr>
<tr>
<td>CV</td>
<td>cyclic voltammetry</td>
</tr>
<tr>
<td>D – A</td>
<td>Donor – Acceptor</td>
</tr>
<tr>
<td>Da</td>
<td>Dalton</td>
</tr>
<tr>
<td>DAT</td>
<td>3,6-diamino-1,2,4,5-tetrazine</td>
</tr>
<tr>
<td>DCM</td>
<td>dichloromethane</td>
</tr>
<tr>
<td>DCT</td>
<td>3,6-dichloro-1,2,4,5-tetrazine</td>
</tr>
<tr>
<td>DFT</td>
<td>density functional theory</td>
</tr>
<tr>
<td>DLS</td>
<td>dynamic light scattering</td>
</tr>
<tr>
<td>DMF</td>
<td>dimethyl formamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethyl sulfoxide</td>
</tr>
<tr>
<td>DPA</td>
<td>diphenylamine</td>
</tr>
<tr>
<td>DPT</td>
<td>3,6-di(pyridyl-2-yl)-1,2,4,5-tetrazine</td>
</tr>
<tr>
<td>DSC</td>
<td>differential scanning calorimetry</td>
</tr>
<tr>
<td>EA</td>
<td>elemental analysis</td>
</tr>
<tr>
<td>FF</td>
<td>fill factor</td>
</tr>
<tr>
<td>GAP</td>
<td>glycidal azide polymer</td>
</tr>
<tr>
<td>GPC</td>
<td>gel permeation chromatography</td>
</tr>
<tr>
<td>HEMA</td>
<td>2-hydroxyethyl methacrylate</td>
</tr>
<tr>
<td>HOMO</td>
<td>highest occupied molecular orbital</td>
</tr>
<tr>
<td>H₁₂MDI</td>
<td>1-isocyanato-4-[(4-isocyanocyclohexyl)methyl]cyclohexan</td>
</tr>
<tr>
<td>IEDDA</td>
<td>inverse electron demand Diels Alder</td>
</tr>
<tr>
<td>IR</td>
<td>infrared</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>LUMO</td>
<td>lowest unoccupied molecular orbital</td>
</tr>
<tr>
<td>MMA</td>
<td>methyl methacrylate</td>
</tr>
<tr>
<td>$M_N$</td>
<td>number average molecular weight</td>
</tr>
<tr>
<td>$M_W$</td>
<td>weight average molecular weight</td>
</tr>
<tr>
<td>Nb</td>
<td>norbornene</td>
</tr>
<tr>
<td>Nb-TTC</td>
<td>norbornene trithiocarbonate</td>
</tr>
<tr>
<td>NLO</td>
<td>nonlinear optics</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>NO</td>
<td>nitric oxide</td>
</tr>
<tr>
<td>NP</td>
<td>nanoparticle</td>
</tr>
<tr>
<td>PCE</td>
<td>power conversion efficiency</td>
</tr>
<tr>
<td>PDI</td>
<td>polydispersity index</td>
</tr>
<tr>
<td>PEG</td>
<td>polyethylene glycol</td>
</tr>
<tr>
<td>PLA</td>
<td>poly(lactic acid)</td>
</tr>
<tr>
<td>PMA</td>
<td>poly(methyl acrylate)</td>
</tr>
<tr>
<td>PS</td>
<td>polystyrene</td>
</tr>
<tr>
<td>PSC</td>
<td>polymer solar cell</td>
</tr>
<tr>
<td>RAFT</td>
<td>reversible addition fragmentation chain transfer</td>
</tr>
<tr>
<td>RDX</td>
<td>rapid detonating explosive</td>
</tr>
<tr>
<td>ROP</td>
<td>ring-opening polymerization</td>
</tr>
<tr>
<td>SEM</td>
<td>scanning electron microscopy</td>
</tr>
<tr>
<td>TCO</td>
<td>trans-cyclooctene</td>
</tr>
<tr>
<td>TEA</td>
<td>triethylamine</td>
</tr>
<tr>
<td>TEOS</td>
<td>triethoxysilane</td>
</tr>
<tr>
<td>TEM</td>
<td>tunneling electron microscopy</td>
</tr>
<tr>
<td>$T_g$</td>
<td>glass transition temperature</td>
</tr>
<tr>
<td>TGA</td>
<td>thermal gravimetric analysis</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TN</td>
<td>tetrazine-naphthalimide</td>
</tr>
<tr>
<td>TPU</td>
<td>tetrazine-polyurethane</td>
</tr>
<tr>
<td>UV</td>
<td>ultra violet</td>
</tr>
</tbody>
</table>
Abstract

This dissertation is composed of 5 chapters detailing advances in the synthesis and post-modification of polymers using tetrazines. The research described herein conveys three new discoveries each of which should forge new fields of research concerning tetrazines in polymer chemistry, that is the use of tetrazines as chemical blowing agents in generating polymer foams, as agents for incorporating large concentrations of antioxidants into polymers, and their attachment to polymers, adding a photodegradable functional unit which alters the refractive index of the materials after degradation.

The first chapter is a review which highlights the use of tetrazines in polymer chemistry as repeat units incorporated into polymers, tools for post-modification, and cross-linkers for the formation of gels. Tetrazines are unique molecules which been utilized in many different types of materials. Their tetra-azo core has provided the basis for preparing high energetic explosive materials, and the high nitrogen content has also been exploited in metal chelating polymers. Being highly electron deficient, the tetrazine ring has found use in donor – acceptor (D – A) copolymers for use in polymer solar cells (PSCs). Its ability to undergo an irreversible cycloaddition reaction without the requirement of metal catalysis, has created an entire field of research in bioorthogonal ligation and has also found use in polymer chain extension, post-modification, and gel formation. The versatility of the tetrazine ring is demonstrated in this review with the shear variety of its applications in polymer chemistry.
The second chapter reports on the discovery of 3,6-dichloro-1,2,4,5-tetrazine’s (DCT) use as a chemical blowing agent in preparing polymer foams. This discovery demonstrates the first reported use of tetrazines as chemical blowing agents, and the production of a new class of polymers foams through exploitation of this chemistry. Nitrogen is released from a cycloaddition reaction between DCT and polybutadiene (PBD). As the reaction proceeds, the foam grows and increases in viscosity eventually setting up into a solid material. The product of the cycloaddition reaction, a dihydropyridazine ring, is demonstrated to provide the foams with a built-in antioxidant, and a change in fluorescence of the foams provides indication for extent of oxidation. Also in this chapter, a new method is proposed for comparing antioxidant properties of small molecules, and two dihydropyridazines are shown to outperform commercial antioxidant BHT with this method.

Chapter 3 follows up on the results from the previous chapter, with the synthesis of four new polymers through solution-based cycloaddition reactions between dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (DMDT) and PBD. Near quantitative conversions results in the formation of two new classes of dihydropyridazine polymers, providing an entirely new class of polymer which contains its own built-in antioxidant on nearly every repeat unit along the polymer backbone. Oxidation of these materials results in an additional 2 new classes of heteroaromatic pyridazine polymers reported for the first time in this chapter. The properties of these new materials are reported and the antioxidant properties of the dihydropyridazine ring are further explored through cyclic voltammetry (CV). Quenching of fluorescence is observed upon oxidation of the materials, providing a
visual indicator for extent of oxidation, and an explanation for the quenching is also provide through CV analysis.

Chapter 4 diverges from tetrazine IEDDA modification of polybutadienes and instead focuses on the post-modification of poly(methyl methacrylate-co-2-hydroxyethyl methacrylate) with DCT to generate photobleachable materials. This chapter represents the first reported use of tetrazine photobleaching in modifying the optical properties of polymers, and the generation of a new copolymer containing pendant tetrazine repeat units. The modified copolymer is demonstrated to be solvent processable, but crosslinks upon heat treatment. Extended UV or ambient light excitation of the copolymer results in degradation of the tetrazine ring and bleaching of the polymer. A refractive index change for the polymer is observed after degradation, leading to the hypothesis that these polymers may find use in optical waveguide materials.

Finally, chapter 5 provides a summation of the dissertation and discusses unfinished projects that can be pursued further by future Loy group graduate students.
Chapter 1

History of Tetrazines in Polymer Synthesis & Modification

1.1 Introduction

Since their initial discovery by Adolf Pinner in 1893, 1,2,4,5-tetrazines also known as symmetrical or s-tetrazines have received extensive attention due to their unique reactivity. The 1,2,4,5-tetrazine family all share the same core structure, and a vast diversity of s-tetrazines have been synthesized to date through variation of the substituents at the 3 & 6 position of the s-tetrazine ring (Figure 1). The tetrazine structure is typically synthesized in two steps by reactions of either imidine, imidate, or nitrile species with hydrazine, followed by oxidation generally with nitric oxides, although oxidation using hypervalent iodine or even light catalyzed oxidation have been reported as well. A lesser used route to 1,2,4,5-tetrazines is through the cycloaddition of 1,3-dipolarophiles as was demonstrated by Stille and Harris, when they prepared the first reported tetrazine polymer in 1966.

![Figure 1: Representative 1,2,4,5-tetrazine structure, numbered per convention.](image-url)
Owing to their four ring nitrogens, 1,2,4,5-tetrazines are electron-deficient heterocyclic species which have the ability to undergo an irreversible inverse electron demand Diels-Alder (IEDDA) reaction, first reported by Carboni & Lindsey in 1959. Unlike with ordinary Diels-Alder reactions where a [4+2]-cycloaddition occurs between an electron-rich diene and an electron-poor dienophile, IEDDA reactions happen between an electron-poor diene, in this case s-tetrazine, and an electron-rich dienophile. While most traditional Diels-Alder reactions are reversible, the unique structure of s-tetrazine leads to the formation of a bicyclic structure upon the [4+2]-cycloaddition (Figure 2). A subsequent retro-[4+2]-cycloaddition results in the release of nitrogen gas, making the tetrazine IEDDA reaction irreversible while generating a dihydropyridazine ring in the process.

![Figure 2: Representative IEDDA reaction of 1,2,4,5-tetrazine. The initial cycloaddition results in a bicyclic intermediate, which undergoes a retro-cycloaddition releasing nitrogen gas and forming a dihydropyridazine ring. Subsequent tautomerization yields the 1,4-dihydropyridazine isomer.](image)

The utility of the tetrazine IEDDA for introducing heterocyclic structures in total synthetic reactions has been demonstrated by Boger, Seitz, and Sauer. Owing to Sauer’s extensive and detailed kinetic study on the rate of reactions of dienophilic species with tetrazines, Fox and Hilderbrand/Weissleder were able to develop trans-
cyclooctene and norbornene-tetrazine ligation systems in 2008 respectively, which have helped spur the field of tetrazine ligation in bioorthogonal chemistry.\textsuperscript{17–19} Shortly afterwards, the tetrazine IEDDA reaction was demonstrated as an effective method for polymer coupling and post-modification, although this area of research has yet to catch on as effectively as its bioorthogonal counterpart.

Finally, tetrazines display unique optical properties for a small molecule. The nitrogen lone pairs situated on the tetrazine ring allow for forbidden n-\(\sigma^*\) transitions through visible light absorption and gives the tetrazines intense coloring not typically common in molecules with their level of conjugation (\textbf{Figure 3}). Substituent effects can lower the \(\pi^*\) orbital and allow for a forbidden n-\(\pi^*\) transition which provides some tetrazines with the ability to fluoresce upon UV or sometimes even visible light excitation.\textsuperscript{20} Tetrazines are also known to be redox active,\textsuperscript{21} and exploiting their redox and optical properties in polymer chemistry provides opportunities into developing sensor materials, which Audebert & colleagues have effectively demonstrated with the preparation of amine sensing nanoparticles, and white light emitting silica nanoparticles. These properties have also lead to extensive exploration into the incorporation of tetrazines in donor – acceptor (D – A) copolymers in polymer solar cells.

\textit{This space intentionally left blank}
Figure 3: Qualitative frontier molecular orbital (FMO) energy diagram showing the shift in FMO energies going from benzene to 1,2,4,5-tetrazine and the effect that electron donating groups at the 3 & 6 positions have on FMO energy levels of 1,2,4,5-tetrazines.\textsuperscript{22}

Because of their many unique properties, tetrazines have been exploited in the design and modification of a variety of different polymer applications. While extensive research has been applied to polymer modification through tetrazine IEDDA chemistry as well as tetrazine incorporation into (D – A) copolymers for use in organic PSCs, other areas have received less attention and it is with hope that this review helps to generate further interest in the design of new tetrazine-based or modified polymers and serve as a reference to those who follow in the footsteps of the authors herein.
1.2 Tetrazines in polymer chemistry

1.2.1 Polymers with Backbone Tetrazine Units Through Cycloaddition and Step-Growth Reactions

The first recorded polymers containing a tetrazine core were reported by Stille & Harris in 1966. In their effort to produce phenyl bridged polypyrazoles through 1,3-dipolar cycloadditions of either isophthaloylphenylhydrazide chloride (1) or terephthaloylphenylhydrazide chloride (3) with diyne monomers, Stille & Harris discovered that when refluxing with trimethylamine in either benzene or THF in the absence of a diyne species, the acid hydrazide chloride would self-dimerize in a 1,3 cycloaddition to form poly(1,4-diphenyl-3,6-m and p-phenylene-1,4-dihydro-1,2,4,5-tetrazine) (2, 4) in high yield (Figure 4A, 4B). Besides noting their synthesis, no mention was given to the properties of these polymers.

It wasn’t until 40 years later that these 1,3-dipolar cycloaddition tetrazine polymers were revisited by Sayed and Higgins, who synthesized the monomer bishydrazanoyl chloride (5) and polymerized it by reacting with 10 equivalents of triethylamine in refluxing chloroform or THF (Figure 4C). The authors were surprised to observe extremely low polydispersity indices (PDIs) and repeated their reaction conditions many times to convince themselves it wasn’t an artifact. The polymers (6) were synthesized up to Mw 90,000 g/mol and had glass transitions (Tg) between 70 – 80 °C depending on molecular weight. Changing the solvent from chloroform to THF resulted in lower molecular weights and a broader PDI, leading the authors to hypothesize a solvent solubility effect on the polymer formation. The authors demonstrated the polymers ability to complex with metals through chelation with cobalt.
The following year, Sayed & Higgins went on to form another 1,3-dipolar cycloaddition tetrazine polymer by being the first to synthesize and polymerize the monomer N,N'-diphenyl-2,6-pyridindioic (bis-hydrانونyl dichloride) (7) (Figure 4D). They determined the best polymerization reaction conditions to be a 4:1 TEA to monomer ratio refluxed for 48 hours at 100 °C in CHCl₃. These conditions yielded polymer (8) in 65% yield with a Mn of 72,000 g/mol and a PDI of 1.14. The polymer was then complexed with cobalt (II) chloride in solution. Thermogravimetric analysis (TGA) was used to determine the extent of cobalt complexation to be 23 wt%.

Figure 4: (A, B) First tetrazine polymers, formed through 1,3-dipolar cycloaddition to form linear poly(1,3,4-triphenyl-1λ⁴,2,4λ⁴,5-tetrazine (2,4). (C) Synthesis of poly(1,4-diphenyl-1λ⁴,2,4λ⁴,5-tetrazine) (5) and through 1,3-dipolarophile cycloaddition poly(1,4-diphenyl-3-(pyridin-2-yl)-1λ⁴,2,4λ⁴,5-tetrazine) (6). (D) Polymerization of N,N'-diphenyl-2,6-pyridindioic (bis-hydrانونyl dichloride) (7) through 1,3-dipolar cycloaddition.
In an effort to prepare high nitrogen containing polymers for use as energetic compounds, Sagot et al. applied microwave irradiation to initiate the polycondensation of pyridine-2,6-diamidrazone (9).\textsuperscript{25} It was determined that the maximum yield obtainable for the polycondensation was 47% using an irradiation power of 40W at 150 °C in DMF over a duration of 20 min (Figure 5A). Yields were reported to decrease with higher power and longer irradiation times. Traditional oxidation with NO gases yielded the fully heteroaromatic tetrazine polymer (11), although some rearrangement of tetrazine repeat units to 4-amino-1,2,4-triazole species was detected using \textsuperscript{15}N NMR. No indication of molecular weight (M\textsubscript{W}) or thermal and mechanical analysis was provided for the polymer. The authors also prepared a hyperbranched alternating tetrazine-triazine polymer matrix (13) through polycondensation of 1,3,5-triazine-2,4,6-tris(carboximidhydrazide) (12) in 180 °C DMSO (Figure 5B). The target material precipitated out of solution as an orange solid and due to its intractable nature proved difficult to fully oxidize. Liquid N\textsubscript{2}O\textsubscript{4} was used in the partial oxidation of 13 and the structure (14) was verified using spectroscopic techniques. No thermal and mechanical analyses were provided for the polymers.

This space intentionally left blank
Figure 5: Synthesis of Poly(2,6-pyridinediyl-s-tetrazinylene) (11) through microwave irradiation of pyridine2,6-diamidrazone (9) and NO gas oxidation of the dihydro intermediate (10) Polycondensation of 1,3,5-triazine-2,4,6-tris(carboximidhydrazide) (12) to form a high nitrogen content hyperbranched triazine/s-tetrazine network (13). Oxidation methods proved unable to fully convert all dihydro tetrazine units to their aromatic counterparts (14).

Incorporation of tetrazines into the backbone of polyurethane chains was successfully demonstrated by reacting 3,6-diaminotetrazine (DAT) with 1-isocyanato-4-[4-isocyanatocyclohexyl)methyl]cyclohexan (H_{12}MDI), using 1,4-butandiol (BD) and adipate diol as hard-block and soft-block chain-extenders, respectively (Scheme 1). Optimization of the reaction conditions were required to compensate for slow reaction kinetics due to the weak nucleophilicity of electron poor DAT (scheme 3). Tetrazine-polyurethane elastomers (TPU) (19) with Mn ranging from 3,500-4,000 g/mol and PDIs of ~1.3 were prepared containing 0-30%:100-70% ratios of DAT to BD. Films of TPU elastomers could be solvent cast, and the polymers were tested for their metal complexation capabilities with cobalt (II) chloride. Using TGA studies to compare
remaining mass above 500 °C for complexed and non-complexed polymers, the authors determined that ~2 equivalents of cobalt would bind to each tetrazine repeat unit. As there was no change in the solubility of 19 upon complexation, an intramolecular complexation mechanism was proposed. Stress-strain comparisons between PU and 19 (10% DAT to BD) revealed an increase in yield stress with tetrazine incorporation (3.2 to 5.9 MPa), and a decrease in yield strain from 15.8 to 9.7%. Upon metal complexation, (10% DAT to BD) yield stress for 19 dropped to 3.7 MPa, and the yield strain became 13.9% which helped to further validate the proposed intramolecular metal complexation.

This space intentionally left blank
Scheme 1: Incorporation of DAT into linear polyurethane elastomers. A one-pot 3-step synthesis is required due to the poor nucleophilicity of DAT. Initially, (15) is prepared by reacting DAT with excess H$_{12}$MDI. Following that, the hard-block PU segments can be grown by reacting 15 with additional H$_{12}$MDI and 1,4-butanediol. Finally, soft-block segments are incorporated by reacting the TPU chain with adipate diol and additional (15).

Three nitrogen-rich polymers (22, 24, 26) were synthesized by reacting equimolar concentrations of 3,6-dihydrazinyl-1,2,4,5-tetrazine (20) with 1,6-hexamethylene diisocyanate (21), 1,4-diisocyanobutane (23), and toluene-2,4-diisocyanate (24) in DMF (Figure 6). The resulting polymers were intractable, but IR spectra matched that of analogous macrocycles prepared in dilute solutions of DMF. Decomposition temperatures of 218.1 °C (22), 226.4 °C (24), and 206.8 °C (26) were measured using DSC, and
showed that these materials were more thermally stable than other energetic polymers used at that time. Due to their higher nitrogen content, the polymers compared well against other energetic materials, and 22 was found to have a larger gas production upon detonation than the energetic glycidal azide polymer (GAP), and a larger heat of combustion than rapid detonating explosive (RDX), GAP, and poly-glycidyl nitrate (polyGLYN).

Figure 6: Formation of high nitrogen content linear polyurethanes through reaction of 3,6-dihydrazinyl-1,2,4,5-tetrazine with diisocyanates. (Adapted from open access article Cohen, A. et al. Novel nitrogen-rich energetic macromolecules based on 3,6-dihydrazinyl-1,2,4,5-tetrazine. – Published by the Royal Society of Chemistry).
1.2.2 Conjugated Tetrazine Polymers Through Electropolymerization and Stille Coupling

Sołoducho et al. were the first to envision the electropolymerization of bis-thiophene and bis-pyrrole functionalized tetrazines\textsuperscript{28}. Using molecular modeling, they compared ionization potentials and electronic populations of 3,6-bis(pyrrol-2-yl)-1,2,4,5-tetrazine (28) with that of 3,6-bis-(4-phenyl-4-thiophene)-1,2,4,5-tetrazine (29) and 3,6-bis(4-[3,4-ethylenedioxy-thiophene])-4,40-bis(phenyl)-1,2,4,5-tetrazine (30) (Figure 7A). In contrast to the pyrrole functionalized tetrazine, which displayed an ionization potential of 8.06 eV and had its main change of electron density localized on the tetrazine ring, the phenylthiophene functionalized tetrazines looked more promising for electropolymerization. Both compounds showed lower ionizations potential than the pyrrole species (6.86 and 6.41 eV respectively) with lower electron density localized on the thiophene units (0.260 e\textendash and 0.283 e\textendash) indicating that these molecules did have the potential to undergo electropolymerization. Following their DFT predications, the group elegantly synthesized 29 & 30, but did not mention any attempt at electropolymerization of the compounds. Around this same time, Audebert et al. had synthesized multiple different heterocycle substituted tetrazine monomers (33-37) to study their electrochemical and spectroscopic properties (Figure 7B).\textsuperscript{21} The tetrazines were found to have high reduction potentials and could undergo both $\pi-\pi^*$ and $n-\pi^*$ transitions, leading the authors to propose their potential use in non-linear optical materials (NLO). They noted that of the 5 molecules, only 3,6-di(1H-pyrrol-1-yl)-1,2,4,5-tetrazine (34) underwent electropolymerization through cyclic voltammetry, but that the polymer
produced was of poor quality. No further characterization details were provided on the polymer. Shortly afterward, Audebert et al. became the first to successfully demonstrate an electrochemical polymerization of thiophene functionalized tetrazines with the polymerization of bis[5-(2-2’-bithienyl)]-s-tetrazine (38) \(^{29}\). The electropolymerization was observed to be reversible up to 50 cycles with a less than 10% loss of electroactivity in the polymer film. Further characterization of the polymer was not reported.

**Figure 7:** (A) Synthesis of 3,6-bis-(4-phenyl-4-thiophene)-1,2,4,5-tetrazine and 3,6-bis(4-[3,4-ethylenedioxythiophene])-4,40-bis(phenyl)-1,2,4,5-tetrazine through Stille coupling. Through DFT analysis, both structures showed potential for electropolymerization. (B) A series of heterocyclic substituted tetrazines studied for their potential to undergo electropolymerization, only 34 was found to polymerize. (C) Structure of bis[5-(2-2’-bithienyl)]-s-tetrazine, the first thiophene-substituted tetrazine monomer discovered to undergo electropolymerization.
Utilizing Stille coupling, Li et al. were the first to synthesize the solution processable semiconducting poly[2,6-(4,4-dihexyl-4H-cyclopenta[2,1-b:3,4-b’]dithiophene)-alt-5,5’-(3,6-bis(4-hexylthienyl-2-yl)-s-tetrazine)] (39) (Figure 8A). Gel permeation chromatography was used to determine the $M_w$ of the copolymer to be 20,000 g/mol with a PDI of 1.41. The polymer displayed good thermal stability up to 240 °C, but no glass transition temperature ($T_g$) was detectable up to the decomposition temperature (250 °C). Thin films of 39 displayed a broad absorption in the visible spectrum from 450-700 nm, and an optical bandgap of 1.68 eV. The HOMO/LUMO energy levels were calculated through cyclic voltammetry (CV) to be -5.34/-3.48 eV respectively, yielding a 1.86 eV electrochemical bandgap. A polymer solar cell was prepared with 39 and (6,6)-phenyl-C71-butyric acid methyl ester (PC71BM) (1/2, w/w), and was demonstrated to have a respectable power conversion efficiency (PCE) of 5.4%.

In a follow-up paper, Li et al. prepared additional derivatives of 39 by altering the alkyl side groups on both the electron-poor bisthienyl-s-tetrazine and electron-rich cyclopenta[2,1-b:3,4-b’]dithiophene monomers, which were then copolymerized in five different combinations (40 a-d) (Figure 8B). Through doing so, the authors were able to explore the effects of substituent size on the solubility, thermal stability, optical, electrochemical, and chain-packing properties of the copolymers. Copolymers of Mn ranging from 11.9 to 29.4 kDa with PDI ranges from 1.50 to 2.14 were prepared. Longer alkyl chains resulted in increased solubility in organic solvents. All copolymers were tested to be stable up to 220 °C, but chain scission would occur through thermal degradation of the tetrazine ring observed near 250 °C. The best optical and electrochemical results came from 39 and a new solar cell containing 39 with 3% 1,8-
diiodooctane (DIO) additive demonstrated the best performance compared to 11 other fabricated devices, having an improved PCE of 5.53%.

In continuing efforts towards optimizing 39, a comparison study was conducted to understand the effect of hexyl substituent positioning on the thiophene ring within the polymer backbone (Figure 8C). Two derivative polymers were prepared with the thiophene hexyl groups facing towards the tetrazine ring (41, 42), intended to sterically prevent observed and unwanted IEEDA side reactions between the tetrazine moiety and fullerene species during solar cell film processing. While the polymers did indeed reduce side-reactions with fullerenes by 28-fold, they had much lower PCE performance in solar devices than 39 which the authors attributed to loose π-π stacking, as the decreased steric hindrance on the thiophene unit gave it more degrees of rotation.

This space intentionally left blank
Figure 8: (A) Structure of poly[2,6-(4,4-dihexyl-4H-cyclepenta[2,1-b:3,4-b']dithiophene)-alt-5,5'-(3,6-bis(4-hexylthienyl-2-yl)-s-tetrazine)]. (B & C) Derivatives of poly[2,6-(4,4-dihexyl-4H-cyclepenta[2,1-b:3,4-b']dithiophene)-alt-5,5'-(3,6-bis(4-hexylthienyl-2-yl)-s-tetrazine)] used for comparison studies of alkyl substituent effects on the properties of the polymer.
In a subsequent paper, the same authors next explored the effect of incorporating bisfuran-s-tetrazine (45) into Donor-Acceptor (D – A) copolymers and compared their properties to the previously studied 39 and 41. The motivation for replacing thiophene with furan linkages was to improve solubility without the need for adding alkyl chains, encourage better \( \pi-\pi \) stacking through creating a more planar backbone, and to increase the (D – A) polymer’s band gap. Copolymers 47a and 47b were prepared through Stille coupling between 3,6-bis(5-bromofuran-2-yl)-s-tetrazine 46 and either benzo[1,2-b:4,5-b’]dithiophene or cyclopenta[2,1-b:3,4-b’]dithiophene, respectively (Figure 9). The two copolymer sizes varied with 47a having a Mn of 52.2 kDa and PDI of 2.81, while 47b had a Mn of 10.7 kDa and PDI of 1.74. Thermal analysis resulted in decomposition of the copolymers occurring slightly above 220 °C, and was once again found to be due to tetrazine fragmentation. While the furan linkage did increase solubility of the polymers, both copolymers fared poorly when used in photovoltaic devices, having PCEs of \(~0.7\%\) compared to the 3.2% of 39. The authors again attributed this to decreased steric allowing more degrees of rotation for the furan linkages, and resulting in inefficient chain conjugation and stacking.

This space intentionally left blank

In an effort to create higher efficiency Donor-Acceptor (D – A) copolymers for use in bulk heterojunction (BHJ) polymer solar cells (PSCs), Zhang et al. synthesized and analyzed four different D – A copolymers using indacenodithiophene (50) as the common donor unit (Figure 10). Four different acceptor groups: bis(thiophen-2-yl)-bithiazole (55a), bis(thiophen-2-yl)-thiazolothiazole (55b), bis(thiophen-2-yl)-tetrazine (55c), and bis(thiophen-2-yl)-benzothiadiazole (55d) were chosen for comparison, and the copolymers were again prepared using Stille coupling. The synthesized tetrazine
copolymers (55c) (Mn 8,700 Da and PDI of 1.53) was measured to be thermally stable up to 271 °C and showed good solubility in CHCl₃, THF, toluene, and chlorobenzene. It performed poorly compared to the other copolymers in photovoltaic device testing with its fill factor (FF) of 38.1% and PCE 3.04% falling below that of 55b and 55d (FF 48.9%, 56.7%, PCE 5.79%, 6.17% respectively), which the authors attributed to a lower hole mobility for 55c.

Figure 10: Synthesis of (D – A) copolymers containing an indacenodithiophene repeat unit and four alternate acceptor groups including bis(thiophen-2-yl)-tetrazine. (Adapted with permission from Zhang, M., Guo, X., Wang, X., Wang, H. & Li, Y. Synthesis and Photovoltaic Properties of D–A Copolymers Based on Alkyl-Substituted Indacenodithiophene Donor Unit. Chem. Mater. 23, 4264–4270 (2011). Copyright (2011), American Chemical Society.)
Wen et al. were the next to explore efforts into incorporating a tetrazine moiety into D–A conjugated copolymers in an effort to reduce the HOMO energy level of the copolymer and improve $V_{oc}$ of the copolymer-based polymer solar cell (Figure 11A). A new D–A conjugated polymer was synthesized by using benzo[1,2-$b$:4,5-$b'$]dithiophene (56) as the donor unit and bisthienyl-s-tetrazine (57) as the acceptor unit. Stille cross-coupling was once again employed to prepare (58), yielding a polymer of Mn 56,000 g/mol and PDI of 2.67. Thermal gravimetric analysis revealed an onset degradation temperature of 276 °C, and UV-Vis showed a broad absorption from 350 to 700 nm for the thin film, indicating that the copolymer could function in a PSC. CV analysis was utilized in order to calculate the HOMO/LUMO energy levels, and found a low-lying HOMO of -5.42 eV and LUMO of -3.58 eV. The copolymer was tested in a photovoltaic device using PC$_{71}$BM as the BHJ acceptor, and after optimization achieved high $V_{oc}$ values of 0.90-0.92 V and a PCE of 3.32% which the authors concluded as a promising result for using the copolymer as a donor material in PSCs.

Further studies on the use of tetrazine acceptor groups in D–A copolymers in PSCs were conducted by Cheng et al. (Figure 11B), when they prepared two copolymers containing benzo[1,2-$b$:4,5-$b'$]dithiophene (59) donor units and either 3,6-Bis(3,4'-dihexyl-2,2'-bithiophen-5-yl)-1,2,4,5-Tetrazine (60) or 3,6-Bis(3,4'-dihexyl-2,2'-bithiophen-5-yl)-1,2,4,5-tetrazine acceptor units (62). Copolymers (61, 63) were synthesized using Stille coupling yielding polymers with Mw of 7.8 and 30.0 kg/mol and PDIs of 1.3 and 2.8, respectively. Both copolymers were found to be soluble in chlorobenzene. Thermal properties of the copolymers were measured with TGA, and onset degradation was observed at 294 °C for 61 and 305 °C for 63. Both copolymers
exhibited broad spectrum absorbance from 300 – 650 nm in thin film form. Cyclic voltammetry was used to predict HOMO/LUMO energy levels and 61 and 63 were found to have low lying HOMOs of -5.39 eV and -5.28 eV, and narrow band gaps supporting their use in PSCs. Bulk heterojunction PSCs made from each copolymer and PC71BM/ZnO/Al displayed high open circuit voltages of ~1.0 V, and resulted in PCEs of ~5.0% when exposed to 1.5 global irradiation of 100 mW/cm².

Figure 11: (A) Synthesis of a (D – A) copolymer containing alternating benzo[1,2-b:4,5-b’]dithiophene & bisthienyl-s-tetrazine units. (Adapted with permission from Wen, S. et al. A benzo[1,2-b:4,5-b’]dithiophene-based copolymer with deep HOMO level for efficient polymer solar cells. Sol. Energy Mater. Sol. Cells 100, 239–245 (2012). Copyright (2012), Elsevier B.V. All rights reserved. (B) Synthesis of benzo[1,2-b:4,5-b’]dithiophene copolymers 61 & 63 with alternating donor units of either 3,6-Bis(3,4’-dihexyl-2,2'-bithiophen-5-yl)-1,2,4,5-Tetrazine (60) or 3,6-Bis(3,4’-dihexyl-2,2'-

DFT calculations on eight copolymers consisting of alternating s-tetrazine and aryl rings were conducted by Moral et al. to better understand the effect aryl groups have on the polymers’ properties (Figure 12A). Band gap values for copolymers 65, 68, and 69 were estimated to be near 2 eV, indicating they have potential value as active materials in PSCs. Modeling of crystal structures provided information on the polymers’ charge transport capabilities and revealed 69 to be the most efficient at electron and hole transport of the eight copolymers. Further calculations confirmed 69 to be the most likely of the copolymers to function as an ambipolar semiconductor, and copolymers 64 and 70 were predicted to function as potential n-type semiconductors.

Liu et al. prepared a D – A copolymer (74) containing 4,8-bis(5,5″-didodecyl-[2,2′:3′,2″-terthiophen]-5′-yl)benzo[1,2-b:4,5-b′]dithiophene as the acceptor unit and 3,6-di(thiophen-2-yl)-1,2,4,5-tetrazine as the donor unit, 75, and compared its properties to 3 other D – A copolymers (Figure 12B). Stille coupling was employed for the polymerization, and a polymer of Mw 61.1 kDa and PDI 1.76 was prepared in an 83% yield. TGA analysis revealed an onset degradation of 329 °C, UV-vis showed broad absorption from 300 to 600 nm, and CV analysis provided a calculated HOMO/LUMO level of -5.61 & -3.65 eV with an energy gap of 1.96 eV for the copolymer. PSCs were tested and an optimum cell with a ratio of 1:3 polymer to PC_{61}BM provided the best
results. Despite optimization, a low PCE of 1.08% was obtained and the authors believed it to be due to the low short circuit density ($J_{sc}$) of the device, caused by an inefficient LUMO energy level offset between the donor and acceptor materials.

Figure 12: (A) Structures of tetrazine-based D-A copolymers used in DFT analysis to understand aryl substituent effect of the polymers' properties (B) Synthesis of copolymers containing 4,8-bis(5,5''-didodecyl-[2,2':3',2''-terthiophen]-5'-yl)benzo[1,2-b:4,5-b']di-thiophene alternate co-units, one being 3,6-di(thiophen-2-yl)-1,2,4,5-tetrazine (75)
1.2.3 Nanoparticle Functionalization

Gross et al. encapsulated a redox-active tetrazine-naphthalimide (TN) (90) species inside β-cyclodextrin-modified polystyrene nanoparticles (92) by initiating self-assembly & nano-precipitation in a THF/H₂O system containing 20% TN by mass (Figure 13A).³⁹ AFM and fluorescence spectroscopy were used to confirm particle formation. Dynamic light scattering (DLS) measurements indicated a hydrodynamic radii range of 138-654 nm with 95.1% of the particles being closer to 138 nm in size and the larger 654 nm sizes being attributed to cluster formation through a proposed host-guest crosslinking. A small hypsochromic shift seen between the λₘₚₓ absorbances of 90 and 92 provided evidence that the tetrazine species were encapsulated within 92. The nanoparticles were verified to be redox-active through cyclic voltammetry (CV), and concentration of encapsulated 90 was calculated to be 1.5 x 10⁻⁴ mol L⁻¹. Due to their redox-active properties, the authors proposed potential uses in catalyst of sensor systems.

A class of amine sensing silica nanoparticles (93) were synthesized by surface functionalization using tetrazines substituted with triethoxysilane (TEOS) groups (Figure 13B).⁴⁰ The silica particles were prepared following the Stöber method, and had diameters measured by dynamic light scattering of ≈140 nm. The tetrazines were synthesized by first reacting 3-(triethoxysilyl)propyl isocyanate (94) with either 1,4-butanediol (95), or tetraethylene glycol (99), followed by facile SₐN₂Ar substitution of 3,6-dichloro-1,2,4,5-tetrazine (97) to form 98 and 101, respectively. Surface functionalization was accomplished over 24 hours under mild acidic conditions, with fluorescence of NPs analyzed at regular time intervals to monitor reaction progress. Elemental analysis (EA)
was used to determine extent of functionalization, and tetrazine concentration was calculated to be 0.26 mmol and 0.34 mmol per gram of NP. The particles displayed broad fluorescence emissions near 560 nm and long fluorescence lifetimes $\tau=148$ ns for 104, and 156 nm for 107, due to the forbidden n-$\pi^*$ transition. Self-quenching effects were observed for the particles, with the shorter chain length displaying greater quenching despite having lower concentrations of tetrazine. Fluorescence quenching was observed for both particles with the addition of diphenylamine (DPA) or triethylamine (TEA), and enhanced quenching was observed with ethanolamine. The particles could be reused after washing with minor loss of material due to their small size. Finally, the surfaces of the particles were demonstrated to be electroactive, which coupled with their fluorescence quenching properties indicated that these materials could have potential uses in amine sensing devices.

In a following article, the same authors sought to develop an electroactive nanoparticle system which would emit white light upon UV excitation (Figure 13D). Following a method developed by Park et al., whereby blocking energy transfer between two different fluorophores, one emitting blue and the other emitting yellow light, effectively results in reproducible white light emission, the authors developed a two fluorophore NP system to carry out this effect. The particles were prepared using a two-step encapsulation/modification method. N-(hydroxyethyl)-1,8-naphthalimide (105), a blue light emitting fluorophore previously shown to enhance tetrazine fluorescence when covalently bound to chloro-substituted tetrazines, was modified with 3-(triethoxysilyl)propyl isocyanate and encapsulated in silica NPs following a previously reported method. Then, surface grafting with 106 provided the desired two fluorophore
NPs. The dual particle system was demonstrated to emit white light when exposed to 330 nm UV irradiation.

Hansell et al. prepared single chain polymer nanoparticles (SNCP) (103), similar to the method first reported by Mecerreyes et al. through the exploitation of tetrazine IEDDA reactions (Figure 13C). RAFT polymerization was employed to generate a series of linear polystyrene-based copolymers containing 5 – 20 mol% of pendant norbornene (Nb) functionalities (102). Slow addition of the functionalized linear polymer dissolved in DMF (10 mM) to an 80 °C DMF solution containing bis(4-(6-methyl-1,2,4,5-tetrazin-3-yl)benzyl) glutarate (104) at 0.5 eq. per Nb unit was determined to be the ideal method for SCNP formation, although a small amount of polymer-polymer coupling was observed in each case. Prior attempts at SCNP formation found the rate of reaction to be too slow at room temperature with only gel formation occurring, and faster addition of the Nb-functionalized polymer lead to polymer-polymer coupling. Discrete particles could be observed from SCNPs formed using an ~30 kDa polymer containing 20% Nb functionality. This method of SCNP formation benefited from an easy purification due to the facile catalyst-free reaction conditions, and the ability to perform the reaction in the presence of air. While higher temperatures were required for SCNP formation using 104 as cross-linker, the authors hypothesized that a more reactive tetrazine species could lower reaction temperatures to ambient conditions.

Topp and Grote prepared the first pendant functionalized tetrazine polymer by post-functionalizing macroporous aminomethylated polystyrene/DVB particles (107) with 3-bromo-6-phenyl-1,2,4,5-tetrazine (108) (Figure 14). Confirmation of the successful functionalization was determined based on elemental analysis and IR comparison to a benzyl amine model compound synthesized by reacting benzylamine with 108. Extent of conversion was calculated through anion exchange capacity of sulfate against chloride, and was determined to be nearly quantitative. The particles were tested for their redox potential, metal absorption selectivity, and metal desorption potential. The redox capabilities of the polymers were shown to be non-existent, indicated by the observed cleavage of the amine-tetrazine bond through hydride attack at the tetrazine carbon when the polymer was reduced with aqueous NaBH₄ solutions. Their metal selectivity results indicated an extraordinarily high selectivity for Palladium even in the presence of base metals, with Pd (II) > Au (III) >> Ir (IV) > Os (IV) > Pt (IV) > Ru (III) > Rh (III). Metal desorption proved to be less fruitful and <1% Pd was collected after extracting 109 with perchloric acid, which the authors attributed to the formation of a metal tetrazine coordinative complex formation on adsorption.
Figure 14: Functionalization of polystryrene nanoparticles through nucleophilic aromatic substitution of 3-bromo-6-phenyl-1,2,4,5-tetrazine.

1.2.4 Verdagyl-Controlled Living polymerizations

Yamada et al. were able to demonstrate the controlled polymerization of polystyrene by using 2-(2-cyano-2-propyl)-1,3,5-triphenyl-1,2,5,6-tetrahydro-1,2,4,5-tetrazine (CPTPV) as a coupling agent. CPTPV was prepared through the disassociation of AIBN in the presence of 1,3,5-tripheynl-verdazyl in refluxing benzene. The polymerizations were run at 110 °C in sealed tubes using three different concentrations of CPTPV, 6, 12, and 24 mmol/L, and were shown to follow first-order kinetics with respect to styrene. A linear dependence was observed between the number average molecular weights ($M_N$) and monomer conversion when the polymerizations were run at both 90 °C and 110 °C. While the authors were able to prepare polymers up to 20 kDa (110), the molecular weight distributions of the polymers were very broad for controlled polymerizations, and PDIs for the polymers were all above 1.5 (Figure 15A). The authors attributed this to be resulting from verdazyl’s thermal instability and degradation, which eventually lead to bimolecular termination and the observed increase in polydispersity.

Teertstra et al. were the next to explore the verdazyl mediated living polymerization of styrene (Figure 15B). Initial attempts at polymerizing styrene at 110
°C using either 1,3,5-triphenyl-6-oxoverdazyl or 1,5-dimethyl-3-phenyl-6-oxoverdazyl and BPO as initiator resulted in 24-29 kDa polymers with monomer conversion percentages in the low to mid 20s, and PDIs that ranged between 1.6 and 1.7. The molecular weight gain and monomer conversion was observed to occur over the first 30 minutes, and no dramatic change was witnessed afterwards for up to 2 hours. Increasing the verdazyl to BPO ratio did not affect these results. Substituting Vazo® 88 as initiator resulted in monomer conversions of only 18% during the first 30 minutes, but was almost immediately followed by a small exotherm and increased viscosity of the reaction mixture, yielding 65% monomer conversion after 50 minutes. Additional polymerizations run using both higher and lower concentrations of verdazyl to Vazo® 88 and lower reaction temperatures did nothing to abate the exotherm. The authors then turned their efforts towards isolating BPO-styrene-verdazyl (BSV) unimers 111 & 112, similar in structure to the nitroxide based unimolecular initiator first synthesized by Hawker.49 Polymerization of styrene with 112 at 125 °C was observed to proceed with an incremental increase in \( M_n \), and much lower PDIs (1.13-1.22) than previously observed. Signs of chain transfer, lower experimental \( M_n \) compared to theoretical and tailing in PDIs at higher conversions, were still observed for this system, and the authors noted they were exploring its cause.

Shortly afterwards, the same group successfully demonstrated a controlled polymerization of both \( n \)-butyl acrylate and polystyrene using verdazyl mediated polymerization (Figure 15C).50 Since a bimolecular initiating pathway using either AIBN or BPO again proved to be unfruitful, a series of four verdazyl unimers 111-114 were prepared and tested with both styrene and \( n \)-butyl acrylate. Use of unimer 111 resulted in
polymers with low PDIs, but no control was observed between calculated and experimental molecular weights. This was predicted to be resultant from a slow disassociation between the verdazyl-styrene bond at the rxn temp of 130 °C. Control was observed with unimer 112 at 125 °C for both styrene and \( n \)-butyl acrylate, but rates of polymerization were slow for styrene, reaching only 40% after 28 h. Switching to unimer 113 resulted in an increase of the rate of styrene polymerization, and no change in \( n \)-butyl acrylate polymerization. Replacing the 3-position substituent with hydrogen on the verdazyl ring of 114 lead to a much faster rate of polymerization for styrene (60% after 7 h), but the rate of polymerization of \( n \)-butyl acrylate was too fast to provide a controlled mechanism for the polymerization. The authors then went on to further establish the living character of verdazyl mediated controlled polymerizations, using unimer 113 to produce well-defined poly(\( n \)-butyl acrylate)-\( b \)-styrene and polystyrene-\( b \)-(\( n \)-butyl acrylate) diblock copolymers through chain extension. The authors mentioned a possible contamination of PS homopolymer in the chain extension of PS with \( n \)-butyl acrylate.

Rayner et al. were the next to explore verdazyl mediated living polymerization of styrene and \( n \)-butyl acrylate.\(^{51}\) Building on Teertstra and Chen et al.’s results, the authors explored substituent effects at the 3-position of 1,5-dimethyl-6-oxoverdazyls and measured the affect they had on the rate and characteristics of the polymerizations. Two new verdazyl unimers with electron donating or withdrawing effects were synthesized from verdazyls 117 & 118 (Figure 15D), and compared to 111 & 114. Styrene polymerizations were carried out using each of the 4 unimers in bulk conditions at 125 °C and compared to a TEMPO unimer initiator. All reactions followed relative linear first order kinetics with respect to monomer consumption. A reduction in the rate of the
polymerizations was observed over the course of the reaction and attributed to the presence of chain termination. A similar rate to that of the TEMPO initiator was achieved with $114$, but phenyl substitution was shown to result in a rate reduction relative to its electronic effects: $R = \text{PhNO}_2 < \text{Ph} < \text{PhOMe}$. In the living polymerization of $n$-butyl acrylate, unimer $117$ was observe to perform much better than the other verdazyl unimers. The same unimer was also demonstrated to mediate living polymerizations of styrene at $100 \, ^\circ\text{C}$, whereas unimer $111$ failed to achieve this. Block copolymers of styrene and $n$-butyl acrylate were prepared to demonstrate the living character of verdazyl mediated polymerizations. Similar to Chen et al.’s work, polystyrene homopolymer was also observed in the chain extension of PS by poly($n$-butyl acrylate), but was less prevalent in the chain extension of poly($n$-butyl acrylate). The results of this study provided additional indication that the structure of the verdazyl radical is central to its effectiveness in living polymerizations.

This space intentionally left blank

1.2.5 Tetrazine IEDDA Polymer Post-Modification

Owing to tetrazine’s ability to undergo rapid and facile IEDDA reactions with strained dienophiles\(^\text{16}\) without the need of metal catalysts or harsh reaction conditions, Barker et al. proposed using tetrazine IEDDA for the post-modification of renewable polymers. Initiating ring opening polymerization of lactic acid with an alkoxy-substituted norbornene, provided a poly(lactic acid) (PLA) polymer with a norbornene end functionality (119) (Figure 16A).\(^\text{52}\) A series of substituted dipyridyl-tetrazines (120 a-d) were reacted with 119, and high conversions were achieved for each modified polymer (121 a-d). Due to the mild reaction conditions (DCM, room temperature), no degradation of the PLA backbone was observed. Ring-opening of norbornene-functionalized lactic acid (122) provided PLA with a repeating norbornene functionalities along its backbone (123). Post-modification with 120 a-d was achieved in the same mild conditions, leading again to high conversions with no observable degradation of the PLA backbone. Demonstration of the ability to use tetrazine IEDDA in forming graft copolymers and amine functionalized PLAs copolymers was accomplished by clicking 120 c & b respectively to 123.

The same groups followed this up with a more comprehensive study on the application of tetrazine-norbornene (Tz-Nb) IEDDA in preparing diblock copolymers.
Hansell et al. first demonstrated that Tz-Nb IEDDA can function orthogonally in a variety of solvents to reversible addition fragmentation chain-transfer (RAFT) agents by clicking dipyridyl tetrazine (120a) to an Nb functionalized thioisocyanate chain transfer agent (Nb-TTC). The tetrazine efficiently coupled to Nb-TTC without degradation of the thioisocyanate functionality in all solvents tested following a rate of DMSO > DMF ≈ EtOH > 1,4-dioxane ≈ THF ≈ DCM. Next a series of diblock copolymers were prepared by reacting Nb end-capped polymers: polystyrene (PS-Nb), N-isopropylacrylamide (PNIPAM-Nb), poly(ε-caprolactone) (PCL-Nb), and poly(δ-valerolactone) (PVL-Nb) with tetrazine functionalized poly ethylene glycol 126 (Figure 16B). Couplings were carried out in H2O for PNIPAM-Nb and DCM for PS-Nb, PCL-Nb, and PVL-Nb, and SEC analysis indicated successful diblock formation for all reactions. Finally, 2-(6-(pyridin-2-yl)-1,2,4,5-tetrazin-3-yl)ethan-1-ol (127) was used to successfully initiate ring opening polymerization of δ-valerolactone (128). The subsequent polymer, 129, was coupled to PVL-Nb to demonstrate that tetrazine ROP initiators provide efficient handles for post-functionalization. While these results displayed the power of Tz-Nb IEDDA reactions in polymer modification, the authors also noted that the difficulty in synthesizing tetrazine starting materials as well as tetrazine’s reactivity towards vinyl monomers provides a substantial barrier to their implementation in polymer modifications.

Hansell and O’Reilly next demonstrated the utility of tetrazine IEDDA click reactions in modifying micellar structures orthogonal to CuAAC azide-alkyne click modification. The authors used RAFT polymerization to prepare an amphiphilic diblock copolymer containing blocks of pendant norbornene and alkyne functionalities along its
backbone, **130** (*Figure 16C*). Micellar structures containing a hydrophobic norbornene-styrene block in their core and hydrophilic alkyne-PEG block for their shell were formed by dissolving the copolymer in THF, followed by the slow addition of water ~2mL/hr. Individual modifications were performed to determine the viability of both click chemistries. Core modification of **132** was conducted by addition of a solution of **120a** in THF, and UV-Vis monitoring indicated the reaction was completed after ~8 hours. Surface modification of **133** was accomplished using an azide-functionalized coumarin molecule designed to become UV active after click modification and therefore providing a method to follow reaction progress. After determining that both core and surface modification could be achieved separately, the authors attempted to run both reactions tandemly, but noted an ~50% decreased efficiency for both reactions. With a slight delay in the addition of tetrazine (20 minutes) to that of the CuAAC reagents or vice versa, the dual modification was successful and had been achieved with little effect on the structure of the micelle **133** as interpreted through DLS. Spectroscopic methods were used to verify that both reactions occurred at high efficiency, effectively demonstrating the utility of tetrazine-norbornene IEDDA chemistry in functionalizing micellar structures orthogonally to CuAAC click chemistry.

*This space intentionally left blank*
Figure 16: (A) Tetrazine IEDDA functionalization of degradable PLA containing end or repeating norbornene units. (Adapted with permission from Macromol. Rapid Commun. 32, 1362–1366 (2011). Copyright (2011) WILEY-VCH Verlag GmbH & Co.) (B) Reaction scheme for the synthesis of PEG-Tz through amide coupling (left), and ring

The surface modification of carbon nanotubes (CNTs) with 3,6-diamino-1,2,4,5-tetrazine (136) was first reported by Zhang et al. in an effort to decrease aggregation and increase their conductivity in epoxy composites (Figure 17).55 The modified nanotubes, 140, were mixed with E-51 epoxy resin (139) and an additional hardening agent then cast into molds and cured in incremental stages between 130-180 °C. TEM analysis revealed a more dispersed network of CNTs in epoxies mixed with modified nanotubes, while aggregation was observed in a control sample. The modified CNT epoxies were determined to have a lower percolation threshold (0.13 wt%) to that of the control (0.51 wt%), which the authors correlated to a significant enhancement in their conductivity.
Figure 17: Modification of CNTs through IEDDA with 3,6-diaminotetrazine provides surface amines which can react with epoxies, and leads to a more uniform dispersion of CNTs in epoxy films and enhanced conductivity.

Preparation of carbohydrate microarrays through the utilization of tetrazine IEDDA chemistry was elegantly demonstrated by Beckmann et al.\textsuperscript{56} Aminopropylsilanized glass slides were surface-functionalized through reaction with 2,5-dioxopyrrolidin-1-yl 4-((6-(pyrimidin-2-yl)-1,2,4,5-tetrazin-3-yl)benzoate (142) to incorporate the tetrazine IEDDA diene handle (Figure 18A). Synthetic carbohydrates
end-functionalized with an alkene or norbornene moiety were then successfully IEDDA clicked to the glass slide using an automated array printer demonstrating the effectiveness of this procedure. Adapting this discovery to microcontact chemistry, Roling et al. demonstrated the utility of tetrazine IEDDA reactions in soft-lithography surface patterning (Figure 1B). Well-defined microstructured patterns were printed on tetrazine functionalized glass slide, using norbornene and cyclooctyne functionalized fluorescent carbohydrate dyes. The modifications with norbornene and cyclooctyne species were shown to work orthogonally and bifunctional surfaces were also prepared with this method. Further demonstrating the utility of tetrazine IEDDA reactions in patterning of self-assembled monolayers (SAMs), undecynyl-functionalized glass slides were printed with 2-(4-(6-(pyrimidin-2-yl)-1,2,4,5-tetrazin-3-yl)benzamido)ethyl 2-bromo-2-methylpropanoate. Following patterning, surface initiated atom transfer radical polymerization (SI-ATRP) was utilized to graft polymethylacrylate (PMA) brushes onto the functionalized glass slide. Well-defined patterns were observed under optical microscopy and atomic force microscopy (AFM) was used to measure the PMA brush height to be 40 nm.
Figure 18: (A) Surface functionalized of aminopropylsilanilized glass slides with 2,5-dioxopyrrolidin-1-yl 4-(6-(pyrimidin-2-yl)-1,2,4,5-tetrazin-3-yl)benzoate to function as click anchors for making carbohydrate microarrays. Adapted with permission from Beckmann, H. S. G., Niederwieser, A., Wiessler, M. & Wittmann, V. Preparation of Carbohydrate Arrays by Using Diels–Alder Reactions with Inverse Electron Demand. Chem. – Eur. J. 18, 6548–6554 (2012). Copyright (2012), WILEY-VCH Verlag GmbH & Co. (B) Surface modification of glass slides with tetrazine for micropatterning through tetrazine IEDDA and attachment of an ATRP initiator for growing graft PMA brushes.
Baumgartner et al. prepared a series of polyesters containing backbone norbornene functionalities through the alternating polymerization of cis-5-norbornene-endo-2,3-dicarboxylic anhydride and various substituted epoxides. To demonstrate the versatility of the polyesters, the authors used thiol-ene and tetrazine-norbornene click chemistries to introduce functional groups onto the norbornene backbone of 158. Functionalization with dipyridyl tetrazine (120a) was conducted at room temperature, resulting in high conversion and drastically increasing the glass transition temperature of 161 after modification (Figure 19).
Figure 19: Functionalization of polymers with repeating norbornene units through thiol-ene and tetrazine IEDDA click chemistries. (Adapted with permission from Baumgartner, R., Song, Z., Zhang, Y. & Cheng, J. Functional polyesters derived from alternating copolymerization of norbornene anhydride and epoxides. Polym. Chem. 6, 3586–3590 (2015). Copyright (2015) with permission of The Royal Society of Chemistry.)

A continuous flow microreactor was designed for the ring-opening polymerization of \( \text{L-lactide} \) using 1,5,7-triazabicyclo[4.4.0]dec-5-ene as a catalyst and was demonstrated by Berg et al. to work effectively with various alcohol initiators including \((4-(6\text{-methyl-1,2,4,5-tetrazin-3-yl})\text{-phenyl})\text{-methanol})\). The microreactor polymerizations produced well-defined poly(lactic acid) (PLA) in high conversions without the need for inert atmosphere. Incorporating a tetrazine handle onto one end of the PLA chain allowed the ability for post-functionalization with (bio)molecules and polymers containing dienophilic functionalities. The authors demonstrated this utility with the attachment of 5-norbornene-2-carboxylic acid, as well as by linking two PLA chains through tetrazine-cyclooctyne end-group click modification.
Jain et al. prepared a series of well-defined homopolymers featuring repeat units of pendant allyl ether moieties through anionic ring-opening polymerization of allyl glycidyl ether 171 as well as copolymers with the inclusion of glycidol (Figure 20A). The polymers were post-functionalized through IEDDA reactions with a variety of tetrazines (165 a-g), and reaction conditions were optimized to achieve >90% conversions for each tetrazine (Figure 20B). Reaction kinetics were monitored in DMSO-d$_6$ using $^1$H NMR, and second-order rate constants of 8.93 x 10$^{-5}$ M$^{-1}$ s$^{-1}$, 7.18 x 10$^{-5}$ M$^{-1}$ s$^{-1}$, and 1.99 x 10$^{-5}$ M$^{-1}$ s$^{-1}$ were obtained for 165 b, f, & g, respectively. The facile reactions, near quantitative conversions, and ability to employ an endless variety of substituted tetrazine compounds in the post-functionalization of poly(allyl glycidyl ethers) displayed the power and utility of tetrazine IEDDA reactions in the modification of polymers bearing pendant alkene repeat units.

This space intentionally left blank
Figure 20: (A) Synthesis of poly(allyl glycidyl ether) and its modification with 1,2,4,5-tetrazines. (B) Structures of tetrazines used to modify poly(allyl glycidal ether) and conduct kinetic rate experiments. (Adapted with permission from Jain, S., Neumann, K., Zhang, Y., Geng, J. & Bradley, M. Tetrazine-Mediated Postpolymerization Modification. Macromolecules 49, 5438–5443 (2016). Copyright (2016) American Chemical Society.)
1.2.6 Tetrazine IEEDA in the Preparation of Hydrogels

Zhou et al. reported on the preparation of hydrogels (170) through IEEDA reactions between norbornene-telechelic PEG oligomers (168) and a tris-tetrazine linker (169) in demonstrating the effectiveness of their network disassembly spectrometry (NDS) in quantifying primary loops and dangling chain imperfections in polymer networks (Figure 21). The gelations were conducted with equimolar concentrations of norbornene and tetrazine functional groups, while varying the initial concentration of norbornene linker from 2 mM to 80 mM. Results from the gelation studies agreed with theoretical predictions and indicated that gels will not form if primary loops are present in concentrations greater than 30% in network junctions. A subsequent reporting by Cok et al. discussed the details of the hydrogel synthesis and analyzed swelling properties of the gels using two different telechelic PEG-norbornene polymers of 6 kDa and 10 kDa sizes. The gelations could be conducted in the presence of the oxidant DDQ, and swelling comparisons between gels with dihydropyridazine and aromatic pyridazine linkages were measured as well. Results indicated that gels made with the larger 10 kDa PEG chains provided greater swelling ratios in water than those made with the 6 kDa linker. The authors were surprised to discover larger swelling ratios for the gels containing oxidized pyridazine linkages than those with dihydropyridazine linkage and suggested the fully aromatic pyridazines were more hydrophilic than their reduced counterparts. A shear modulus of the 6 kDa gel was reported to be 2.6 kPa. Due to the facile preparation of the hydrogels along with the ability to prepare them in the presence...
of an oxidant, the authors believed this synthetic approach to be a reliable method for forming model networks with potential uses in various applications.

**Figure 21:** Ideal hydrogel structure prepared from reacting telechelic norbornene monomer (168) with tris-tetrazine linker (169). (Adapted with permission from Zhou, H. et al. Counting primary loops in polymer gels. Proc. Natl. Acad. Sci. 109, 19119–19124 (2012).)
Exploiting the rapid reaction kinetics of IEDDA reactions between strained trans-cyclooctene (TCO) dienophiles and tetrazines, Zhang et al. developed an interfacial system combining the two to prepare 3-dimensional hydrogel structures.\(^{63}\) By adding a tetrazine-functionalized polysaccharide, hyaluronic acid (171), to aqueous solutions containing \textit{bis}-TCO end-capped PEG crosslinkers (172) (Figure 22A), the authors were able to generate hydrogel microspheres and channels through slow diffusion of the crosslinker into the hydrogel core (Figure 22B). Addition of a TCO-functionalized fluorescent tag to the reaction mixture allowed spatial resolution of the hydrogels using confocal microscopy.

Liu et al. next used the TCO-tetrazine interfacial polymerization techniques to prepare linear multiblock copolymers from a biphasic ethyl acetate: water system.\(^{64}\) A \textit{bis}-TCO monomer containing a hydrophobic dodecane chain (173) was synthesized for the organic soluble block, and two \textit{bis}-tetrazine monomers with hydrophilic PEG spacers were synthesized for the water soluble block, 174 \& 175 (Figure 22C). Inclusion of a cell-adhesive peptide in between the PEG chains of 175 was intended to promote attachment of fibroblasts and myoepithelial-like cells. Rapid polymerization occurred at the biphasic interface, allowing meter-long fibers to be pulled from the interface until \(\sim 70\%\) of the \textit{bis}-tetrazine was consumed (Figure 22D). Copolymers of up to Mw 530 kDa were synthesized and DSC analysis indicated a semi-crystalline morphology with broad melting transitions observed at 53 °C and 34 °C for copolymers with consisting of 174 and 175 respectively. Young’s moduli of 120 MPa for 174 and 106 MPa for 175 were determined through AFM modulus mapping.

Tetrazine-norbornene IEDDA reactions were used in the synthesis of supramolecular metallo-hydrogels (181) by Kawamoto et al. PEG chains of Mw 2 kDa, end-capped with dipyridyl tetrazine molecules, 179, were reacted with substoichiometric
amounts of tris-norbornene crosslinker, 180, and gelation was induced by the addition of Ni(ClO₄) (Figure 23). The versatility of a non-toxic metallo-hydrogel prepared using Fe(ClO₄) was demonstrated by incorporating either photocleavable doxorubicin (DOX) or an enzymatically cleavable peptide into the metallogel matrix using tetrazine-norbornene IEDDA. When the respective gels were exposed to either UV irradiation or the enzyme chymotrypsin, their incorporated small molecules were released into solution, which demonstrated their utility to function as a controlled-release delivery material in biological systems.

**Figure 23:** The synthesis of supramolecular metallo-hydrogels through tetrazine-norbornene IEDDA crosslinking followed by metal complexation. (Adapted with permission from Kawamoto, K., Grindy, S. C., Liu, J., Holten-Andersen, N. & Johnson, J. A. Dual Role for 1,2,4,5-Tetrazines in Polymer Networks: Combining Diels–Alder Reactions and Metal Coordination To Generate Functional Supramolecular Gels. ACS Macro Lett. 4, 458–461 (2015). Copyright (2015) American Chemical Society)
Alignate hydrogels, consisting of (1,4)-linked β-D-mannuronic and α-L-guluronic acid repeating units were prepared by mixing solutions of alignate biopolymers functionalized with either benzylamino tetrazine, 182, or norbornene methanamine groups, 181 (Figure 24A). Under ambient conditions, the tetrazine-norbornene IEDDA reaction produced stable hydrogels 183 within an hour, with only small amounts of bubble formation from nitrogen gas release. The gels were easily modified using post-gelation thiol-ene chemistry on residual unreacted norbonenenes to attach cell adhesive peptides. They demonstrated cytompatibility towards forming 2-dimensional cell cultures as well as cell encapsulation while causing minimal inflammation to tissue in in-vivo studies. The same groups shortly followed up with the reporting of an injectable gelatin hydrogel using gelatin polymers modified with the same tetrazine-norbornene system utilized in forming their alignate hydrogels (Figure 24B). The functionalized gelatin polymers, 184 & 185, could be injected subcutaneously in mice where the mixture would undergo spontaneous crosslinking and hydrogel formation, with minimal tissue inflammation being observed in vivo. The hydrogels, 186, were demonstrated to support cell attachment, and underwent biodegradation without the need of any additional synthetic steps allowing cellular infiltration and 3D culturing.

This space intentionally left blank
Figure 24: (A) Combining alginic acid biopolymers functionalized with pendant norbornene and tetrazine moieties results in the formation of hydrogel matrix. (Adapted with permission from Desai, R. M., Koshy, S. T., Hilderbrand, S. A., Mooney, D. J. & Joshi, N. S. Versatile click alginate hydrogels crosslinked via tetrazine–norbornene chemistry. Biomaterials 50, 30–37 (2015). Copyright (2015) Elsevier Ltd.). (B) Applying this same chemistry to gelatin biopolymers results in the rapid formation of biocompatible gelatin hydrogels. (Adapted with permission from Koshy, S. T. et al. Click-Crosslinked Injectable

1.3 Conclusion

The usage of tetrazines in polymer chemistry has become more prevalent recently, owing mostly to their ability to modify polymers and cross-link through IEDDA reactions. This review has demonstrated their use in multiple applications, from metal chelating polymers, high nitrogen energetic materials, D – A copolymers for organic PSCs, click modification of polymers through tetrazine IEDDA, redox active nanoparticles for sensor applications, as well as their use in the formation of biocompatible hydrogels. It is unique for one molecule to provide so many different applications in polymer chemistry, but in agreement with Hansell and O’Reilly, the difficulty in tetrazine synthesis as well as their reactivity towards unsaturated monomers does create a challenge for the polymer chemist trying to work with tetrazines. Despite this challenge, the range with which a small molecule which be utilized in so many unique ways for developing novel polymeric materials will continue to lure more researchers to the challenge, and it is our hope that this review will also help to encourage others to pick up that challenge.
Chapter 2

Transforming polybutadiene with tetrazine click chemistry into self-indicating, antioxidant foams

2.1 Introduction

Antioxidants protect polymers against oxidative damage to the extent that their eventual depletion dictates the lifetime of the polymer.\textsuperscript{68–70} The amount of antioxidants (hindered phenols, aryl amines or phosphites) used is limited by their poor solubility in polymers and their attenuation of the polymers’ mechanical properties through plasticization.\textsuperscript{71} One powerful method for circumventing both of these limitations is to synthesize macromolecular antioxidants.\textsuperscript{72,73} This method also eliminates the potential environmental or health problems resultant from blooming or leaching of antioxidants,\textsuperscript{74,75} but it requires the synthesis of specialized monomers which increase the cost of the polymers. An alternative approach is simple, chemical modification of existing, commodity polymers to install antioxidant groups in numbers sufficient to substantially increase the lifetime of the polymer.\textsuperscript{76}

This is now achievable using a new class of antioxidants, 1,4-dihydropyridazines, which can be attached through click reactions of 1,2,4,5-tetrazines with polymers bearing reactive C=C bonds, such as polybutadiene. Tetrazine-alkene click chemistry, also known
as the Carboni-Lindsey reaction, is an inverse [4+2] Diels-Alder cycloaddition between an electron-rich alkene and the electron-poor diene 1,2,4,5-tetrazine. The initial cycloaddition is immediately followed by a retro-[4+2] cycloaddition, which affords dihydropyridazine and a molecule of nitrogen (Figure 25A). Aromatization of dihydropyridazines to pyridazines provides two hydrogen atom equivalents for terminating radical chain reactions, just as with 1,4-cyclohexadiene or 1,4-dihydropyridine antioxidants (Figure 25B). Generally applied to click or bioorthogonal modification of macromolecules with norbornenyl, trans-cyclooctenyl, ethynyl, dicyclopentadienyl, or allyl ether groups, the Carboni-Lindsey reaction has yet to be used to modify the more mundane C=C bonds of common macromolecules, such as polybutadiene or styrene-butadiene rubber. Herein, we describe the first application of tetrazine click chemistry towards chemically modifying polydienes with antioxidant dihydropyridazine groups while exploiting the release of nitrogen gas as the reaction’s chemical byproduct to foam the solidifying polymers.

This space intentionally left blank
Figure 25: (A) Carboni-Lindsey reaction of polybutadiene with tetrazines as reactive modifiers and chemical blowing agents for the production of poly(dihydropyridazine) foams, shown completely converted. (B) The dihydropyridazine acts as a two H atom donor antioxidant oxidizing to the heteroaromatic polypyridazines.

2.2 Results & Discussion

2.2.1 Click Modification of Polybutadienes

DCT reacts as soon as it is dissolved in PBD, acting as a chemical blowing agent and giving rise to viscous dark orange solutions bubbling with the nitrogen gas released from the Carboni-Lindsey reaction. Different 1,4-dihydropyridazine products result when using PBDs with either cis/trans (PBD14) or predominately vinylic (PBD12) conformations. The product of the reaction of DCT with PBD14 can be described as a copolymer of butadiene and 4,5-dimethylene-3,6-dichloro-1,4-dihydropyridazine, poly(1,4-butadiene-co-4,5-dimethylene-3,6-dichloro-1,4-dihydro-pyridazine) (187) (Figure 26A). The product from PBD12 is poly(1,2-butadiene-co-4-vinyl-3,6-dichloro-1,4-dihydropyridazine) (191). As the cycloaddition products from PBD and DCT result in
the formation of dihydropyridazine rings, an additional oxidation step, 189, is required to generate the heteroaromatic pyridazine ring. Oxidation of 187 and 191 afford either poly(1,4-butadiene-co-4,5-dimethylene-3,6-dichloropyridazine) (190), or poly(1,2-butadiene-co-4-vinyl-3,6-dichloropyridazine) (192), respectively.

**Figure 26:** Liquid PBD (A) is blended neat with DCT and nitrogen release from the Tz-IEDDA reaction results in foaming (B, C). Dependent on the type of PBD used, different product results are observed. Foams produced from lower viscosity PBD14 will collapse over 72-120 hours (D) and an intractable material forms through interchain crosslinking (188). Using higher viscosity PBD12 produces a brittle foam that retains its shape indefinitely and is soluble in halogenated solvents (E). Thermoset soft foams (F) are generated from PBDOH (193). Polymers synthesized in solution (191, 192) must be
accompanied with in-situ oxidation (189) otherwise cross-linking upon precipitation results in intractable products.

As noted above, foaming reactions between PBD and DCT were run solvent-free since the PBDs used in this study were all viscous liquids at room temperature. While DCT was found to be soluble in liquid PBD (Figure 26B), we also explored other tetrazine species: 3,6-diphenyl-1,2,4,5-tetrazine, 3,6-di(pyridin-2-yl)-1,2,4,5-tetrazine, dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (DMDT) and 3,6-bis(3,5-dimethyl-1H-pyrazol-1-yl)-1,2,4,5-tetrazine, but found them to be relatively insoluble in PBD and did not pursue them further in this study. Due to the viscosity of the PBDs, mechanical mixing of DCT was required to create a uniform homogenous solution of the two, which we found necessary to initiate the foaming reaction. Mixing provided deep orange, viscous solutions that immediately began to bubble and foam as nitrogen gas was released (Figure 26C, 26D). At 25 mol% conversion, tetrazine-alkene click chemistry will generate approximately 26 cm³ of N₂ from 1.15 mmol of DCT when it’s used to modify 5.00 mmol of PBD, resulting in a volume expansion of more than 10-fold as the foam grows from less than 0.5 cm³ to just over 5 cm³. As the viscosity increases, the expansion ceases and the solution eventually solidifies into an orange foam over the course of 30 minutes to 3 hours, e.g. hydroxyl-functionalized polybutadiene (PBDOH) click modified with 25 mol% DCT solidified as an opaque, orange foam within 0.5-1 h. With curing overnight, the color of the polymeric foams faded to a light tan color at room temperature as the residual unreacted DCT was exhausted or to dark brown when cured at
60 °C, of which the color is believed to result from thermal oxidation of the dihydropyridazine rings.

The qualities of the foams can be altered by the choice of PBD that is blended with DCT. The foams made from lower viscosity PBD14 (2.7-3.0 Pa·s, Aldrich) and 25 mol% DCT, 187, were tacky and elastomeric following formation, but would collapse within 3-5 days of setting (Figure 26E). The collapsed polymer was initially soluble in halogenated and ethereal solvents, but became intractable over time. The cross-linking is predicted to be caused through nucleophilic attack between a dihydropyridazine unit’s amine on one chain with the imidoyl chloride species on a dihydropyridazine unit of a neighboring copolymer chain (188). Lower percentages of chlorine in the elemental analysis of 187 help to support this claim of intramolecular cross-linking. Through repeated cross-linking, the viscous polymer became an intractable dark-brown thermoset over the course of 3 weeks. Using higher viscosity PBD12 (3-10 Pa·s, Aldrich) provided brittle thermoplastic foams (191), which retained their shape indefinitely after formation (Figure 26F) The orange coloration of the foam remained after formation and was caused by residual unreacted DCT. The foams were soluble in aromatic, chlorinated, and ethereal solvents after formation, but cross-linking was observed after dissolution and an intractable white precipitate formed in solution within 24 hours after the foam had been dissolved. Click modification of hydroxyl-terminated polybutadienes (1.5 Pa·s, Aldrich) with 12.5, 25, or 45 mol% DCT (193A-C, respectively) afforded insoluble thermoset foams (Figure 26G). Despite the viscosity of PBDOH being lower than that of PBD14, all of the thermoset foams retained their shape after formation through cross-linking by nucleophilic attack of the PBD hydroxyl end groups with the reactive carbon center of the
dihydropyridazine’s imidoyl chloride moiety. Lower chlorine percentages in the elemental analyses for the foams helps supports this claim. Modification with 12.5 mol% DCT provided a more elastomeric foam, 193A, and using higher concentrations of DCT lead to increased rigidity in the foams. Foams made with 45 mol% DCT, 193C, contained unreacted crystalline tetrazine and were more brittle.

2.2.2 Structure of Click Modified Polymers

*Table 1*: Extent of conversion and thermal properties of copolymers produced from the modification of polybutadienes with DCT.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Conc. DCT (mol%)</th>
<th>PBD Type</th>
<th>PBD $M_n$, $M_w$ (Da)</th>
<th>PBD $T_g$ (°C)</th>
<th>Solvent-free or solution product</th>
<th>Extent conver.</th>
<th>Product $M_n$, $M_w$ (Da)</th>
<th>Product $T_g$ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>187</td>
<td>25</td>
<td>1,4 cis/trans</td>
<td>6494 22209</td>
<td>-100 °C</td>
<td>Solvent free: Foam/collapsed</td>
<td>25%</td>
<td>8184 36238</td>
<td>95</td>
</tr>
<tr>
<td>190</td>
<td>100</td>
<td>1,4 cis/trans</td>
<td>6494 22209</td>
<td>-100 °C</td>
<td>Solution: light brown ppt</td>
<td>48%</td>
<td>9975 17432</td>
<td>53</td>
</tr>
<tr>
<td>191</td>
<td>25</td>
<td>1,2 vinylic</td>
<td>3042 4414</td>
<td>-20 °C</td>
<td>Solvent free: Foam/brittle</td>
<td>23%</td>
<td>4200 5984</td>
<td>5</td>
</tr>
<tr>
<td>192</td>
<td>100</td>
<td>1,2 vinylic</td>
<td>3042 4414</td>
<td>-20 °C</td>
<td>Solution: white ppt</td>
<td>51%</td>
<td>4519 6551</td>
<td>85</td>
</tr>
<tr>
<td>193 A</td>
<td>12.5</td>
<td>Hydroxyl terminated</td>
<td>—</td>
<td>-100 °C</td>
<td>Solvent free: Foam</td>
<td>Insol.</td>
<td>Insol.</td>
<td>—</td>
</tr>
<tr>
<td>193 B</td>
<td>25</td>
<td>Hydroxyl terminated</td>
<td>—</td>
<td>-100 °C</td>
<td>Solvent free: Foam</td>
<td>Insol</td>
<td>Insol</td>
<td>45</td>
</tr>
<tr>
<td>193 C</td>
<td>45</td>
<td>Hydroxyl terminated</td>
<td>—</td>
<td>-100 °C</td>
<td>Solvent free: Foam</td>
<td>Insol</td>
<td>Insol</td>
<td>100</td>
</tr>
</tbody>
</table>

The extent of click modification (*Table 1*) was estimated by comparing new dihydropyridazine $^1$H NMR resonances to those of the residual butadiene alkenes (cis: 5.51, trans: 5.64 ppm, vinyl: 4.94 & 5.40 ppm), allylic (cis: 2.08 ppm, trans 2.06 ppm)
or vinyl backbone (1.18 & 2.11 ppm) peaks, labeled with asterisks in Figure 27A-C. In all three of the CDCl₃ soluble polymers made using 25 mol% DCT, integration of these peaks revealed 23-25 mol% of the butadiene repeat units were converted into vinyl dihydropyridazine groups in 191 or dimethylene dihydropyridazine groups in 187. Where both 1,2- and 1,4-regiochemistries were present in a 20% 1,2-addition polybutadiene, DCT showed no selectivity between either regioisomer. In 191, the backbone methylene (1.5 ppm) and methine resonances (1.8 ppm) are partially obscured by the methylene and methine peaks of the 1,2-butadiene backbone, while the dihydropyridazine ring methylene (2.75 ppm) is just downfield from the 1,2-butadiene methine. The backbone methylenes in samples of 187 were also found at 1.4 ppm and 2 ppm while the ring methine peak was near δ 2.5 ppm. Tautomerization of 4,5-dihydropyridazines to the 1,4-dihydropyridazines, well known from reaction of small molecule alkenes with tetrazines, was confirmed by the presence of an NH resonance between 8-10 ppm in all of the solvent-free click modified polymers. The molecular weights of the modified copolymers increased proportionally to their respective PBDs with what would be expected for their equivalent DCT modification (Table 1).

With solvent-free modification of polybutadienes, no more than 45% DCT could be dissolved in PBD as using higher concentrations of DCT would result in a run-off exothermic reaction that lead to significant scorching of the foams and the generation of a grey-colored acidic gas. Thermoset foam 193C was brittle compared to the other thermoset foams made using less DCT concentrations and residual orange DCT crystals remained trapped in the foam after formation and curing. Elemental analysis of 193C after Soxhlet extraction with CHCl₃ indicated that only 27% of DCT reacted with the
PBDOH, and provided an upper limit to the amount of modification that can be achieved through neat mixing. To achieve higher conversion percentages, solution-based attempts to quantitatively click-modify PBD were conducted in methylene chloride with 100 mol% DCT. The solution-based modification attempts proved to be a frustrating endeavor due to the reactivity of the dihydropyridazine units’ imidoyl chloride functionalities, and upon precipitation the polymers would immediately crosslink and become intractable brown solids. *In-situ* oxidation of the dihydropyridazine groups with dimethyl dioxirane (DMDO) before precipitation provided a method to obtain soluble linear polymers after click modification, as DMDO converted the reactive dihydropyridazine ring into its more stable heteroaromatic pyridazine variant and afforded either 190 or 192 (Figure 26A) in 52% and 58% conversions, respectively.

*This space intentionally left blank*
Figure 27: Solution 1H NMR of (A) 191, (B) 192, and (C) 187 and solid state 13C NMR spectra of (D) 191, (E) 192, and (F) 190.

In the $^1$H NMR spectrum of 192, the aliphatic region of the spectrum ($\delta$ 1-3.5 ppm) is a continuous, complex absorption arising from overlapping peaks and line broadening (Figure 27B). The broad NH peak from the dihydropyridazine precursor has been replaced by a new sharper singlet from the pyridazine ring’s sole aromatic hydrogen, indicating the oxidation was successful. In the $^1$H NMR spectrum of 190 samples, this peak is neither expected nor observed (see appendix A). IR comparisons between the dihydropyridazine copolymers 187 and 191 with that of their oxidized counterparts 190 and 192 show the disappearance of two distinct bands upon oxidation, the N-H stretch at $\nu = 3198$ cm$^{-1}$ or 3420 cm$^{-1}$ respectively, and the sharp
dihydropyridazine ring C=C stretch for both copolymers at ν = 1682 cm⁻¹ (see appendix A).

Solid state ¹³C NMR was required for analysis of the insoluble thermosets and its excellent signal to noise was also helpful in providing spectral details of the oxidized copolymers prepared through solution polymerizations. In the solid state NMR spectra (Figures 27D-F), the peaks from the unreacted butadiene repeat units are also labeled with asterisks. In the materials with the dihydropyridazine groups intact (Figures 27D, 27F), the spectrum resonances for the backbone methylenes and methines from both butadiene residues and dihydropyridazine groups appear between 20—45 ppm. The carbons in the dihydropyridazine rings lie downfield around the butadiene C=C resonances. In the ¹³C spectrum for 191 (Figure 27D), an additional peak at 170 ppm provides confirmation of the presence of unreacted DCT. In the spectrum for 192 (Figure 27E), the two carbons bearing chloride groups on the pyridazine ring are located at 158 and 148 ppm, while the aromatic CH and the quaternary carbon where the ring is attached to the polymer backbone are observed at 130 ppm and 140 ppm, respectively. The minor peak at 100 ppm may indicate that a small amount of epoxidation of the alkene bonds did occur from 189. In the spectrum for the symmetric 190, there are only the two expected pyridazine carbons at 158 and 140 ppm. An additional small peak at 105 ppm may be due to a small amount of epoxide formation as well.

2.2.4 Thermal Properties & Microstructure

DCT click conversion of the flexible and disordered polybutadienes into more rigid and massive poly(dichlorodihydropyridazines) and poly(dichloropyridazines) changed the liquid precursors into solid elastomers, thermoplastics or thermosets. Which was
obtained was dependent mostly on how much DCT was used for the modification and on the viscosity of the starting polymer. PBD14 (2.7-3.0 Pa·s) has a T_g of -100 °C while 25% modification with DCT increased the T_g to 7 °C for 187, and 52% modification and oxidation raised it to 66 °C for 190 (Table 1). Onset degradation temperatures for the copolymers were 308 and 299 °C, respectively. The predominantly vinylic PBD12 (3-10 Pa·s) has a higher T_g of -20°C and its copolymers’ glass transition temperatures were also higher than those made from PBD14, 28 °C for 191 and 143 °C for the 58% functionalized 192. Onset degradation temperatures for these copolymers were 318-319 °C, but slight mass loss was observed beforehand. Mass loss beginning at 100 °C in 191 could be attributed to the degradation of unreacted DCT. The lower viscosity PBDOH (1.5 Pa·s) produced thermoset foams with lower glass transitions, which increased with extent of modification -45, -5, and 11 °C for 193A, 193B, & 193C, respectively. Onset degradation temperatures for the thermoset copolymers were similar to PBDOH (450 °C), ranging from 436—456 °C.

The pore sizes for the 187 foams were non-uniform and pores as large as millimeters in diameter could be observed visually, with SEM imaging indicating the presence of an open cell network having smaller pores in the range of 10s to 100s of micrometers (see appendix A). The non-uniformity of cell size and shape for 187 foams is likely attributed to both the absence of a stabilizing surfactant in their formation and the low viscosity of the PBDOH used. The foams were tested and found to be insoluble in methanol, hexanes, toluene, chloroform, and THF. Swelling was observed in toluene, chloroform, and THF, with the largest observed expansion occurring in THF. Thermoset foams could be formed in molds and cubic samples of 10 mm^3 were prepared for density
measurements and compression testing. Samples of 193B were found to have a density of 0.22 g/cm³, and compression testing provided a compressive strength of 40.67 ± 1.81 kPa at 25% deformation and a modulus of 0.436 ± 0.013 MPa. Thermoplastic 191 foams provided a slightly more uniform open cell pore structure (see appendix A), but pore sizes still ranged from micron to millimeter diameters throughout the foams. The foams generated using PBD12 were too brittle to mold, and compressive testing could not be obtained.

2.2.5 Dihydropyridazines as Free Radical Inhibitors

Although 1,4-dihydropyridazines are well-known to undergo oxidative aromatization, their use as antioxidants has to the best of our knowledge not been reported to date. To test their antioxidant capabilities, we designed a simple method which can be used to provide a quick, qualitative and comparative analysis of an antioxidant’s ability to inhibit radical polymerization (Figure 28A). First, a control system, 194, was prepared from neat solutions of 75 mol% styrene (ST), 25 mol% divinylbenzene (DVB), and 1 mol% AIBN, which after mixing were degassed and then heated to 70 °C to initiate polymerization. Over the course of 11 minutes, the solutions’ viscosities were observed to increase as the polymers grew in molecular weight and cross-linking from the DVB resulted in the formation of glassy gels. The gelation times of the controls were used to establish a baseline for which to compare inhibitive effects of the antioxidants. Next, a known antioxidant was tested to compare its inhibition effects to 1,4-dihydropyridazines. Addition of 1 mol% butylated hydroxytoluene (BHT) to solutions of ST/DVB/AIBN before polymerization, 195, resulted in a modest increase in gelation time (13 minutes). Finally, two dihydropyridazines were examined and prepared
in situ by first adding 1 mol% of either DCT, 196, or DMET, 197, to solutions of ST/DVB/AIBN. The tetrazines reacted with the styrenic alkenes to form their 1,4-dihydropyridazine analogs, and reaction progress was easily monitored by a distinctive color change from orange/red to yellow. Following that, the solutions were degassed and heated to 70 °C to initiate polymerization. Both 1,4-dihydropyridazines were observed to outperform 195 in inhibiting the radical polymerization, with 196 extending gelation time to 20 minutes, and 197 extending gelation time more than 10-fold to an astounding 120 minutes! While the styrenic 1,4-dihydropyridazines proved to be more effective in inhibiting radicals than BHT, their oxidized pyridazine analogs were unfortunately colored (Figure 28B), a trait known to occur in other aromatic amine antioxidants.86,87 Ultimately, this coloration limits the antioxidant applications of 196 and 197, but the results of these gelation studies provide evidence that additional analyses of the antioxidant properties of dihydropyridazines are warranted.
**Figure 28:** (A) Evaluation of antioxidant properties of BHT (195), dichlorodihydropyridazine (196) and dimethyl dihydropyridazine dicarboxylate (197) by inhibition of free radical polymerization and gelation of styrene/divinylbenzene solutions. (B) Chemical structures of each inhibitor are provided above their respective gels, and gelation times are listed showing the improved inhibition of dihydropyridazines over the commercial antioxidant BHT.

The demonstration that 1,4-dihydropyridazines have antioxidant properties implies that the polymers discussed in this article are inherently antioxidant-rich. A unique aspect of the foams is the ability to visually observe the extent of their oxidation through fluorescence. It was recently reported that certain dihydropyridazine species can fluoresce under UV excitation, and the 193 foams were observed to fluoresce yellow light after 24 hr curing. After 6 months, the 193B foams fluorescence changed to white light.
light emission ($\lambda_{\text{max}} = 506$ nm), similar to that of the parent 3,6-dichloropyridazine (Figure 29). Monitoring the change in fluorescence provides an indication of extent of oxidation. By examining the foam’s cross-section it becomes evident that the permeation of air to the foam interior and therefore its oxidation was occurring at a slower rate, as the white fluorescence was much less pronounced compared to that of the exterior. While not within the scope of this study, the white fluorescence of 3,6-dichloropyridazine is an interesting discovery not mentioned in prior literature,\textsuperscript{89,90} and the potential for making white light emitting devices from this commercially available small molecule or derivatives of it could be an intriguing pursuit.

![Image](image_url)

**Figure 29:** (left) Solid DCP fluoresces white light upon Long-Wave UV excitation. (middle) The outside layer of a 6-month aged sample of 193B emitting white fluorescence under the same conditions indicating that 1,4-dihydropyridazine units on the foam surface have undergone air oxidation. (right) Slow diffusion of air into the foam leads to a more gradual oxidation in the foam interior, evident when observing a freshly-cut cross-section of 6-month aged 193B.
2.3 Conclusion

In summary, we have discovered new classes of antioxidants in dihydropyridazines, chemical blowing agents in tetrazines, and prepared new antioxidant-rich butadiene-dihydropyridazine copolymer foams through the inverse electron demand Diels Alder reaction between 3,6-dichloro-1,2,4,5-tetrazine and polybutadiene. When dissolved in viscous alkene-rich PBDs, DCT undergoes a Carboni-Lindsey cycloaddition/retro-cycloaddition reaction which releases nitrogen gas as a chemical byproduct that foams the resultant copolymer. The modification imparts mechanical properties into a liquid elastomer. Glass transitions increase, but onset degradation temperatures decrease with extent of modification compared to that of PBD. Lower viscosity PBDs will result in foams which collapse over time, while higher viscosity or hydroxyl terminated PBDs produced either organics soluble or thermoset foams, respectively. The product of this cycloaddition, 1,4-dihydropyridazine, imparted the polymers with their own built-in antioxidants, and radical inhibition experiments were used to demonstrate their enhanced effectiveness over commercially used antioxidant BHT. Extent of oxidation can be followed visually as the copolymer foams change fluorescence from yellow to white as they become oxidized. DMDT showed enhanced radical inhibition over DCT, and we are currently pursuing studies into antioxidant polymers predominately composed of dimethyl ester dihydropyridazine functionalites. This chemistry shows potential for use in generating foamed materials using other liquid polymers that contain alkene substituents, and in making cheap antioxidant polymers that are highly resistant to oxidation. We are also currently in the process of determining other possible tetrazine candidates that function as chemical blowing agents with polydiienes.
2.4 Experimental Section

Poly(1,4-butadiene-co-4,5-dimethylene-3,6-dichloro-1,4-dihydro-pyridazine) \textit{\textsuperscript{(25)}}

collapsed foam: \textit{\textsuperscript{(187)}}

To a glass scintillation vial (20 mL volume) was added poly-1,4-butadiene (0.270 g, 5.00 mmol) and 3,6-dichloro-1,2,4,5-tetrazine (0.188 g, 1.25 mmol). The mixture was blended with a glass stir rod until a bright orange foaming paste was generated. The reaction was left to proceed for 24 h under ambient conditions. The orange foam ceased growing after 3 h, and became a light tan color after 24 h (0.432 g). After 72 h the foam had collapsed into a brown intractable resin. $^1$H NMR (499 MHz, Chloroform-$d$, $\delta$) 9.01 (s, 0.1H), 6.74 (s, 0.3H), 5.92 – 4.82 (m, 2.2H), 3.57 (s, 0.1H), 3.02 – 2.70 (m, 0.6H), 2.65 (s, 0.3H), 2.55 – 2.25 (m, 0.7H), 2.11 (q, $J = 3.4$, 2.8 Hz, 4H), 1.90 – 0.85 (m, 1.4H); $^{13}$C NMR (126 MHz, CDCl$_3$, $\delta$): 140.64, 129.71, 27.53, 27.39, 27.35, 27.32, 27.22, 26.25; IR (ATR, SiO$_2$): $\nu = 3208$ (br, $\nu_s$(NH)), 3110 (br, $\nu_s$(NH)), 3007, 2924, 2857, 2148, 1680 (s, $\nu_s$(dihydropyridazine C=C)), 1530, 1452, 1401, 1310, 1220, 1173., 1076, 971, 912, 888, 829, 7423, 674, 624, 589, 567, 552 cm$^{-1}$; GPC: (PS stds, THF): Mn, Mw, PDI = 8184, 36238 Da, 4.43. Anal. Calcd: C$_{2064}$H$_{2046}$Cl$_{420}$N$_{420}$: C 64.06, H 6.57, Cl 21.05, N 8.32; found: 64.43, H 8.10, Cl 16.92 from difference, N 10.55.

Poly(1,4-butadiene-co-(4-vinyl (6%))-4,5-dimethylene (18%)-3,6-dichloro-1,4-dihydro-pyridazine) collapsed foam: \textit{\textsuperscript{(187')}}

To a 20 mL glass scintillation vial was added poly-1,2-1,4-butadiene (0.270 g, 5.00 mmol) and 3,6-dichloro-1,2,4,5-tetrazine (0.175 g, 1.16 mmol). The mixture was stirred at room temperature until the tetrazine was completely dissolved and gas generation
could be observed in the bright orange foaming liquid. The foam continued to expand for an additional 30 minutes. After 24 h, the color of the foam had changed to a light peach-yellow color with a small amount of what appeared to be unreacted orange dichlorotetrazine specks contained within it and the foam was observed to fluoresce yellow under UV light. Mass of product after 24 h (0.401 g). After 1 week, the foam had collapsed into an orange-brown intractable resin. $^1$H NMR (499 MHz, Chloroform-$d$, $\delta$): 9.13 (s, 0.3H), 5.39 (d, $J = 21.7$ Hz, 2H), 5.12 (s, 0.1H), 4.97 (s, 0.3H), 2.85 (s, 0.2H), 2.62 (s, 0.3H), 2.45 (s, 0.2H), 2.30 (d, $J = 29.8$ Hz, 0.2H), 2.06 (d, $J = 22.8$ Hz, 4H), 1.67 (d, $J = 41.8$ Hz, 1H), 1.42 (s, 0.2H), 1.28 (s, 0.4H); $^{13}$C NMR (126 MHz, CDCl$_3$, $\delta$): 142.75, 140.70, 129.72, 114.58, 46.42, 43.82, 38.28, 34.23, 32.81, 29.53, 29.15, 27.52, 27.32, 24.40, 23.95; IR (ATR, SiO$_2$): $\nu = 3199$ (br, $\nu_\text{s}$(NH)), 3121 (br, $\nu_\text{s}$(NH)), 3007, 2919, 2851, 1681 (s, $\nu_\text{s}$(dihydropyridazine C=C)) , 1448, 1311, 1175, 1076, 969, 914, 742, 666, 626, 575, 553 cm$^{-1}$; GPC (PS stds, THF): Mn, Mw, PDI = (peak 1) 25361, 27089 Da, 1.07 (peak 2) 11826, 12001 Da, 1.02; Anal. calcd. for C$_{1070}$H$_{1434}$Cl$_{114}$N$_{114}$: C 64.47, H 7.25, Cl 20.27, N 8.01; found: C 65.47, H 7.69, Cl 12.21, N 9.62.

*Poly(1,4-butadiene-co-4,5-dimethylene-3,6-dichloropyridazine)* (100) linear polymer: (190)

A 50 mL 14/20 1-neck round-bottom flask was charged with poly-1,4-butadiene (0.216 g, 4.00 mmol), DCT (0.604 g, 4.00 mmol), dichloromethane (20 mL), and a Teflon-coated magnetic stir bar. The bright orange solution was degassed with argon for 30 minutes and then refluxed for 72 h during which time the solution became an opaque dark brown color. The reaction was then cooled to room temperature (23 °C) and a separate solution of freshly prepared dimethyl dioxirane in acetone (4.0 mL) was added to the flask, and
stirred for 1 hr. During this time the reaction solution became slightly more transparent. After 1 hr, the solution was concentrated under dynamic vacuum, dissolved in THF (2 mL) and precipitated into methanol (20 mL). The precipitate was collected and dried with vacuum filtration, then dried further by heating to 45 °C under high vac. to yield a light brown solid (0.407 g). $^1$H NMR (499 MHz, DMSO-$d_6$, δ) 5.38 (s, 2H), 2.77 (s, 3H), 2.20 (s, 2H), 1.87 (s, 2H), 1.37 (s, 3H). $^{13}$C NMR (20 kHz, CPMAS, δ) 157.68, 141.75, 129.74, 68.27, 27.58, 17.41; IR (ATR, SiO$_2$): ν = 3009, 2944, 2866, 1637, 1527, 1447, 1396, 1311, 1151, 1075 1019, 917, 797, 739, 585 cm$^{-1}$; GPC: (PS stds, THF): Mn, Mw, PDI = 9975, 17432 Da, 1.75; Anal. calcd for 51% conversion C$_{2064}$H$_{2046}$Cl$_4$N$_{420}$: C 52.01, H 4.32, Cl 31.30, N 12.37, found: C 52.50, H 5.30, Cl 29.1 by difference, N 13.10.

Poly(1,2-butadiene-co-4-vinyl-3,6-dichloro-1,4-dihydropyridazine (25) thermoplastic foam: (191)

To a glass scintillation vial (20 mL volume) was added poly-1,2-butadiene (0.270 g, 5.00 mmol) and 3,6-dichloro-1,2,4,5-tetrazine (0.188 g, 1.25 mmol). The mixture was blended with a glass stir rod until a bright orange foaming paste was generated, and the reaction was left to proceed for 24 h under ambient conditions. The orange foam ceased growing after 2 h, and retained its shape after formation (0.416 g) $^1$H NMR (400 MHz, Chloroform-$d$, δ) 8.58 (s, 0.1H), 5.45 (d, $J = 173.7$ Hz, 1.2H), 4.95 (d, $J = 10.3$ Hz, 2.0H), 3.23 – 2.28 (m, 0.5H), 2.06 (d, $J = 62.2$ Hz, 1.5H), 1.68 – 0.84 (m, 2.7H); $^{13}$C NMR (20 kHz, CPMAS): δ 170.18, 156.41, 143.39, 129.94, 115.96, 39.64; IR (ATR, SiO$_2$): ν = 3241(br, ν$_a$(NH)), 3077, 2973, 2919, 2846, 1892, 1834, 1682 (s, ν$_a$(dihydropyridazine C=C)), 1636, 1560, 1452, 1418, 1377, 1312, 1237, 1137, 1077, 996,
Poly(1,2-butadiene-co-4-vinyl-3,6-dichloropyridazine) (100) linear polymer: (192)

A 50 mL 14/20 1-neck round-bottom flask was charged with poly-1,2-butadiene (0.216 g, 4.00 mmol), 3,6-dichloro-1,2,4,5-tetrazine (0.604 g, 4.00 mmol), dichloromethane (20 mL), and a Teflon coated magnetic stir bar. The bright orange solution was degassed with argon for 30 minutes and then refluxed for 72 h during which time the solution developed a slight dark brown color but remained transparent. The reaction was cooled to room temperature (23 °C) and a brown residue was observed to have formed on the sidewalls of the flask. A solution of freshly prepared dimethyl dioxirane in acetone (4.0 mL) was added to the flask, and the reaction was stirred for 1 hr. During this time the solution became more transparent. After 1 hr, the reaction solution was concentrated under reduced pressure before precipitating into hexanes. The precipitate was collected and dried with vacuum filtration, then dried further by heating to 45 °C under high vac. to yield a white powder (0.448 g). $^1$H NMR (400 MHz, DMSO d$_6$, δ): 8.04 (s, 1H), 5.31 (s, 1H), 4.86 (s, 2H), 3.62–0.78 (m, 8H); $^{13}$C NMR (20 kHz, CPMAS, δ): 157.18, 142.15, 129.40, 116.90, 101.96, 39.74, 17.92; FT-IR (ATR, SiO$_2$): ν = 3074, 2922, 2852, 1696, 1639, 1560, 1452, 1419, 1380, 1326, 1136, 1080, 1051, 998, 916, 857, 833, 797, 760, 721, 693, 626, 614, 592, 573, 546, 493, 471, 449, 439, 419 cm$^{-1}$; GPC: (PS stds, THF): Mn, Mw, PDI = 4616, 5930 Da, 1.28; Anal. calcd for 58% conversion C$_{424}$H$_{399}$Cl$_{96}$N$_{96}$:
C, 49.72; H, 3.93; Cl, 33.23; N, 13.13; found: C 50.63, H 4.83, Cl 30.78 by difference, N 13.76.

*Hydroxyl-functionalized poly(1,4-butadiene-co-4,5-dimethylene-3,6-dichloropyridazine)*
*(12.5) thermoset foam: (193A)*

To a 20 mL plastic weighing cup was added hydroxyl-functionalized poly-1,4-butadiene (0.272 g, 5.04 mmol) and 3,6-dichloro-1,2,4,5-tetrazine (0.094 g, 0.62 mmol). The mixture was stirred until the tetrazine was completely dissolved and gas generation could be observed in the bright orange foaming paste. The orange foam continued to rise under an open air environment at 25 °C for 30 additional minutes before ceasing to grow any further. After 24 h, the color of the foam had changed to a light tan color and the foam was observed to fluoresce yellow under UV light. Mass of product after 24 h (0.346 g, 99%) IR (KBr): ν = 3240 (br, νs(NH)), 3074, 3005, 2920, 2848, 2151, 1679 (s, νs(dihydropyridazine C=C)), 1511, 1444, 1380, 1345, 1308, 1251, 1215, 1177, 1077, 995, 967, 912, 830, 727, 667, 624, 489 cm⁻¹; Anal. calcd for C₉₄H₁₃₂Cl₃N₆O₆: C 72.91, H 8.59, Cl 6.87, N 5.43, O 6.20; found: C 72.23, H 8.82, Cl 7.56, N 5.65, O 5.74 by difference.

*Hydroxyl-functionalized poly(1,4-butadiene-co-4,5-dimethylene-3,6-dichloropyridazine)*
*(25) thermoset foam: (193B)*

To a 20 mL plastic weighing cup was added hydroxyl-functionalized poly-1,4-butadiene (0.271 g, 5.03 mmol) and 3,6-dichloro-1,2,4,5-tetrazine (0.189 g, 1.25 mmol). The mixture was stirred until the tetrazine was completely dissolved and gas generation could be observed in the bright orange foaming paste. The orange foam continued to rise under
an open air environment at 25 °C for an approximately 30 additional minutes before ceasing to grow any further. After 24 h, the color of the foam had changed to a light peach-yellow color and the foam was observed to fluoresce yellow under UV light. Mass of product after 24 h (0.408 g, 96%) 13C NMR (20 kHz, CPMAS): δ170.82, 147.36, 142.67, 130.56, 116.01, 42.51, 33.16, 28.34; IR (KBr): 3232 (br, νs(NH)), 3077, 3004, 2919, 2850, 2150, 1678 (s, νs(dihydropyridazine C=C)), 1511, 1445, 1383, 1310, 1251, 1219, 1178, 1135, 1075, 995, 968, 728, 665, 622, 488 cm⁻¹; Anal. calcd for C₉₀H₁₃₁Cl₆N₁₁O₆: C 66.66, H 7.40, Cl 11.92, N 8.64, O 5.38; found: C 65.57, H 7.95, Cl 11.66, N 8.73, O 6.09 by difference.

*Hydroxyl-functionalized poly(1,4-butadiene-co-4,5-dimethylene-3,6-dichloropyridazine) (45)* thermoset foam: (193C)

To a 20 mL plastic weighing cup was added hydroxyl-functionalized poly-1,4-butadiene (0.271 g, 5.02 mmol) and 3,6-dichloro-1,2,4,5-tetrazine (0.337 g, 2.23 mmol). The mixture was stirred until the tetrazine was completely dissolved and gas generation could be observed in the bright orange foaming paste. The orange foam continued to rise under an open air environment at 25 °C for an approximately 30 additional minutes before ceasing to grow any further. After 24 h, the color of the foam had changed to a light peach-yellow color and the foam was observed to fluoresce yellow under UV light. Mass of product after 24 h (0.520 g, 95%) IR (KBr): 3349 (br, νs(NH)), 3070, 3009, 2965, 2922, 2852, 2145, 1682 (s, νs(dihydropyridazine C=C)), 1613, 1510, 1447, 1433, 1381, 1339, 1299, 1239, 1218, 1178, 1082, 1012, 996, 969, 914, 829, 757, 722, 664, 629, 563, 474 cm⁻¹; Anal. calcd for C₁₀₈H₁₃₂Cl₁₄N₂₀O₆: C 56.33, H 5.78, Cl 21.55, N 12.17, O 4.17;
experimental before CHCl₃ extraction: C 59.31, H 7.01, Cl 15.38; N 11.66; after CHCl₃ extraction found: C 64.15, H 7.55, Cl 11.99, N 9.28.

**Antioxidant Gelation Delay Study**

*Control sample: styrene (Styr); divinyl benzene (DVB), AIBN (194)*

A 20 mL glass scintillation vial was charged with styrene (4.167 g, 40.01 mmol), divinylbenzene (1.728 g, 13.27 mmol), AIBN (0.108 g, 0.66 mmol), and a magnetic stir bar. The vial was capped with a rubber septum and the solution purged with argon while stirring for 30 minutes. The vial was kept under positive pressure with argon, transferred to a 70 °C oil bath and left undisturbed. The solution was observed to have gelled after 11 minutes, and after 13 minutes Trommsdorff autoacceleration led to fissures forming in the gel and smoke filling the vial. After removal from the oil bath, the product was observed to be an opaque white solid.

*Control sample: styrene (Styr); divinyl benzene (DVB), butylatedhydroxy toluene (BHT), AIBN (195)*

A 20 mL glass scintillation vial was charged with styrene (4.165 g, 39.99 mmol), divinylbenzene (1.745 g, 13.40 mmol), BHT (0.145 g, 0.66 mmol), AIBN (0.108 g, 0.66 mmol), and a magnetic stir bar. The vial was capped with a rubber septum and the solution purged with argon while stirring for 30 minutes. The vial was then transferred to a 70 °C oil bath and left undisturbed. The solution was observed to have gelled after 13 minutes and the vial was removed from the oil bath yielding a transparent colorless gel.
DCT sample: styrene (Styr); divinyl benzene (DVB), DCT, AIBN (196)

A 20 mL glass scintillation vial was charged with styrene (4.162 g, 39.96 mmol), 3,6-dichloro-1,2,4,5-tetrazine (0.100 g, 0.66 mmol), and a magnetic stir bar. The tetrazine began reacting with styrene upon addition and vigorous nitrogen bubbling was observed in the orange solution. The vial was capped with a rubber septum and degassed with argon for 45 minutes while stirring, during which time the solution became a transparent dull peach color. After 45 minutes, divinylbenzene (1.732 g, 13.30 mmol), and AIBN (0.108 g, 0.66 mmol), were added to the flask. The vial was recapped and the solution purged with argon with stirring for an additional 30 minutes. The vial was kept under positive pressure with argon, transferred to a 70 °C oil bath and left undisturbed. The solution was observed to have gelled after 20 minutes, and after 23 minutes Trommsdorff autoacceleration led to fissures forming in the gel and smoke filling the vial. After removal from the oil bath, the product was observed to be an opaque peach solid.

DMET sample: styrene (Styr); divinyl benzene (DVB), DMET, AIBN (197)

A 20 mL glass scintillation vial was charged with styrene (4.166 g, 40.00 mmol), dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (0.131 g, 0.66 mmol), and a magnetic stir bar. The tetrazine began reacting with styrene immediately upon addition and vigorous nitrogen bubbling was observed in the solution. The vial was capped with a rubber septum and degassed with argon for 1.5 hr while stirring, during which time the solution became a transparent bright yellow color. After 1.5 h, divinylbenzene (1.736 g, 13.33 mmol), and AIBN (0.108 g, 0.66 mmol), were added to the flask. The vial was recapped and the solution purged with argon with stirring for an additional 30 minutes. The vial was kept
under positive pressure with argon, transferred to a 70 °C oil bath and left undisturbed. The solution was observed to have gelled after 120 min, and after 170 minutes Trommsdorff autoacceleration led to fissures forming in the gel and smoke filling the vial. After removal from the oil bath, the product was observed to be an opaque yellow solid.
Chapter 3

Fluorescent anti-oxidant macromolecules through click modification of polybutadiene with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate

3.1 Introduction

While click modification of polymers with tetrazines has become broadly utilized due to its ability to be carried out in both aqueous and organic solutions at high conversions, low temperatures, and in the absence of a catalyst, most of this focus has been aimed towards its use in bioorthogonal chemistry where a tetrazine covalently bound to a fluorophore can be clicked to a biopolymer expressing unsaturated moieties. Its utility in modifying synthetic polymers has only seen a modest gain in popularity since Barker et al. clicked tetrazines to norbornene functionalized poly(lactic acid), but the versatility of polymer modification using tetrazine click chemistry can easily be observed by the variety of its applications. From carbohydrate microarrays, micropatterning of self-assembled monolayers, core modification of micelles orthogonal to copper click chemistry, and the formation of hydrogel networks, tetrazine click chemistry has demonstrated itself to be a powerful tool for polymer modification, although most of its applications have been through acting as an anchor for cross-linking or the attachment of a desired functional group.
The formation of either dihydropyridazine or pyridazine-rich polymers has never been the end goal of tetrazine click modification, even in the two demonstrated cases where polymers containing norbornene and allyl glycidal ether repeat units were fully converted with tetrazine. Tetrazine reacts with electron-rich dienophiles through an inverse electron demand Diels Alder [4+2]-cycloaddition followed by a retro-[4+2]-cycloaddition, also known as the Carboni-Lindsey reaction. The original intention of the Carboni-Lindsey reaction was aimed towards developing new forms of pyridazine, so it’s only fitting that it has now been utilized in the modification of commercial polybutadiene with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate to form two new classes of polydihydropyridazines and polypyridazines. Dihydropyridazines were recently demonstrated by us to function as antioxidants, and dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate was shown to be over 9x more effective than commercial antioxidant butylated hydroxytoluene (BHT) in the radical inhibition of a styrene/divinylbenzene polymerization. By reacting dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate with polybutadiene, near quantitative conversion of the butadiene backbone with DMDT installs repeating units of dihydropyridazine, creating antioxidant-rich polymers which can provide indication of their oxidation extent through quenching of fluorescence.

3.2 Results & Discussion

3.2.1 Click modification of polybutadienes.

We previously demonstrated the advantages of using a tetrazine click reaction in modifying liquid alkene-rich elastomer polybutadienes (PBDs) through the reaction of 3,6-dichloro-1,2,4,5-tetrazine (DCT) with polybutadiene (PBD). DCT was found to be soluble in PBD and would react upon dissolution, releasing nitrogen gas and creating a
copolymers foam. The incorporated dihydropyridazine rings were demonstrated to function as built-in antioxidants, and outperformed butylated hydroxytoluene (BHT) in radical inhibition experiments. Dihydropyridazines prepared from the reaction of DMDT with styrene were also tested, and demonstrated to be 6x more effective at radical inhibition than DCT-based dihydropyridazines, and 9x more effective than BHT. Based on these results, it was decided to pursue functionalizing PBD with DMDT in order to prepare a new class of polymers which contain near quantitative amounts of antioxidant repeat units.

Scheme 2: (right) Reaction scheme showing the synthesis of poly(dimethyl 1,4-dihydropyridazine-3,6-dicarboxylates) (197, 198) from polybutadienes and their oxidation with DDQ to poly(dimethyl pyridazine-3,6-dicarboxylates) (198, 200). (left) Synthesis of small molecule dimethyl 1,4-dihydropyridazine-3,6-dicarboxylates (201, 203) by reacting DMDT with either cyclohexene or 1-hexene and their subsequent reaction with DDQ.
Unlike with DCT, DMDT was not soluble enough in PBD to generate a foam. A click reaction did occur with heating to 60 °C, and nitrogen gas was observed to generate small gas pockets in the PBD, but DMDT’s relative insolubility resulted in a reaction which was too slow to produce a foamed material (see appendix B). Further modifications were carried out in solution, and DMDT was found to be reactive with PBD in THF. Rapid gas generation was observed upon dissolution of the two in THF, and reaction progress could be followed visually. The initially dark red solution resulting from the tetrainze n-σ* transition faded as the reaction proceeded to a pale-yellow color upon completion and exhaustion of the tetrazine species (Figure 30B). Modifications were conducted on both predominately 1,2-addition polybutadiene (PBD12), and 1,4-addition polybutadiene (PBD14) using equimolar equivalents of DMDT. Refluxing conditions in THF over 17 hours under a positive nitrogen pressure resulted in near quantitative conversions based on NMR integration and elemental analysis for both types of PBDs. In contrast to solution run modifications with DCT and PBD, no cross-linking was observed upon precipitation in methanol or ether and solution-run modifications of PBD with DMDT afforded soluble thermoplastic polymers. Reactions of DMDT with PBD12 (Scheme 1) generated poly(dimethyl 4-vinyl-1,4-dihydropyridazine-3,6-dicarboxylate) (199), and PBD14 produced poly(dimethyl 4,5-dimethylene-1,4-dihydropyridazine-3,6-dicarboxylate) (197). Oxidation of the dihydropyridazine polymers with DDQ in THF yielded poly(dimethyl 4-vinylpyridazine-3,6-dicarboxylate) (200) and poly(dimethyl 4,5-dimethylpyridazine-3,6-dicarboxylate) (198) quantitatively based on NMR integration. The dihydropyridazine polymers displayed good solubility in CHCl3, THF, DMF, and DMSO, and were found to be insoluble in hexanes, ether, and
methanol. The oxidized polymers shared similar solubilities to their dihydropyridazine analogs, but were also found to be insoluble in THF.

![Scheme for the synthesis of poly(dimethyl 4,5-dimethylene-1,4-dihydropyridazine-3,6-dicarboxylate) from the IEDDA reaction between PBD14 and DMDT (197)](image)

**Figure 30:** (A) Scheme for the synthesis of poly(dimethyl 4,5-dimethylene-1,4-dihydropyridazine-3,6-dicarboxylate) from the IEDDA reaction between PBD14 and DMDT (197) (B) Reaction progress can be monitored visually as the dark red color of DMDT gradually fades to a light yellow solution as the rxn proceeds indicating the complete conversion of DMDT to dihydro pyridazine.

### 3.2.2 Structure of click modified polymers.

The $^1$H NMR spectra of 199 shows a strong methyl peak between $\delta$ 3.82-3.85 ppm which was used as a basis for determining extents of conversion (Figure 31B). The distinct NH peak between 8-9 ppm can be observed for both polymers, and a series of peaks between 1-3.5 ppm are from the polymer backbone hydrogens. For 199, a broad peak at 5.74 ppm could easily be mistaken for residual alkene resonances from PBD12, but comparison with the model compound dimethyl 4-butyl-1,4-dihydropyridazine-3,6-dicarboxylate indicates this peak is resultant from the vinylic proton on the dihydropyridazine ring.
(Figure 31B). $^1$H NMR of the oxidized vinyl pyridazine polymer 200 provides additional evidence of this structure, as the peak at 5.74 ppm disappears after oxidation. Following oxidation, integration of the broad peak at 4.70 ppm, interpreted as residual PBD, was used to establish a conversion percentage for the click reaction between DMDT and PBD12, providing evidence of an 89% conversion (Figure 31C). For 197, a small peak at 5.27 ppm remained from unreacted PBD, and integration for 198 after DDQ oxidation provided evidence for 2% residual PBD, and a 98% conversion for the modification of PBD14 with DMDT. The IR spectra for 197 and 199 show a strong C=O stretch at $\nu = 1731 \, \& \, 1717 \, \text{cm}^{-1}$, respectively and a broad N-H stretch at $\nu \approx 3376 \, \text{cm}^{-1}$. After oxidation, a residual broad peak remained at $\nu = 3437 \, \text{cm}^{-1}$ for 198, and $\nu = 3617 \, \text{cm}^{-1}$ for 200, and was also observed in both small molecules. This peak commonly observed in IR spectra for pyridazines, $^{95-97}$ can be attributed to known hydrogen bonding interactions between water and pyridazine, $^{98}$ and provides explanation for high percentages of hydrogen and oxygen in elemental analysis for the oxidized polymers. $^1$H NMR of 200 and 198 show the disappearance of the dihydropyridazine ring NH peak, indicating the oxidation proceeded to completion. In 200, a new peak appears at 7.97 ppm and is assigned to the aromatic pyridazine ring proton (Figure 31C). This peak is not observed for 198 as there are no protons on its pyridazine ring. Residual butadiene peaks are not apparent for any of the polymers in $^{13}$C NMR spectra showing the conversion of PBD14 into 197, and its subsequent oxidation to 198 (Figure 31 D-F, respectively). No residual butadiene peaks are also seen in the $^{13}$C spectrum for 197 and the polymers’ peaks match those of their respective monomers 201 – 202 providing evidence that the predicted structures are accurate (see appendix B).
Figure 31: (A) $^1$H NMR PBD12 (B) $^1$H NMR of 199, both NH and C=C-H peaks can be observed at 8-9 ppm and 5.74 ppm, respectively (C) $^1$H NMR of 200 showing the disappearance of the dihydro NH and C=C-H peaks, and a new peak at 7.97 ppm from the pyridazine ring hydrogen. (D) $^{13}$C NMR of PBD14 (E) $^{13}$C NMR of 197 showing no peaks from residual PBD14 (F) $^{13}$C NMR of 198 showing more defined peaks as the oxidized pyridazine ring is now symmetric. CDCl$_3$ used for both proton and carbon NMR.

3.2.3 Thermal Properties

Modification of PBD with DMDT dramatically increased the glass $T_g$s of the resultant polymers from that of the original PBDs. Compared to PBD12 (-41 °C), the $T_g$ of 199 was measured to be 147 °C through DSC, which changed little upon oxidation to 200 (145 °C). The $T_g$ of 197 increased to 125 °C from PBD14 (-100 °C), and increased slightly upon oxidation to 139 °C. The polymers’ thermal stability decreased with
modification, and thermal gravimetric analysis (TGA) showed onset degradation for the dihydropyridazine polymers occurred at 256 °C for 199 and 263 °C for 197 (Figure 32). Oxidation decreased thermal stability even further and onset degradation for 200 to 217 °C, and 188 °C for 198. For each polymer, initial mass losses of ~ 36% provided evidence that decarboxymethylation was the initiator of degradation, and indicates that the methyl ester groups are a thermal weak link on the materials.

**Figure 32:** Thermal degradation of polymers synthesized through DMDT click reactions with PBD14 (left), and PBD12 (right).
3.2.4 Optical and Electrochemical Properties

*Table 2:* Absorption and emission data for dihydropyridazine/pyridazine polymers and small molecules prepared from DMDT click

<table>
<thead>
<tr>
<th>Compounds</th>
<th>$\lambda_{\text{abs}} / \lambda_{\text{ems}}$ (nm)</th>
<th>$\varepsilon$ L mol$^{-1}$ cm$^{-1}$</th>
<th>Stokes shift (nm)</th>
<th>$\Phi_f$</th>
</tr>
</thead>
<tbody>
<tr>
<td>197</td>
<td>335/445</td>
<td>2899.9</td>
<td>110</td>
<td>0.1</td>
</tr>
<tr>
<td>198</td>
<td>318/-</td>
<td>704.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>199</td>
<td>336/451</td>
<td>2031.4</td>
<td>115</td>
<td>0.003</td>
</tr>
<tr>
<td>200</td>
<td>326/-</td>
<td>500.6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>201</td>
<td>364/459</td>
<td>2941.9</td>
<td>95</td>
<td>0.008</td>
</tr>
<tr>
<td>202</td>
<td>300/452</td>
<td>291.2</td>
<td>152</td>
<td>-</td>
</tr>
<tr>
<td>203</td>
<td>328/454</td>
<td>2361.2</td>
<td>126</td>
<td>0.004</td>
</tr>
<tr>
<td>204</td>
<td>319/443</td>
<td>503.7</td>
<td>124</td>
<td>-</td>
</tr>
</tbody>
</table>

$\lambda_{\text{abs}} / \lambda_{\text{ems}}$ measured in CHCl$_3$

$\Phi$ measured in DMF and calculated in comparison to coumarin 151 in ethanol

The dihydropyridazine polymers and their small molecule analogs were found to be fluorescent under UV irradiation, which correlates with previously reported instance of dihydropyridazine fluorescence.$^88$ Both 197 & 198 displayed little to no absorption in the visible region, and appeared as yellow and off-white solids after precipitation. Both dihydropyridazine polymers absorbed in the UV ($\lambda_{\text{max}}$ 335 & 336 respectively), with emission upon long-wave UV excitation producing blue light $\lambda_{\text{max}}$ 445 & 451 nm (*Table 2*). Their small molecule analogs 201 & 203 displayed similar fluorescent properties, although 197 was found to have a much larger quantum yield $\phi_f = 0.1$ than its small molecule analog $\phi_f = 0.003$ (201), potentially resulting from intrachain push-pull effects between dihydropyridazine units.$^{99,100}$ It was very interesting to see quenching of fluorescence upon oxidation to the fully aromatic pyridazine ring for both polymers (Figure 33B) and small molecules, and turns out to be beneficial for the materials’ use as
antioxidants as it provides them with a built-in indicator to monitor the extent of oxidation.

*Figure 33:* Image of dihydropyridazine polymers 197 & 199 and their oxidized form 198 & 200 (left). Quenching of fluorescence is observed in the polymers after oxidation (right).

The electrochemical properties of small molecules 201-204 were investigated to further understand the antioxidant properties of dihydropyridazines 201 & 203, and to better understand the fluorescence quenching observed in the oxidized pyridazines 202 & 204. Anodic potential sweeps of 201 & 203 revealed that both molecules undergo an irreversible 1-electron chemical oxidation with low Ep/2 potentials of 0.61V and 0.81V, respectively (*Figure 34A*). This indicates favorable electron donation for both compounds, and provides evidence that 201 acts as a better antioxidant than 203, donating its electrons at a lower oxidation potential. Cathodic sweeps of oxidized compounds 202 & 204 show 3 reduction peaks for both compounds with Ep/2 of -2.02V, -2.33V, and -2.62V for 202, and -1.81V, -2.33V, and -2.62V for 204 (*Figure 34B*). The
first reduction for both molecules is quasi-reversible with $E_{1/2}$ reduction potentials of -1.97V for 202, and -1.87V for 204, while the second and third reductions are irreversible. The low $E_{1/2}$ potentials for 202 & 204 indicates that both oxidized molecules are better electron acceptors than known fluorescence quenchers quinolone ($E_{1/2} = -2.0V$) and pyridine ($E_{1/2} -2.66V$),\textsuperscript{101,102} and demonstrates that electron transfer interactions are likely involved in the observed quenching for the oxidized pyridazines.

**Figure 34:** (A) Anodic sweep of 201 and 203 showing an irreversible 1-electron oxidation for both dihydropyridazine species. (B) Cathodic sweep of 202 and 204 showing 3 distinct reduction peaks. The first peak is quasi-reversible, but the second and third are irreversible indicating either a geometric or chemical change is occurring upon reduction. Both scans conducted with a sweep rate of 100 mV/s. Counter electrode: platinum wire; reference electrode: Ag/AgNO\textsubscript{3}
3.3 Conclusion

The facile modification of polybutadienes with DMDT resulted in a dramatic transformation of the initial polymers and converted liquid elastomers into solid poly(dimethyl 1,4-dihydropyridazine-3,6-dicarboxylate) thermoplastics with glass transition temperatures ranging from 125-147 °C. High conversion percentages between 89-98% were achieved through reacting equimolar amounts of DMDT and PBD in refluxing THF, allowing near quantitative addition of antioxidant repeat units to a polymer chain. Oxidation with DDQ in THF converted the polymers to their heteroaromatic poly(dimethyl pyridazine-3,6-dicarboxylate) analogs, which became insoluble after oxidation allowing for simple purification. TGA analysis revealed that poly(dimethyl 1,4-dihydropyridazine-3,6-dicarboxylates) are more stable before oxidation and mass loss percentages were used to determine that the methyl ester group creates a thermal weak link on both the reduced and oxidized polymers. Poly(dimethyl 1,4-dihydropyridazine-3,6-dicarboxylates) and small molecule model compounds fluoresce from long-wave UV excitation, emitting blue light (λ_{max} = 445 - 451 nm). This fluorescence was observed to quench after oxidation, and cyclic voltammetry was used to indicate fluorescence quenching involves electron transfer interactions. Low oxidation potentials for dimethyl 1,4-dihydropyridazine-3,6-dicarboxylate small molecules provided further evidence for their antioxidant properties, and quenching of fluorescence provides a simple and powerful visual tool for monitoring extent of oxidation for these antioxidant-rich materials.
3.4 Experimental Section

dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (DMDT)

To a 250 mL, 3-neck, 24/40 round-bottom flask was added dimethyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (2.700 g, 13.49 mmol), dichloromethane (150 mL), and a magnetic stir bar. A separate 250 mL, 3-neck, 24/40 round-bottom flask was prepared with conc. HCl (16.90 mL), a magnetic stir bar, and then cooled to 0 °C in an ice bath. An addition funnel containing aqueous sodium nitrite (11.2 g, 162 mmol) dissolved in DI H₂O (27 mL) was attached to the HCl flask, and the aqueous sodium nitrite was added dropwise to the cooled HCl and generated a dark brown NOₓ gas. The gas was fed into the reaction solution through a 1.5 cm glass tube under a steady stream of dry nitrogen, and the solution began to turn dark red. After 3 hours, an additional 16 mL of HCl was added to the acid flask, and an additional amount of aqueous sodium nitrite (11.2 g, 162 mmol) in DI H₂O (27 mL) was added dropwise to the acid, while continuing to bubble the brown NOₓ gas into the reaction flask. After 3 hours, the reaction flask was detached from the gas line, and the DCM and residual gases were removed under dynamic vacuum. The resulting dark red crystals were collected with vacuum filtration and rinsed with -5 °C methanol until the filtrate was a light red color, then dried under vacuum to yield DMDT as a dark red crystalline solid (2.483 g, 93%). mp: 174-176 °C, (173-175 °C)1; ¹H NMR (400 MHz, Chloroform-d, δ): 4.22 (s, 6H); ¹³C NMR (101 MHz, CDCl₃, δ): 160.51, 159.26, 54.78.
poly(dimethylene 4,5-dimethyl-1,4-dihydropyridazine-3,6-dicarboxylate) (197)

To a 100 mL 1-neck round-bottom flask was added poly-1,4-butadiene (0.270 g, 5.00 mmol), DMDT (1.090 g, 5.50 mmol), THF (25 mL) and a magnetic stir bar. The dark red solution was attached to a condenser, flushed with nitrogen, placed under positive nitrogen pressure, and heated to 66 °C and stir for 24 hours. After 24 hours, the dark orange solution was cooled to room temperature 23 °C, concentrated to 5 mL under vacuum, and precipitated into 50 mL diethyl ether. The precipitate was collected with vacuum filtration and dried under high vacuum for 72 hours, yielding a light-yellow powder (1.016 g, 89%). \(^{1}\)H NMR (499 MHz, Chloroform-\(d\), \(\delta\)): 8.52 (s, 1H), 5.27 (s, 0.14H), 3.82 (s, 6H), 3.38 (m, 1H), 3.04 – 0.79 (m, 3H); \(^{13}\)C NMR (126 MHz, CDCl\(_{3}\), \(\delta\)): 164.74, 162.02, 131.46, 125.57, 52.61, 37.18, 30.54, 28.22, 26.95; IR (KBr): \(\nu = 3375.70\) ((br, \(\nu_s\)(NH)), 3000, 2953, 2854, 1731 (s, \(\nu_s\)(C=O)), 1708, 1640, 1592, 1439, 1334, 1257, 1198, 1161, 1106, 9567, 875, 818, 777, 735, 636, 556, 502, 425 cm\(^{-1}\); GPC (PS Stds, DMF): Mn, Mw, PDI = 12479, 28815 Da, 2.14; Anal. calcd for C\(_{4062}\)H\(_{4884}\)N\(_{806}\)O\(_{1612}\): C 53.73, H 5.42, N 12.40, O 28.44, found: C 53.51, H 5.78, N 12.57, O 28.14; \(T_g = 125\) °C.

poly(dimethylene 4,5-dimethylpyridazine-3,6-dicarboxylate) (198)

To a 25 mL 1-neck 14/20 round-bottom flask was added polyDHP (0.448 g, 2.14 mmol), 5 mL of THF, and a magnetic stir bar. The yellow solution was stirred at ambient temperature (23 °C) and DDQ (0.522 g, 2.30 mmol) was added, turning the solution a dark black color. After 24 hours the light brown solution was triturated with methanol (10 mL) then poured into a separate flask containing methanol (90 mL) and stirred for 5 minutes. The precipitate was collected with vacuum filtration, rinsed with methanol and
dried under high vacuum 72 hours to yield poly(DP) as a cream colored solid (0.435 g, 98%). $^1$H NMR (499 MHz, CDCl$_3$, $\delta$): 5.35 (s, 0.04H), 4.24 – 3.41 (m, 6H), 3.07 (s, 3.5H), 2.62 – 0.98 (m, 1.5H); $^{13}$C NMR (126 MHz, CDCl$_3$, $\delta$): 165.54, 153.99, 139.08, 53.68, 27.76; IR (KBr): $\nu$ = 3436.76, 3007.35, 2956.33, 2855.43, 1732.22 (s, $\nu_s$ (C=O)), 1638, 1536, 1441, 1382, 1269, 1198, 1146, 1108, 1036, 962, 822, 781, 755, 649 cm$^{-1}$; GPC (PS Stds, DMF): Mn, Mw, PDI = 7915, 10507 Da, 1.34; Anal. calcd for C$_{4062}$H$_{4078}$N$_{806}$O$_{1612}$: C 54.22, H 4.57, N 12.51, O 28.70; found: C 53.69, H 5.13, N 12.46, O 28.72; $T_g$ = 139 °C.

dimethyl 4-vinyl-1,4-dihydropyridazine-3,6-dicarboxylate (199)
To a 100 mL 1-neck round-bottom flask was added polybutadiene (0.270 g, 5.00 mmol), DMDT (1.090 g, 5.50 mmol), THF (25 mL) and a magnetic stir bar. The dark red solution was attached to a condenser, flushed with nitrogen, placed under positive nitrogen pressure, and heated to 66 °C and stir for 24 hours. After 24 hours, the dark orange solution was cooled to room temperature 23 °C, concentrated to 5 mL under vacuum, and precipitated into 50 mL methanol. The precipitate was collected with vacuum filtration and dried under high vacuum for 72 hours, yielding a white powder (0.992 g, 87%). $^1$H NMR (499 MHz, CDCl$_3$, $\delta$): 9.46 – 7.60 (m, 1H), 5.39 (s, 1H), 3.85 (s, 6H), 1.49 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$, $\delta$): 164.79, 161.49, 133.83, 130.26, 107.97, 52.55, 34.04; IR (KBr): $\nu$ = 3377.08 (br, $\nu_s$(NH)), 3002, 2954, 2853, 1717 (s, $\nu_s$(C=O)), 1591, 1440, 1347, 1286, 1197, 1165, 1118, 1006, 957, 862, 817, 758, 736, 686, 613, 565, 512, 459 cm$^{-1}$; GPC (PS Stds, DMF): Mn, Mw, PDI = 8673, 10429 Da, 1.20;

120
Anal. calcd for C₈₂₀H₉₈₄N₁₆₄O₃₂₈: C 53.57, H 5.39, N 12.49, O 28.54, found: C 52.80, H 5.82, N 12.00, O 29.38; T₉ = 147 °C.

**poly(dimethyl 4-vinylpyridazine-3,6-dicarboxylate) (200)**

To a 25 mL 1-neck 14/20 round-bottom flask was added PolyVHP (0.448 g, 2.14 mmol), 5 mL of THF, and a magnetic stir bar. The yellow solution was stirred at ambient temperature (23 °C) and DDQ (0.522 g, 2.30 mmol) was added, turning the solution a dark black color. After 24 hours the solution had turned an opaque brown color and a light colored precipitate had formed. The solution was triturated with methanol (10 mL), and dark brown viscous solid precipitate formed on the bottom of the flask. The solvent was removed under vacuum, and the solid was dissolved in DCM then precipitated into THF. The precipitate was collected with vacuum filtration, rinsed with THF and methanol then dried under high vacuum for 72 hours to yield PolyVP as a white solid (0.381 g, 86 %). ¹H NMR (499 MHz, Chloroform-d, δ): 7.97 (s, 1H), 4.70 (s, 0.36H), 3.88 (m, 6H), 1.81 (m, 3H);¹³C NMR (126 MHz, CDCl₃, δ): 163.91, 151.99, 144.23, 126.83, 53.68, 34.54; IR (KBr): ν = 3617, 3445, 3008, 2956, 2859, 1724, 1638, 1578, 1530, 1387, 1258, 1197, 1140, 997, 956, 882, 824, 778, 709, 610 cm⁻¹; GPC (PS Stds, DMF): Mn, Mw, PDI = 10687, 12021 Da, 1.12; Anal. calcd for C₈₂₀H₈₂₀N₁₆₄O₃₂₈: C 54.05, H 4.54, N 12.61, O 28.80, found: C 55.69, H 5.40, N 12.79, O 26.12; T₉ = 145 °C.

**Dimethyl 2,4a,5,6,7,8-hexahydrophthalazine-1,4-dicarboxylate (201)**

To a 10 mL, 1-neck, 24/40 round-bottom flask was added DMDT (0.100 g, 0.505 mmol), DCM (2 mL), and a magnetic stir bar. To the transparent dark red stirring solution was
added cyclohexene (0.100 mL, 0.987 mmol) and slow gas generation was observed. The reaction was stirred for 18 minutes, while over the course of time the solution had become a pale transparent yellow color. The solution was transferred to a separatory funnel, then extracted with DI water (1 x 10 mL), brine (1 x 10 mL) and dried over anhydrous sodium sulfate. The dried solution was filtered through a cotton plug and the solvent removed by rotary evaporation to yield a pale yellow solid (0.126 g, 99% yield).

\[
\text{mp (MeOH): 105 -106 °C, (107 °C); } ^1\text{H NMR (400 MHz, CDCl}_3, \delta): 7.86 \text{ (s, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.63 - 3.56 (m, 1H), 3.50 (ddd, J = 11.3, 3.4, 0.9 Hz, 1H), 2.11 - 2.01 (m, 1H), 2.01 - 1.92 (m, 1H), 1.91 - 1.83 (m, 2H), 1.81 - 1.45 (m, 4H).}^{13}\text{C NMR (101 MHz, CDCl}_3, \delta): 165.25, 162.59, 131.04, 130.65, 119.72, 52.34, 52.27, 37.32, 34.22, 30.27, 29.67, 26.77. \text{ IR (KBr): } \nu = 3359, 3192, 3071, 3019, 3006, 2952, 2937, 2924, 2854, 1718, 1703, 1659, 1603, 1476, 1442, 1411, 1391, 1343, 1318, 1295, 1276, 1261, 1221, 1195, 1180, 1158, 1110, 1080, 1055, 1032, 1019, 998, 985, 912, 889, 838, 820, 806, 782, 767, 717, 644, 565, 484, 430 \text{ cm}^{-1}.
\]

**Dimethyl 5,6,7,8-tetrahydrophthalazine-1,4-dicarboxylate (202)**

To a 10 mL, 1-neck, 24/40 round-bottom flask was added DMDT (0.100 g, 0.505 mmol), DCM (2 mL), and a magnetic stir bar. To the transparent dark red stirring solution was added cyclohexene (0.100 mL, 0.987 mmol) and slow gas generation was observed. The reaction was stirred for 20 minutes, while over the course of time the solution had become a pale transparent yellow color. DDQ (0.123 g, 0.542 mmol) was added to the reaction solution and a cream-colored precipitate formed almost immediately. The slurry was stirred for an additional 30 min, and then the solid was removed by filtering through
a cotton plug. The solution was then washed with saturated aqueous sodium bicarbonate solution (3 x 10 mL) DI water (1 x10 mL), brine (1 x 10 mL) and then dried over anhydrous sodium sulfate. After drying, the solution was filtered through a cotton plug, and the solvent removed through rotary evaporation to yield a light yellow/white solid (0.126 g, 99% yield). mp (MeOH): 129 – 131 °C, (131-132 °C). $^1$H NMR (499 MHz, CDCl$_3$, δ): 4.05 (s, 6H), 3.86 (dd, $J = 13.1$, 0.8 Hz, 1H), 3.00 (ddd, $J = 6.7$, 4.2, 2.6 Hz, 4H), 1.90 – 1.84 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$, δ): 165.36, 153.07, 138.70, 53.26, 25.73, 21.10; IR (KBr): ν = 3438, 3344, 3038, 2997, 2950, 2882, 2850, 1731, 1596, 1566, 1526, 1444, 1411, 1392, 1368, 1340, 1307, 1282, 1262, 1223 1197, 1162, 1102, 1032, 997, 985, 949, 911, 901, 877, 842, 820, 800, 779, 755, 732, 711, 692, 626, 574, 511, 486 cm$^{-1}$.

**Dimethyl 4-butyl-1,4-dihydropyridazine-3,6-dicarboxylate (203)**

To a 10 mL, 1-neck, 24/40 round-bottom flask was added dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (0.100 g, 0.505 mmol), DCM (2 mL), and a magnetic stir bar. To the transparent dark red stirring solution was added 1-hexene (0.100 mL, 0.806 mmol) and rapid gas generation was observed. The reaction was stirred for 7 minutes, while over the course of time the solution had become a pale transparent yellow color. The solution was transferred to a separatory funnel, then extracted with DI water (1 x 10 mL), brine (1 x 10 mL) and dried over anhydrous sodium sulfate. The dried solution was filtered through a cotton plug and the solvent removed by rotary evaporation to yield a yellow viscous liquid (0.123 g, 97% yield). $^1$H NMR (400 MHz, CDCl$_3$, δ): 8.22 (s, 1H), 5.93 (dd, $J = 6.3$, 2.4 Hz, 1H), 3.85 (d, $J = 3.0$ Hz, 6H), 3.64 (ddd, $J = 7.7$, 6.3, 5.2 Hz, 1H), 1.51 –
1.37 (m, 2H), 1.28 (dd, \(J = 7.5, 3.8\) Hz, 4H), 0.93 – 0.81 (m, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\), \(\delta\)): 164.95, 161.90, 134.33, 129.47, 110.78, 52.68, 52.65, 33.55, 31.71, 27.29, 22.68, 14.05; IR (KBr): \(\nu = 3360, 2957, 2933, 2873, 2102, 1731, 1585, 1532, 1440, 1390, 1342, 1268, 1198, 1131, 993, 960, 913, 824, 765, 732, 447\) cm\(^{-1}\).

**Dimethyl 4-butylpyridazine-3,6-dicarboxylate (204)**

To a 10 mL, 1-neck, 24/40 round-bottom flask was added dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (0.100 g, 0.505 mmol), DCM (2 mL), and a magnetic stir bar. To the transparent dark red stirring solution was added 1-hexene (0.100 mL, 0.806 mmol) and rapid gas generation was observed. The reaction was stirred for 10 minutes, while over the course of time the solution had become a pale transparent yellow color. DDQ (0.123 g, 0.542 mmol) was added to the reaction solution and a cream-colored precipitate formed almost immediately. The slurry was stirred for an additional 15 min, and then the solid was removed by filtering through a cotton plug. The solution was then washed with saturated aqueous sodium bicarbonate solution (3 x 10 mL) DI water (1 x10 mL), brine (1 x 10 mL) and then dried over anhydrous sodium sulfate. After drying, the solution was filtered through a cotton plug, and the solvent removed through rotary evaporation to yield a peach colored liquid that over two weeks crystallized to a yellow semi-crystalline liquid (0.126 g, 99% yield). \(^1\)H NMR (499 MHz, CDCl\(_3\), \(\delta\)): 8.11 (s, 1H), 4.09 (s, 3H), 4.07 (s, 3H), 2.94 – 2.90 (m, 2H), 1.69 – 1.61 (m, 2H), 1.46 – 1.37 (m, 2H), 0.96 (t, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\), \(\delta\)): 165.18, 164.37, 154.31, 151.67, 143.65, 128.98, 53.65, 53.43, 32.04, 31.69, 22.63, 13.88; IR (KBr): \(\nu = 3638, 3446, 3001, 2957,\)
2934, 2873, 1731, 1631, 1581, 1531, 1441, 1390, 1264, 1204, 1136, 1086, 988, 959, 913, 870, 824, 776, 746, 733, 712, 616, 448 cm$^{-1}$.

This space intentionally left blank
Chapter 4

Bleaching of copolymers containing photodegradable pendant chloroalkoxy tetrazines groups: a potential approach towards preparing low-cost photoresists and optical waveguides

4.1 Introduction

The photodecomposition of s-tetrazines has been widely researched since the initial studies on their UV and visible light induced degradation,\textsuperscript{103,104} but its application in polymer chemistry has yet to be proposed. Tetrazine photodegradation results when a photon is absorbed through either a $\pi-\pi^*$ transition or $n-\pi^*$ transition and decays to the zero-point singlet state, if a second photon is absorbed before relaxation of the first, an undiscovered series of intermediates will form leading to thermal decay of the tetrazine core into N$_2$ and two equivalents of RCN.\textsuperscript{105–108} Photodegradable polymers find utility as materials in photoresists\textsuperscript{109,110} and optical waveguides,\textsuperscript{111–114} providing the ability for patterning through light-induced degradation of designated regions on a polymer film, followed by removal of the exposed region with a developing solution.

To date, modification of synthetic polymers with tetrazine moieties has been mostly focused on installing an end-chain handle for inverse electron demand Diels Alder functionalization, polymer chain extension, and crosslinking.\textsuperscript{52,53,62} Aside from nanoparticle surface functionalization,\textsuperscript{46,115,41,116} linear polymers containing pendant tetrazine groups have been all but overlooked in the literature,\textsuperscript{117} and no reporting on
their photodegradation has been mentioned. Herein we report the synthesis of poly(methyl methacrylate-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate)), and demonstrate the ability of its tetrazine ring to photodegrade when exposed to UV and ambient light. Combined with its demonstrated ability to be solvent cast into films and thermally crosslinked, this material provides a simple method to modify common polymers for use in photoresists and optical waveguides.

Scheme 3: (A) Synthesis of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (206) from reaction of DCT with 2-hydroxyethyl methacrylate (HEMA). No poly(2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) homopolymer (207) resulted from attempts at radical polymerization with AIBN, presumably due to radical inhibition by the tetrazine species. (B) Synthesis of poly(methyl methacrylate-co-2-hydroxyethyl methacrylate) (209) from AIBN initiated polymerization of methyl methacrylate (MMA) and HEMA. Post-modification of 207 with DCT produced poly(methyl methacrylate-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) in near quantitative conversions.
4.2 Results & Discussion

4.2.1 Synthesis of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) and the development of a pendant tetrazine copolymer.

Initially an effort to prepare poly(2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) homopolymer (207) was attempted through an AIBN initiated radical polymerization of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (206). To that effect, 205 was synthesized by reacting DCT with 2-hydroxyethyl methacrylate in refluxing DCM and in the presence of 2,4,6-collidine, a method adapted from previously reported syntheses of alkoxychloro tetrazines.\textsuperscript{20} Altering the conditions from stirring at room temperature to refluxing in DCM resulted in increased yields and better isolation for 205, a dark red viscous liquid obtained in 91% yield. After isolation, attempts were conducted to radically polymerize the monomer in 70 °C toluene using 1-5 mol% of AIBN as initiator. All attempts at polymerization failed to produce either polymer or even oligomer, and it was determined that the tetrazine was acting as a radical inhibitor,\textsuperscript{118,119} preventing chain growth from occurring either through chain transfer at carbon-chlorine bond or by the ring itself.

As a work around to forming 206, post-modification of poly(2-hydroxyethyl methacrylate) with DCT was attempted in DMSO, but resulted in an intractable red solid predicted to be due to crosslinking between unmodified hydroxyl groups and modified pendant chloroalkoxy tetrazine groups. It was determined that a copolymer consisting of HEMA and MMA repeat units would allow for functionilization of the HEMA groups with DCT, while having MMA dispersed along the chain would decrease the amount of crosslinking occurring during post-modification and increase solubility of the final
polymer (207). Multiple efforts provided an indicator for the extent of HEMA (≤ 10%) which could be incorporated into the copolymer, and allow for DCT post-modification without crosslinking. A HEMA/MMA copolymer containing 8% HEMA and 92% MMA 207 was synthesized through radical polymerization with AIBN, and post-modified with DCT in refluxing DCM to yield the desired product (208). Modification was determined to be near quantitative based on NMR integration and molecular weight gain, and the resulting light pink polymer was found to be insoluble in H₂O, MeOH, EtOH, hexanes, soluble in THF, DMF, and halogenated solvents, and it could also be cast into transparent dark red films with relative ease from chloroform.

4.2.2 Structure of copolymers and 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate)

The 1H NMR of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) (205) (Figure 35A) shows two distinct peaks at δ 4.64 and 4.92 ppm which are assigned to the methylene protons in 205’s ethyl chain, and a singlet at 1.94 ppm assigned to the lone methyl group protons of the methacrylate. Analysis of 207 shows a strong methyl peak at 3.60 ppm from the MMA repeat unit’s methyl ester (Figure 35B). The two methylenes in its HEMA ethyl chain are seen further upfield at δ 3.85 and 4.12 ppm, as the electron withdrawing tetrazine group is not present to deshield these protons. Integration of the methylene peaks in relation to the methyl ester peak provides evidence for 8% HEMA functionality in the copolymer, and agrees well with elemental analysis results. Size exclusion chromatography of 207 shows an M_n of ~42 kDa and M_w of ~65 kDa with a PDI of 1.52. After modification with DCT, the methylene peaks are observed to shift downfield to 4.49 and 4.90 ppm (Figure 35C), aligning well with the methylene peaks in
the model compound. Integration of these peaks in relation to the methyl ester singlet at 3.59 as well as the complete disappearance of the HEMA methylene peaks in Figure 35C shows that the modification was near quantitative. This is supported by SEC, showing modification did little to change the M\textsubscript{n} of the copolymer (41 kDa), but the M\textsubscript{w} of the copolymer (73 kDa) increased accordingly with its predicted conversion percentage.

\textsuperscript{13}C NMR of 205 shows the two methylene carbons at 62 and 68 ppm, and three peaks further downfield at 164, 166, and 167 ppm assigned to its carbonyl carbon, and the two tetrazine ring carbons (Figure 35D). In copolymer 206, the methylene peaks on the HEMA units are weaker due to only being present in 7\% concentration, but can be observed just slightly upfield to those of the monomer’s methylenes at 61 and 67 ppm (Figure 35E). A methyl peak from the methyl ester on the MMA repeat units is observed at 52 ppm and the carbonyl peaks are further downfield at 177-178 ppm as the alkene’s conjugative effect is no longer present in the polymer. The \textsuperscript{13}C spectrum of tetrazine modified polymer 207 shows two distinct peaks appear from the carbons on the tetrazine rings at 165 and 167 ppm, with little effect on the rest of the carbons in the polymer (Figure 35F). It is interesting to see that the post-modification had an effect on the stereoconfiguration of the polymer backbone, as the upfield alkyl peaks are remarkably cleaner in both the proton and carbon spectra (Figures 35C, 35F).
Figure 35: $^1$H NMR of (A) 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) (205), (B) poly(MMA-co-HEMA) (207), and (C) poly(MMA-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (208). $^{13}$C NMR of (D) 205, (E), 207, and (F) 208

4.2.3 Thermal and photochemical properties

Table 3: Thermal properties of 207 & 208, and photochemical properties of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (205) and 208

<table>
<thead>
<tr>
<th>Compounds</th>
<th>$M_n$ ($M_w$ (Da))</th>
<th>$T_g$ (°C)</th>
<th>$\lambda_{abs}$ (nm)</th>
<th>$\varepsilon$ (L mol$^{-1}$ cm$^{-1}$)</th>
<th>$\lambda_{ems}$ (nm)</th>
<th>Stokes shift (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>205</td>
<td>-</td>
<td>-</td>
<td>329 520</td>
<td>2960.5 689.1</td>
<td>557 557</td>
<td>228 35</td>
</tr>
<tr>
<td>207</td>
<td>42881, 65306</td>
<td>113</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>208</td>
<td>41097, 73965</td>
<td>122</td>
<td>329 518</td>
<td>-</td>
<td>557 557</td>
<td>228 39</td>
</tr>
</tbody>
</table>
The thermal properties for 207 and 208 were collected using both TGA and DSC. No distinct change in onset degradation temperatures were observed for either copolymer, with both occurring at 211 °C, although thermal degradation appears slower for 208 than 207 after onset (see appendix C). DSC analyses revealed a slight increase in the glass transition temperature upon modification, with 208 having a $T_g$ of 122 °C, while the unmodified copolymer 207 had a $T_g$ of 113 °C (Table 3). An interesting aspect of the tetrazine modified copolymer, 208, was discovered when exploring the possibility of melt processing at 150 °C. Samples of 208 with 2% residual unreacted HEMA repeat units would crosslink with pendant tetrazine units during melt pressing (Figure 36A), forming an intractable red solid disc. Compared to tetrazine modified copolymers before heat treating which can be reversibly dissolved in CHCl₃ and solvent cast into films (Figures 36B, 36C), the heat treated polymer became a thermoset and would only swell in CHCl₃ due to the low cross-link density (Figures 36D, 36E).
Figure 36: (A) Tuning the extent of post-functionalization with tetrazine provides polymers that display both thermoplastic and thermoset properties. (B & C) A solvent cast film can be readily dissolved in chloroform. (D & E) Melt processing of copolymers with residual hydroxyl groups results in crosslinking, and swelling is observed when the film is exposed to chloroform.

Table 3 shows the photochemical properties for the tetrazine modified small molecule (205), and copolymer (208). Films prepared from 208 were dark red in color (Figure 37A) owing to the tetrazine n-σ* transition ($\lambda_{\text{max}} = 519$ nm), and would fluoresce
orange light ($\lambda_{\text{max}} = 557$ nm) upon excitation with UV ($\lambda = 329$ nm) (Figure 37B). The polymers appeared opaque when fluorescing, and were demonstrated to act as UV light filters (Figure 37B). Intriguingly, photobleaching of 207 was observed with extended UV excitation as well as extended exposure to ambient light (Figure 36C). Comparison of IR spectra for 207, and 208 before and after bleaching indicates the complete degradation of the tetrazine ring, and reversion back to unmodified 207 (see appendix C).

Figure 37: (A) An image of a film of 207 cast from CHCl₃ (B) Two films sandwiched above a UV light source, a black halo on the top film shows that the polymer underneath it is absorbing the incoming light (C) A film cast from THF that has been exposed to ambient light for 2 years, followed by further bleaching with 365 nm light for 7 days

Refractive index measurements were conducted on samples of the same film before and after photobleaching and the results are displayed in Table 4. After 48 hours of exposure to UV light ($\lambda_{\text{max}} = 365$ nm), a distinct refractive index change was observed in the bleached film with a $\Delta$ near 0.01 observed at transmission wavelengths 633, 816, 1305, and 1554 nm. These results indicate that photobleachable polymers functionalized
with tetrazine or containing tetrazine additives may be a useful addition to current materials used in the design optical waveguides.

**Table 4: Refractive index change of poly(methyl methacrylate-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate)**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>nm</th>
<th>TE(_{\text{normal}})</th>
<th>TE(_{\text{bleached}})</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>207</td>
<td>633</td>
<td>1.504</td>
<td>1.493</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>816</td>
<td>1.498</td>
<td>1.489</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>1305</td>
<td>1.492</td>
<td>1.484</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>1554</td>
<td>1.491</td>
<td>1.483</td>
<td>0.008</td>
</tr>
</tbody>
</table>

**4.3 Conclusion**

A new tetrazine-functionalized monomer, 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate was synthesized and demonstrated to be a radical inhibitor in AIBN initiated reactions. Poly(methyl methacrylate-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) (207) was synthesized through the facile post-modification of poly(MMA-co-HEMA) with DCT. The copolymer exhibits similar optical properties to chloroalkoxy tetrazine, having a deep red color from an n-\(\pi^*\) excitation, and orange fluorescence from \(\pi-\pi^*\) excitation. The addition of tetrazine to the HEMA units of 207 increases the T\(_g\) of the copolymer slightly, and provides an anchor for nucleophilic crosslinking. The radical inhibiting properties and strong UV absorbance of the attached tetrazine provide the polymer with protection from both radical oxidation and UV-degradation. Photobleaching of the tetrazine moiety occurs with extending excitation from either UV or ambient light, and bleaching results in a change in the refractive index for the copolymer. The change in refractive index upon bleaching may indicate potential applications in optical waveguide materials. Combined with the ability of the materials to
crosslink under heat treating, this chemistry also has the potential to be used in photoresists or other thermoset materials/adhesives which can be broken down to smaller organics soluble molecules with extended exposure to light.

4.4 Experimental Section

2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (205)

To a 50 mL, 1-neck, 24/40, round-bottom flask was added 2-hydroxyethyl methacrylate (0.500 mL, 4.11 mmol), 3,6-dichloro-1,2,4,5-tetrazine (0.758 g, 5.02 mmol), DCM (25 mL), and a magnetic stir bar. The solution was heated to reflux and 2,4,6-collidine (0.575 mL, 43.51 mmol) was added through the condenser, which was subsequently rinsed with dichloromethane (2 mL). During the addition of 2,4,6-collidine, the solution change from a transparent orange color to a dark reddish purple color. After 1 hr, the reaction was removed from heat and the opaque dark purple solution was concentrated under dynamic vacuum, then purified on a silica column (DCM, 2% MeOH). The solvent was removed under dynamic vacuum, and then further dried under high vacuum for 120 hours, yielding a dark red viscous liquid (0.917 g 91%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 6.12 (dq, $J = 1.4$, 1.0 Hz, 1H), 5.61 (p, $J = 1.6$ Hz, 1H), 4.99 – 4.87 (m, 2H), 4.69 – 4.57 (m, 2H), 1.94 (dd, $J = 1.6$, 1.0 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 167.12, 166.69, 164.83, 135.76, 126.66, 68.36, 61.82, 18.36; IR (KBr): $\nu$ = 2959, 2929, 1720 (s, C=O), 1637, 1486, 1447, 1380, 1349, 1316, 1295, 1241, 1197, 1165, 1121, 1035, 930, 883, 850, 815, 802, 724, 693, 652, 555 cm$^{-1}$. 
Failed polymerization of poly(2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) homopolymer (206)

To a 5 mL, 1-neck, 14/20, round-bottom flask was added 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate \((205)\) (0.500 g, 2.04 mmol), AIBN (0.017 g, 0.102 mmol), toluene (2 mL), and a magnetic stir bar. The dark red solution was degassed with nitrogen for 1 hr, and then placed under positive pressure with nitrogen. The solution was heated to 70 °C using a sand bath for 17 hours, during which time no viscosity change was observed. After 17 hours, the solution was removed from heated and concentrated under dynamic vacuum. NMR indicated showed no indication of polymer/oligomer formation.

poly(methyl methacrylate-co-2-hydroxyethyl methacrylate) (207)

To a 10 mL 1-neck 14/20 round-bottom flask was added 2-hydroxyethyl methacrylate (0.200g, 1.54 mmol), methyl methacrylate (2.000 g, 20.00 mmol), AIBN (0.035 mg, 0.21 mmol), toluene (2 mL), and a magnetic stir bar. The transparent colorless solution was degassed with nitrogen for 30 minutes, and then heated to 65 °C for 3 hours. The colorless high viscosity reaction solution was quenched by removing the flask from heat and exposing to air. The copolymer was precipitated first into methanol, forming a sludge, collected, dried, and then precipitated into hexanes where a white powdery precipitate formed. The solid was collected via vacuum filtration, and dried under high vac. to yield a white powder (1.145 g, 52%) \(^1H\) NMR (499 MHz, CDCl\(_3\), \(\delta\)): 4.12 (s, 0.17H), 3.85 (s, 0.17H), 3.59 (s, 3H), 2.82 (d, \(J = 103.6\) Hz, 0.07H), 2.23 – 0.61 (m, 7H); \(^13\)C NMR (125 MHz, CDCl\(_3\), \(\delta\)): 178.16, 177.86, 176.99, 67.07, 60.76, 54.62, 54.34, 51.96, 45.24, 45.06, 44.85, 44.72, 36.24, 34.83, 34.68, 31.75, 29.23, 25.45, 22.82, 20.87, 18.93, 16.69, 14.29, 11.61; IR (KBr): \(\nu = 3538\) (br, O-H), 3445 (br, O-H), 2997, 2952,
2845, 1731 (s, C=O), 1486, 1389, 1450, 1244, 1194, 1149, 1063, 1022, 989, 966, 914, 842, 810, 751, 482 cm⁻¹; GPC (PS stds, THF): Mn, Mw, PDI = 42881, 65306 Da, 1.52. Anal. calcd. for C₃₂₄H₅₂₀O₁₂₀: C 59.63, H 8.03, O 32.35; found: C 58.63, H 8.80, O 32.35 by difference TGA onset degradation (°C) 211; Tₜᵣᵢₜ = 113 °C.

*poly(methyl methacrylate-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate (208)*

To a 25 mL, 1-neck, 14/20, round-bottom flask was added 207 (0.750 g, 0.58 mmol 2-hydroxyethyl methacrylate functionality), 3,6-dichloro-1,2,4,5-tetrazine (0.150 g, 0.99 mmol), dichloromethane (15 mL), and a magnetic stir bar. The transparent orange solution was heated to reflux and 2,4,6-trimethylpyridine (0.132 mL, 0.10 mmol) was added to the flask. The solution change from orange to purple, and then settled as a transparent dark red color. The reaction was refluxed for 13 hours, during which time it had turned a dark purple color. The reaction was removed from heat, concentrated under dynamic vacuum, and precipitated into methanol. The pink precipitate was collected via vacuum filtration and rinsed with excess methanol until the filtrate became colorless. The polymer was dried under high vac. to yield a light pink powder (0.804 g, 99% yield) ¹H NMR (499 MHz, CDCl₃, δ): 4.90 (s, 0.17H), 4.49 (s, 0.17H), 3.59 (s, 3H), 2.10 – 1.69 (m, 2H), 1.50 – 1.34 (m, 0.26H), 1.28 – 1.16 (m, 0.15H), 1.02 (s, 1H), 0.92 – 0.70 (m, 2H); ¹³C NMR (125 MHz, CDCl₃, δ): 178.12, 177.82, 177.67, 177.12, 177.00, 166.58, 164.77, 67.78, 61.77, 54.53, 54.34, 52.73, 51.93, 45.03, 44.68, 19.12, 18.88, 16.63; IR (KBr): 3550, 3438 (w, O-H), 2996, 2951, 2842, 1731 (s, C=O), 1486, 1449, 1384, 1344, 1270, 1243, 1195, 1149, 1064, 989, 966, 931, 842, 827, 810, 751, 557, 480 cm⁻¹; GPC
(PS stds, THF): Mn, Mw, PDI = 41097, 73965 Da, PDI 1.80; Anal. calcd for 
C$_{3320}$H$_{5160}$Cl$_{40}$ N$_{160}$ O$_{1320}$: C 57.08, H 7.45, Cl 2.03, N 2.31, 30.23; TGA onset 
degradation (°C) 211; T$_g$ = 122 °C.

This space intentionally left blank
Chapter 5

Conclusions and future work

5.1 Conclusion

This body of work has demonstrated that there are still many different possibilities for exploiting the reactivity of tetrazines in polymer synthesis and modification. Previous research had focused on the utility of IEDDA reactions for attaching important functionalities to polymers, chain extension, crosslinking in gel formation, and interfacial polymerization. We can now include tetrazine’s use as a chemical blowing agent to that list, as chapter 2 has established that the nitrogen released from tetrazine IEDDA reactions can be used effectively to foam liquid dienophile-rich polymers. The foaming of PBD with DCT resulted in the generation of a new class of butadiene-dihydropyridazine copolymer, and represented the first reported instance where the dihydropyridazine moiety was the end-goal product, not just a byproduct of a reaction meant to install additional functionalities. The dihydropyridazine ring added antioxidant properties to the foams, and their oxidation lead to a fluorescence change from yellow to white, providing a method to monitor the extent of oxidation.

To demonstrate the antioxidant properties of dihydropyridazines, a new method was developed for providing fast qualitative comparisons on the antioxidant properties of small molecules. Monitoring the delay in gelation times of a styrene/divinyl benzene radical polymerization in the presence of antioxidant provided a visual indicator of
radical inhibition, in effect their ability to function as an antioxidant. When compared to a controlled gelation run with no antioxidant, 3,6-dichloro-4-phenyl-1,4-dihydropyridazine was demonstrated to be 4.5x more effective at radical inhibition than commercial antioxidant BHT. An additional dihydropyridazine, dimethyl 4-phenyl-1,4-dihydropyridazine-3,6-dicarboxylate, was also tested using this method, and shown to be nearly 55x more effective at radical inhibition than BHT.

Solution based studies revealed that the dihydro-dichloropyridazine unit was too reactive to achieve complete modification of PBD with DCT, and only a maximum of ~50% conversion was achieved following in-situ oxidation with DMD. Oxidation was required for isolation, as the dihydro-dichloropyridazines were observed to crosslink upon precipitation through nucleophilic substitution between their amine and imidoyl chloride functional groups. This established that DCT was not an ideal tetrazine species for developing antioxidant-rich linear polymers as it was all but impossible to isolate a fully converted dihydropyridazine polymer through solution based chemistry. With this final result and the observation that Dimethyl 4-phenyl-1,4-dihydropyridazine-3,6-dicarboxylate performed better as an antioxidant than 3,6-dichloro-4-phenyl-1,4-dihydropyridazine, it was determined that reacting DMDT with PBD to synthesize solution-based linear antioxidant-rich polymers was worth pursuing.

Chapter 3 followed up on the results from the previous chapter, with the synthesis of two dimethyl 1,4-dihydropyridazine-3,6-dicarboxylate polymers through solution-based IEDDA reactions between DMDT and either PBD14 or PBD12. High conversions (89% & 98%) were obtained using equimolar concentrations of DMDT and PBD14 or PBD12, respectively. Both dihydropyridazine polymers were observed to emit blue light
upon UV excitation, and an intrachain push-pull effect was observed in poly(dimethyl 4,5-dimethylene-1,4-dihydropyridazine-3,6-dicarboxylate, which resulted in a large quantum yield increase over that observed for small molecule analog dimethyl 2,4a,5,6,7,8-hexahydrophthalazine-1,4-dicarboxylate. Quenching of fluorescence occurred upon oxidation of both dihydropyridazine polymers and small molecules, and was indicated as a potential method for monitoring oxidation extent of the materials. Both polymers also became insoluble in THF following oxidation. Cyclic voltammetry was conducted on the small molecule model compounds to better understand the oxidation and fluorescence quenching occurring in the polymers. CV showed 1-electron electrochemical oxidations for both dihydropyridazine small molecules, and both oxidations occurred at low potentials indicating that they were favorable reactions. Reduction sweeps of the oxidized small molecules revealed both compounds underwent three 1-electron reductions, and the lower potentials alluded to the involvement of electron transfer interactions in the quenching of fluorescence observed following oxidation. Modification of common elastomer PBD with DMDT proved to be an effective method for installing antioxidant units onto a dienophile-rich polymer backbone, and a unique method of forming a new class of thermoplastic polymers from cheap commercially available liquid elastomers.

Finally, chapter 4 diverged from tetrazine IEDDA modification of polybutadienes and instead focused on the post-modification of poly(MMA-co-HEMA) with DCT, to generate photobleachable materials. Initial attempts to prepare a pendant tetrazine homopolymer from the radical polymerization of 2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) did not result in polymer, or even oligomer formation, and it
was deemed that the tetrazine ring was inhibiting radical propagation. Attempts at post-modifying poly(HEMA) resulted in intractable red solids, and were not pursued further. It was determined that a copolymer of ~90% MMA and ~10% HEMA repeat units provided a material that could be post-modified with DCT, but would not crosslink during the modification and remained solvent processable afterwards. The polymer could be cast into transparent dark red films using CHCl$_3$, and were observed to fluoresce orange under UV excitation while becoming visually opaque in the process. Extended irradiation with either UV or ambient light resulted in the photodegradation of the tetrazine ring, supported by IR comparisons before and after $h\nu$ exposure, and bleaching of the film was observed visually. A distinct change in refractive index was observed upon bleaching, and the use of tetrazines as photobleachable agents in optical waveguide materials was proposed. Partially modified copolymers were demonstrated to crosslink upon thermal processing, creating a photodegradable linked network. This observation lead to the proposal for using these polymers in the design of low-cost photoresist materials.

The diversity of the applications for the materials presented in this dissertation demonstrates only a fraction of the potential and versatility that the tetrazine group has to offer in polymer applications. It is my hope that this document helps to inspire further innovations in the field, as well as additional improvements on the applications mentioned herebefore. I would like to thank those who have come before me in this field, as your discoveries have helped to inspire me as well.
5.2 Future Work

5.2.1 Tetrazines as chemical blowing agents (Organosilicon foams)

While exploring possibilities in expanding the scope of liquid dienophiles that will foam when mixed with DCT, we discovered poly(allylsiloxane) functioned as a compatible polymer. The foaming reaction occurs at a much faster rate than with PBD, and cooling of the system to 5 °C was required to prevent scorching. DCT proved itself to be too reactive for scale-up, but additional tetrazines should be explored as chemical blowing agents in making organosilicon foams. An additional project that should be explored based on observations from this is a rate study on tetrazine IEDDA reactions with allyl siloxanes. It appears there may be a β-silicon rate effect on these reactions which has yet to be reported in the literature. On one occasion in my research, the addition of 1 mmol allyltriethoxysilane to a solution of DMDT in THF lead to the near-complete ejection of solvent from the flask from rapid nitrogen generation and an immediate color change from red to yellow for the remaining solution. Needless to say, care should be taken when conducting these experiments.

Figure 38: Organosilicon foams from DCT IEDDA reaction with poly(allylsiloxane)
5.2.2 Tetrazines as chemical blowing agents (1,2,4,5-tetrazine blowing agent)

In an effort to develop a better chemical blowing agent for the PBD foaming system, we set our aims on a PBD soluble tetrazine that could be produced in less than five synthetic steps and lacked reactive halogen groups that could off-gas after foam formation. The parent 1,2,4,5-tetrazine proved to fulfill these requirements, and is currently demonstrating to outperform DCT in a variety of ways. The synthetic pathway for 1,2,4,5-tetrazine is only 2 steps, and can be carried out in a one pot reaction in 52% yield (not optimized). The reactions are better controlled, and scorching has not been observed under conditions where it would happen with DCT. The foams produced from 1,2,4,5-tetrazine show a much more well-defined open pore network under SEM, and the reactions can be carried out at room temperature. This initial project is nearing completion, but 1,2,4,5-tetrazine shows promise as a useful chemical blowing agent for making foams from other liquid dienophile-rich polymers, i.e. poly(allylsiloxane).

This space intentionally left blank
**Figure 39:** (A) Images of soft foams prepared from the IEDDA reaction between 1,2,4,5-tetrazine and PBD (B) SEM image of the soft-foam, showing a much more uniform open cell network than SEMs of DCT based foams.

### 5.2.3 Poly(MMA-co-2-((6-chloro-1,2,4,5-tetrazin-3-yl)oxy)ethyl methacrylate) photoresists

The initial studies for chapter 4 have lead us to the hypothesis that these and other tetrazine polymers can be utilized in making negative photoresist materials. Additional research is required to prove whether this hypothesis is correct, and further DCT modification of poly(MMA-co-HEMA) should be conducted. Thermally processed tetrazine modified copolymers containing 2\% unreacted HEMA functional groups were demonstrated to crosslink, and were observed to swell when exposed to CHCl₃. With optimization to achieve a higher crosslink density and prevent swelling, while also
avoiding crosslinking during post-modification with DCT, photolithography experiments can be conducted on thermally treated thin films as a demonstration of this method’s viability.
Appendix A

Chapter 2 Supporting Information

This Appendix is included to provide experimental details and supporting information for Chapter 2: Transforming polybutadiene with tetrazine click chemistry into self-indicating, antioxidant foams

A.1 Materials

All chemicals were purchased from the chemical suppliers and used without further purification. Polybutadiene (containing 20% 1,2 addition, 80% cis- and trans- 1,4, listed avg M_n ca. 5,000), polybutadiene (listed avg M_n ~3000), polybutadiene (predominantly 1,2-addition), polybutadiene (hydroxyl functionalized, listed avg M_n ~1200), and guanidine hydrochloride - Aldrich. Hydrazine hydrate (100%, 64% hydrazine) and trichloroisocyanuric acid (99%) - Acros Organics. Methylene chloride (certified ACS stabilized), and 1,4 dioxane (certified ACS) - Fischer Chemical. Acetonitrile (HPLC grade) and methanol (GR ACS) - EMD Millipore. Hexanes (ACS grade) - Macron, chloroform-d (CDCl_3, 0.05 % v/v TMS) and dimethyl sulfoxide-d6 (D, 99.9%) - Cambridge Isotope Laboratories. 3,6-dichloro-1,2,4,5-tetrazine was prepared according to literature procedures. DMDO was synthesized immediately prior to use following the procedure of Mikula et al.
A.2 Instrumentation

$^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were obtained using either a Bruker AVIII 400 MHz or a Bruker DRX 500 MHz spectrometer with chemical shifts referenced to TMS (δ 0.00) ppm for $^1$H and CDCl$_3$ (δ 77.0 ppm) for $^{13}$C. CP-MAS was obtained using a Varian VNMRS 400MHz NMR spectrometer operating at 100.5246 MHz for 13C (9.6 T static magnetic field). The NMR probe was a 1.6 mm triple resonance T3 High-speed MAS probe (Varian, Palo Alto, CA). All $^{13}$C spectra collected at 20 kHz MAS using 2 ms contact time with ramped-amplitude CP (1H power of 86 kHz matching conditions) with 131 kHz TPPM 1H high power decoupling. Adamantane was used as an external chemical shift reference with the 38.6 ppm for $^{13}$C spectrometer. Size exclusion chromatography (SEC) was performed in a tetrahydrofuran (THF) mobile phase on either an Acquity APC system (Waters) using three 4.6 mm 150 mm Acquity APC XT columns (450 Å, 2.5 µm; 125 Å, 2.5 µm; and 45 Å, 1.7 µm) connected in series and a refractive index detector calibrated with polystyrene standards, or a Waters 1515 isocratic pump running three 5-µm PLgel columns (Polymer Labs, pore size 104, 103 and 102 Å) at a flow rate of 1 mL/min with a Waters 2414 differential refractometer and a Waters 2487 dual-wavelength UV-vis spectrometer calibrated with polystyrene standards. Thermogravimetric analysis (TGA) was performed with a Q50 TGA (TA instruments) from 40 °C to 800 °C at a rate of 20 °C/min under a nitrogen atmosphere. Differential scanning calorimetry (DSC) was conducted with a Q100 DSC (TA Instruments) with heat cool heat cycles at a heating rate of 20 °C/min and a cooling rate of 5 °C/min. Data from the second heating cycle is reported. Elemental Analyses (C, H, N, Cl) were acquired from ALS Environmental services and (C, H, N) from Numega.
Resonance Labs. Infrared (IR) spectra were obtained with a Thermo/Nicolet Avatar 360 FT-IR using a Voltex, Inc. HeNe Laser source, and using either a Harrick MVP-Pro™ Single Reflection ATR Microsampler, NaCl plates, or in KBr pellet form. Compression testing was performed using an Instron 5542.

A.3 Experimental

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{NH} & \quad \text{H-Cl} \\
\text{H}_2\text{N} & \quad \text{N} & \quad \text{NH}_2 & \quad \text{H-Cl}
\end{align*}
\]

1,4-dioxane reflux 2 hrs

\[97\%\]

\text{Triaminoguanidine monohydrochloride}

To a 500 mL three-neck round-bottom flask, set-up for mechanical stirring was added guanidine monohydrochloride (19.12 g, 0.20 mol), and 1,4-dioxane (100 mL) creating a white slurry. Hydrazine monohydrate (34.00 mL, 0.70 mol) was added in one addition, and the solution was heated to reflux for 2 hours with stirring. During reflux, the guanidine HCl was observed to have dissolved completely into solution. After 2 hours, a white precipitate had formed, and the solution was cooled to ambient temperature. The precipitate was collected via vacuum filtration, and rinsed with 1,4-dioxane until the filtrate was colorless. The product was dried overnight under high vacuum, yielding a white powder (27.33 g, 97% yield). mp 225 °C decomposes, (228 °C); \textsuperscript{13}C NMR (100 MHz, CDCl₃, δ): 159.54.
To a slurry of triaminoguanidine monohydrochloride (17.00 g, 121 mmol) in 300 mL of DI water, was added 2,4-pentanedione (25.00 mL, 245 mmol) dropwise over 10 min. During the addition, the solution turned yellow briefly before becoming a dark orange color. After the addition, the temperature of the solution had increased to 45 °C, and it was stirred at this temperature for an additional 30 minutes. The solution was then heated to 70 °C for 2.5 hours, during which time a yellow precipitate formed in the reaction vessel. After 2.5 hours, the solution cooled to room temperature and then the precipitate was collected via vacuum filtration and rinsed with DI water. The product was dried overnight under high vacuum to yield a bright yellow powder (12.02 g, 73% yield). mp 148-151 °C, (150 °C); ^1H NMR (400 MHz, Chloroform-\(d\), \(\delta\)): 8.06 (s, 2H), 5.95 (dd, \(J = 1.0, 0.5\) Hz, 2H), 2.48 (d, \(J = 0.9\) Hz, 6H), 2.21 (s, 6H); ^13C NMR (101 MHz, CDCl\(_3\), \(\delta\)): 150.06, 145.90, 142.41, 109.99, 13.95, 13.61.
3,6-bis(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine

To a 500 mL round-bottom flask, was added sodium nitrite (2.81 g, 41 mmol), DI water (100 mL), and dichloromethane (50 mL). The reaction solution was then cooled to 0 °C before adding 3,6-bis(3,5-dimethylpyrazol-1-yl)-1,2-dihydro-1,2,4,5-tetrazine (3.88 g, 14 mmol). Acetic acid (7.60 mL, 70 mmol) was added to the solution dropwise. After addition, the solution was stirred until gas generation had ceased, and the color had changed from yellow to a dark red color. A 5% solution of aqueous potassium carbonate was added until the reaction solution was neutralized. The organic layer was collected, and the aqueous layer was extracted three additional times with dichloromethane. The organic fractions were combined, and the solvent removed with rotary evaporation. The red crystals were then further purified by vacuum filtration, and rinsing with DI water, followed by methanol, until the filtrate was light red in color. The bright red powder was dried overnight under vacuum at ambient temperature, and had a final mass of (2.91 g, 75% yield). mp 224-226 °C, (223-225 °C); $^1$H NMR (400 MHz, Chloroform-$d$, δ): 6.20 – 6.18 (m, 2H), 2.71 (d, $J = 1.0$ Hz, 6H), 2.39 (s, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 159.40, 154.57, 143.88, 14.80, 13.99.
3,6-dihydrazinyl-1,2,4,5-tetrazine

To a solution of 3,6-bis(3,5-dimethylpyrazol-1-yl)-1,2,4,5-tetrazine (6.11 g, 23 mmol) in 100 mL of acetonitrile, was added hydrazine monohydrate (3.00 mL, 62 mmol). During the addition, the solution changed from a dark red to a dark maroon color. The solution was heated to reflux for 2 hours, and then allowed to cool to ambient temperature. The precipitate was collected via vacuum filtration, and rinsed with acetonitrile. The dark maroon powder was dried overnight under vacuum at ambient temperature and had a final mass of (2.58 g, 80% yield). mp 144-146 °C, decomposed (137-138, 160-162 °C) $^{13}$C NMR (101 MHz, CDCl$_3$, δ): 163.38 ppm.

This space intentionally left blank
3,6-dichloro-1,2,4,5-tetrazine (DCT)

A slurry of 3,6-dihydrazinyl-1,2,4,5-tetrazine (2.56 g, 18 mmol) in acetonitrile (100 mL) was cooled to 0 °C. After cooling, excess trichloroisocyanuric acid (10.45 g, 45 mmol) dissolved in acetonitrile (50 mL) was added to the slurry dropwise. During the addition, the solvent changed to a bright orange color, and gas evolution was observed. After the addition, the system was warmed to 23 °C and then stirred for an additional 30 min. The precipitate was removed by vacuum filtration, and the solvent was removed from the filtrate via rotary evaporation leaving behind an orange powder. The orange powder was extracted with a 1:1 mixture of hexanes:dichloromethane and filtered through a silica plug. The bright orange crystals were dried overnight under vacuum at ambient temperature and then further purified by sublimation to yield (1.961 g, 72%). mp 144-147 °C, decomposed; $^{13}$C NMR(101 MHz, CDCl$_3$, δ): 168.24 ppm.

This space intentionally left blank
A.4 SEM of Foams

SEM of 193B (left) and 191 (right)

A.5 NMR Spectra

$^1$H NMR poly-$l$,4-butadiene (PBD14) (CDCl$_3$)
$^{13}$C NMR of poly-1,4-butadiene (PBD14) (CDCl$_3$)

$^1$H NMR of poly-1,2-butadiene (PBD12) (CDCl$_3$)
$^{13}C$ NMR of poly-1,2-butadiene (PBD12) (CDCl$_3$)

$^1H$ NMR for 191 (CDCl$_3$)
$^{13}$C NMR for 191 (20 kHz CPMAS)

$^1$H NMR 187 (CDCl$_3$)
$^{13}$C NMR 187 (CDCl$_3$)

$^1$H NMR for 190 (DMSO-d$_6$)
$^{13}C$ NMR for 190 (20 kHz CPMAS)

$^1H$ NMR for 192 (DMSO-d$_6$)
$^{13}\text{C NMR for 192 (20 kHz CPMAS)}$

$^{13}\text{C NMR of PBDOH (CDCl}_3\text{)}$

161
A.6 IR Spectra

IR of 3,6-dichloro-1,2,4,5-tetrazine (DCT) (ATR-SiO₂)
IR of poly-1,2-1,4-butadiene (NaCl)

IR of poly-1,4-butadiene (PBD14) (NaCl)
IR of poly-1,2-butadiene (PBD12) (NaCl)

IR of hydroxyl-functionalized poly-1,4-butadiene (PBDOH) (NaCl)
IR of 187 (ATR-SiO₂)

IR of 191 (ATR-SiO₂)
IR of 190 (ATR-SiO₂)

IR of 193B (ATR-SiO₂)
IR of 193C (ATR-SiO₂)

A.7 TGA
Appendix B

Chapter 3 Supporting Information

This Appendix is included to provide experimental details and supporting information for Chapter 3: Fluorescent anti-oxidant macromolecules through click modification of polybutadiene with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate

Figure B1: Foaming attempts – (Left) neat mixing of DMeT with Pbd and subsequent heating to 90 °C, (right) adding DCM as solubilizer followed by heating to 40 °C. While not efficient for a pbd system, does show promise for an elastomer that can dissolve the tetrazine.

B.1 Instrumentation

$^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were obtained using either a Bruker AVIII 400 MHz or a Bruker DRX 500 MHz spectrometer with chemical shifts referenced to TMS ($\delta$ 0.00) ppm for $^1$H and CDCl$_3$ ($\delta$ 77.0 ppm) for $^{13}$C. Size exclusion
chromatography (SEC) was performed in a dimethylformamide mobile phase on a Waters 1515 isocratic pump running three 5-µm PLgel columns (Polymer Labs, pore size 104, 103 and 102 Å) at a flow rate of 1 mL/min with a Waters 2414 differential refractometer and a Waters 2487 dual-wavelength UV-vis spectrometer calibrated with polystyrene standards. Thermogravimetric analysis (TGA) was performed with a Q50 TGA (TA instruments) from 40 °C to 800 °C at a rate of 10 °C/min under a nitrogen atmosphere. Differential scanning calorimetry (DSC) was conducted with a Q100 DSC (TA Instruments) with heat cool heat cycles at a heating rate of 10 °C/min and a cooling rate of 5 °C/min. Data from the second heating cycle is reported. Elemental Analyses (C, H, N) were performed by Numega Resonance Labs. Infrared (IR) spectra were obtained with a Thermo/Nicolet Avatar 360 FT-IR using a Voltex, Inc. HeNe Laser source in KBr pellet form (1 mg per 100 mg KBr). Cyclic Voltammetry was conducted in freshly distilled THF with 0.2M, 0.3M nBu₄NPF₆ (oxidation, reduction respectively) electrolyte concentrations using a Gamry potentiostat and 1 mM of compound. A 3mm glassy carbon disc functioned as the working electrode, with a platinum wire counter electrode and Ag/AgNO₃ as the reference electrode. All data is referenced to ferrocene.

B.2 Materials

All chemicals were purchased from their listed chemical suppliers and used without further purification unless otherwise noted. Polybutadiene (containing 20% 1,2 addition, 80% cis- and trans-1,4, listed avg Mₙ ca. 5,000, GPC (THF) Mₙ 6494, Mₘ 22209, DP: 3.42), poly-1,2-butadiene GPC (THF) Mₙ 3042, Mₘ 4414, DP: 1.45), glycine ethyl ester hydrochloride, cyclohexene, and 1-hexene were purchased from Aldrich (St. Louis, MO). Cyclohexene and 1-hexene were passed through a column of alumina.
before using. Sodium hydroxide and methanol (ACS grade) were purchased from EMD Millipore (Billerica, MA). Hexanes (ACS grade) came from Macron Fine Chemicals (Center Valley, PA). Chloroform-d (CDCl₃, 0.05 % v/v TMS) and dimethyl sulfoxide-d₆ (D, 99.9%) were obtained from Cambridge Isotope Laboratories (Tewksbury, MA).

**B.3 Experimentals**

*Synthesis of ethyl diazoacetate:*

\[
\begin{align*}
\text{O} & \quad \text{N}^+ \text{NH}_3^+ \quad \text{Cl}^- & \quad \text{NaNO}_2, 5\% \text{ aq. H}_2\text{SO}_4 \\
\text{DCM, H}_2\text{O}, 0^\circ\text{C, 15 min} & \quad 79.4\% & \quad \text{O} \quad \text{N}^-\text{N}^- \\
\end{align*}
\]

To a 500 mL beaker set up behind a blast shield was added glycine ethyl ester hydrochloride (30.000 g, 0.215 mol), 60 mL DI H₂O, 120 mL DCM, and a magnetic stir bar. The solution was cooled to 0 °C in an ice bath before the addition of 4M aqueous sodium nitrite (60 mL), followed by a 5% aqueous sulfuric acid solution (10 mL). After the addition, the biphasic solution began to turn yellow and gas generation was observed. The reaction was run for 15 minutes, after which time the organic phase was transferred to a flask containing 0 °C saturated sodium carbonate solution (120 mL). The mixture was stirred briefly, and the bright yellow organic phase was separated from the dark yellow aqueous phase, then dried over sodium sulfate. The solution was filtered through a cotton plug, and the solvent removed through rotary evaporation until yellow product was observed to be distilling over, yielding a bright yellow liquid (19.49 g, 79% (11% residual DCM by NMR integration)). ¹H NMR (400 MHz, CDCl₃, δ): 4.73 (s, 1H), 4.21
(q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$, δ): 166.91, 60.94, 46.24, 14.52.

Caution: Product is potentially explosive, and NO gas is toxic proper equipment and fume hoods should be used during synthesis and care should be taken during workup.

*Synthesis of sodium 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate:*

A 250 mL 24/40 3-neck round-bottom flask equipped for mechanical stirring was charged with sodium hydroxide (32.0 g, 800 mmol) and DI H$_2$O (50 mL). The solution was stirred until the sodium hydroxide had dissolved and then was heated to 60 °C in a sand bath. Ethyl diazoacetate (19.45 g, 170.5 mmol) was added dropwise maintaining a temperature near 60 °C throughout the addition. The solution changed color from yellow to mustard brown during the addition and precipitate was observed to have started to form after 10 minutes of heating. The reaction was run for 1.5 h, during which time the solution had become a yellow-brown slurry, then removed from heat and allowed to cool to ambient temperature (23 °C). After cooling, the solution was transferred to a 500 mL Erlenmeyer flask, and 95% ethanol (250 mL) was added to the flask and mixed with magnetic stirring. After allowing the precipitate to settle, the solution was decanted from the flask. This process was repeated 4 additional times, and the precipitate was collected.
via vacuum filtration, rinsed with ethanol, and dried over vacuum to yield a tan colored solid (16.25 g, 88%).

*Synthesis of 1,4-dihydro-1,2,5-tetrazine-3,6-dicarboxylic acid:*

![Chemical structure of 1,4-dihydro-1,2,5-tetrazine-3,6-dicarboxylic acid]

To a 250 mL 1-neck 24/40 round-bottom flask was added sodium 1,4-dihydro-1,2,5-tetrazine-3,6-dicarboxylate (16.200 g, 75.00 mmol), DI H₂O (16 mL) and ice (16 g), and a magnetic stir bar. The slurry was stirred and concentrated hydrochloric acid (30 mL) was added in one addition generating a light-yellow paste. After 5 minutes of stirring, the paste was diluted with 100 mL of 5 °C DI H₂O and stirred for an additional 10 minutes. The reaction was diluted with an additional 100 mL of 5 °C DI H₂O immediately prior to collection of the solid via vacuum filtration. The paste was rinsed with 25 mL 5 °C H₂O and dried under vacuum to yield a yellow solid (4.22 g, 33%). mp: 142-143 °C, (144-148 °C).

*This space intentionally left blank*
**Synthesis of dimethyl 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate:**

![Chemical Structure]

A 100 mL 1-neck 24/40 round bottom flask containing anhydrous methanol (27 mL) and a magnetic stir bar was cooled to -78 °C in a dry ice/acetone bath. Thionyl chloride (4.40 mL, 60.65 mmol) was added dropwise to the cooled methanol, followed by 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylic acid (4.039 g, 23.46 mmol) and an additional volume of anhydrous methanol (28 mL). The solution was warmed to ambient temp (23 °C), and then heated to 40 °C at which time it had changed to a dark opaque brown color. After 17 h the solution had turned a transparent dark orange color, and a dark orange solid had formed on the bottom of the flask. The solution was cooled to ambient temperature (23 °C), and the solid collected with vacuum filtration. The orange solid was purified through Soxhlet extraction using DCM. The DCM was removed through rotary evaporation, yielding an orange fibrous solid (2.79 g, 59%). mp: 173-174 °C, (171-172 °C); \(^1\)H NMR (400 MHz, CDCl\(_3\), δ): 7.51 (s, 2H), 3.92 (s, 6H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\), δ): 159.18, 138.23, 53.87.
Synthesis of dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate:

To a 250 mL 1-neck 24/40 round-bottom flask was added 1,4-dihydro-1,2,4,5-tetrazine-3,6-dicarboxylate (2.700 g, 13.50 mmol), DCM (125 mL), and a magnetic stir bar. In a separate 250 mL 3-neck 24/40 round-bottom flask, concentrated HCl (17 mL) and a magnetic stir bar were added. The flask was cooled in an ice bath before the dropwise addition of an aqueous solution of sodium nitrite (11.2 g in 27 mL DI H₂O). The evolved brown gases were bubbled into the tetrazine solution through a 1 mm glass tube attached to a 24/40 adapter which contained a vent tube (adapted liquid N₂ cold trap top piece) under a stream of nitrogen. The transparent orange solution began to turn a transparent dark red color over time, and a second charging of NO gas was generated using the same procedure as listed above after 3 h. The dark red reaction solution was stirred for an additional 3 h, then disconnected from the NO feed line. The DCM and residual NO gases were removed through rotary evaporation in a fume hood, and the resulting red crystalline solid was further purified by rinsing with cold methanol (0 °C, 25 mL) to yield a bright red crystalline solid (2.483 g, 93%) mp: 174-176 °C, (173-175 °C); ¹H NMR (400 MHz, CDCl₃, δ): 4.22 (s, 1H); ¹³C NMR (101 MHz, CDCl₃, δ) 160.51, 159.26, 54.78. **Caution: Toxic NO gas fumes are generated during this step, therefore the reaction should be run in a fume hood preferably with a NaOH trap to convert excess NO gases into sodium nitrite.**
B.4 NMR Spectra

$^1H$ NMR for 201 (CDCl$_3$)

$^{13}C$ NMR for 201 (CDCl$_3$)
$^1$H NMR for 197 (CDCl$_3$)

$^{13}$C NMR for 197 (CDCl$_3$)
$^1H$ NMR for 202 (CDCl$_3$)

$^{13}$C NMR for 202 (CDCl$_3$)
$^1$H NMR for 198 (CDCl$_3$)

$^{13}$C NMR for 198 (CDCl$_3$)
$^1$H NMR for 203 (CDCl$_3$)

$^{13}$C NMR for 203 (CDCl$_3$)
$^1$H NMR for 199 (CDCl$_3$)

$^{13}$C NMR for 199 (CDCl$_3$)
$^1$H NMR for 204 (CDCl$_3$)

$^{13}$C NMR for 204 (CDCl$_3$)
\(^1\)H NMR for 200 (CDCl\(_3\))

\(1^3\)C NMR for 200 (CDCl\(_3\))
B.5 Comparison NMR Spectra
\[ \text{Diagram of chemical structures with NMR spectra.} \]

\[ \text{NMR spectra for different compounds.} \]

\[ \text{Fl (ppm) scale.} \]

\[ \text{Peaks at various ppm values.} \]
B.6 IR Spectra

188
## B.7 GPC Data

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Mn</th>
<th>Mw</th>
<th>Mp</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBD12(^\Theta)</td>
<td>3042</td>
<td>4414</td>
<td>3748</td>
<td>1.45</td>
</tr>
<tr>
<td>199(^\Phi)</td>
<td>8673</td>
<td>10429</td>
<td>9253</td>
<td>1.20</td>
</tr>
<tr>
<td>200(^\Phi)</td>
<td>10687</td>
<td>12021</td>
<td>10869</td>
<td>1.12</td>
</tr>
<tr>
<td>PBD14(^\Theta)</td>
<td>6494</td>
<td>22209</td>
<td>15489</td>
<td>3.42</td>
</tr>
<tr>
<td>197(^\Phi)</td>
<td>12479</td>
<td>28815</td>
<td>21128</td>
<td>2.14</td>
</tr>
<tr>
<td>198(^\Phi)</td>
<td>7915</td>
<td>10507</td>
<td>8309</td>
<td>1.34</td>
</tr>
</tbody>
</table>

*Figure 1: GPC results showing size increase on IEDA functionalization and after oxidation*

\(^\Theta\)Traces run in THF

\(^\Phi\)Traces run in DMF

\(^\Omega\)Higher molecular weight peaks fell outside range of calibration standards

This space intentionally left blank
B.8 Cyclic Voltammetry

Oxidation 1
Scan Rate: 100 mV/s
Small Mol. Conc: 1 mM
Electrolyte (nBu4N.PF6) Conc: 0.2M
Electrode: 3mm glassy carbon disk

Oxidation 2
Scan Rate: 100 mV/s
Small Mol. Conc: 1 mM
Electrolyte (nBu4N.PF6) Conc: 0.2M
Electrode: 3mm glassy carbon disk
**Oxidations**
Scan Rate: 100 mV/s
Small Mol. Conc: 1 mM
Electrolyte (nBu4N.PF6) Conc: 0.2M
Electrode: 3mm glassy carbon disk

**Reduction**
Scan Rate: 100 mV/s
Small Mol. Conc: 1 mM
Electrolyte (nBu4N.PF6) Conc: 0.2M
Electrode: 3mm glassy carbon disk
B.9 UV-Vis Spectra (all samples were dissolved in CHCl₃)

Reduction 2
Scan Rate: 100 mV/s
Small Mol. Conc: 1 mM
Electrolyte (nBu4N.PF₆) Conc: 0.2M
Electrode: 3mm glassy carbon disk
Absorbance vs. Wavelength (nm) for different concentrations.

- 0.1 mM
- 0.2 mM
- 0.4 mM
- 0.6 mM
- 0.8 mM
- 1.0 mM

Graphs show the absorbance at different wavelengths for varying concentrations.

Equations and R² values are provided:

1. \( y = 500.56x - 0.0058 \), \( R^2 = 0.99848 \)
2. \( y = 2941.9x + 0.0058 \), \( R^2 = 0.99984 \)
Absorbance

Wavelength (nm)

0.2 mM

0.4 mM

0.6 mM

0.8 mM

1.0 mM

y = 291.24x - 0.024

R² = 0.98997

0

0.05

0.1

0.15

0.2

0.25

0.3

Concentration (M)

0

0.0002

0.0004

0.0006

0.0008

0.001

0.0012

Absorbance

Concentration (M)

0

0.0002

0.0004

0.0006

0.0008

0.001

0.0012

Absorbance

Wavelength (nm)

0.1 mM

0.2 mM

0.4 mM

0.6 mM

0.8 mM

1.0 mM

y = 2361.2x - 0.0541

R² = 0.99953

0

0.0002

0.0004

0.0006

0.0008

0.001

0.0012

Absorbance

Concentration (M)
B.10 Fluorimeter (all samples were dissolved in CHCl₃)
B.11 Quantum Yield Data

197 (DMF), coumarin 151 (ethanol)
Quantum yield: 0.099, Excitation max: 340 nm, Emission max: 407 nm

201 (DMF), coumarin 151 (ethanol)
Quantum yield: 0.004, Excitation max: 373 nm, Emission max: 462 nm
199 (DMF), coumarin 151 (ethanol)
Quantum yield: 0.003, Excitation max: 352 nm, Emission max: 448 nm

203 (DMF), coumarin 151 (ethanol)
Quantum yield: 0.008, Excitation max: 373 nm, Emission max: 448 nm
Appendix C

Chapter 4 Supporting Information

This Appendix is included to provide experimental details and supporting information for Chapter 4: Bleaching of copolymers containing photodegradable pendant chloroalkoxy tetrazines groups: a potential approach towards preparing low-cost photoresists and optical waveguides

C.1 Materials

The following chemicals were purchased from their listed chemical suppliers and used without further purification or as listed. Guanidine hydrochloride – (Aldrich), Hydrazine hydrate (100%, 64% hydrazine) and trichloroisocyanuric acid (99%) – (Acros Organics), methylene chloride (certified ACS stabilized), and 1,4 dioxane (certified ACS) – (Fischer Chemical), acetonitrile (HPLC grade) and methanol (GR ACS) – (EMD Millipore), Hexanes (ACS grade) – (Macron), chloroform-d (CDCl₃, 0.05 % v/v TMS) – (Cambridge Isotope Laboratories). Methyl methacrylate (Aldrich) and 2-hydroxyethyl methacrylate – (Aldrich) were purified by passing through a plug of activated alumina before use. AIBN – (Asta Tech Inc.) was recrystallized in methanol and stored at -5 °C. 3,6-dichloro-1,2,4,5-tetrazine was prepared according to procedures by Coburn et al.,¹⁶ Chavez et al.,¹⁷ and Helm et al.,¹⁸ purified according to the method put forth by Gong et al.¹⁹
C.2 Instrumentation

$^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were obtained using either a Bruker AVIII 400 MHz or a Bruker DRX 500 MHz spectrometer with chemical shifts referenced to TMS ($\delta$ 0.00) ppm for $^1$H and CDCl$_3$ ($\delta$ 77.0 ppm) for $^{13}$C. CP-MAS was obtained using a Varian VNMRS 400MHz NMR spectrometer operating at 100.5246 MHz for $^{13}$C (9.6 T static magnetic field). The NMR probe was a 1.6 mm triple resonance T3 High-speed MAS probe (Varian, Palo Alto, CA). Size exclusion chromatography (SEC) was performed in a tetrahydrofuran (THF) mobile phase on a Waters 1515 isocratic pump running three 5-$\mu$m PLgel columns (Polymer Labs, pore size 104, 103 and 102 Å) at a flow rate of 1 mL/min with a Waters 2414 differential refractometer and a Waters 2487 dual-wavelength UV-vis spectrometer calibrated with polystyrene standards. Thermogravimetric analysis (TGA) was performed with a Q50 TGA (TA instruments) from 40 °C to 800 °C at a rate of 10 °C/min under a nitrogen atmosphere. Differential scanning calorimetry (DSC) was conducted with a TA 2920 modulated DSC with heat cool heat cycles at a heating rate of 10 °C/min and a cooling rate of 5 °C/min. Data from the second heating cycle is reported. Elemental Analyses (C, H, N) were acquired from Numega Resonance Labs. Infrared (IR) spectra were obtained with a Thermo/Nicolet Avatar 360 FT-IR using a Voltex, Inc. HeNe Laser source, and using either a Harrick MVP-Pro™ Single Reflection ATR Microsampler, NaCL plates, or in KBr pellet form. Photobleaching experiments were conducted using a Cure Zone 2 UV Flood Curing System equipped with a 400 watt metal halide lamp having a 80 mw/cm$^2$ output in the UVA region and a peak intensity at 365 nm.
C.3 Experimentals

See appendix section A3 for experimentals on the synthesis of 3-,6-dicholoro-1,2,4,5-tetrazine.

C.4 NMR Spectra

$^1H$ NMR of 205 (CDCl$_3$)
$^{13}$C NMR Spectra of 205 (CDCl$_3$)

$^1$H NMR of 207 (CDCl$_3$)
$^{13}$C NMR Spectra of 207 (CDCl$_3$)

$^1$H NMR of 208 (CDCl$_3$)
$^{13}$C NMR Spectra of 208 (CDCl$_3$)

C.5 IR Spectra

IR spectrum of 207 (KBr)
**IR Spectrum of 208 (KBr)**

![IR Spectrum of 208 (KBr)](image)

**IR comparison of 207, 208, and photobleached 208 (KBr)**

![IR comparison of 207, 208, and photobleached 208 (KBr)](image)
C.6 Absorbance & Emission Spectra

Absorbance and Emission Spectrum for 205 (0.01 mM in CHCl₃)

Absorbance and Emission Spectrum for 208 (CHCl₃) (0.01 mM in CHCl₃)
C.7 TGA Data

*TGA comparison of 207 and 208*

This space intentionally left blank
Permissions
References


