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14. ABSTRACT

In this STIR project we have investigated the development of a new class of semi-rigid, highly-tailorable copolymeric materials based on purines. Synthetic efforts have been based on step-growth polymerization using Stille cross-couplings of halogenated purines and aryl-organotin reagents. These studies have demonstrated the first-ever synthesis of copolymers containing purine units as the chain backbone. With the feasibility of producing these novel materials demonstrated, a wide variety of efforts have been devoted to increasing the molecular weight of the copolymer through choice of solvent, catalyst, design of the monomeric building blocks, and reaction

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purine, copolymer, cross-coupling, materials

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19a. NAME OF RESPONSIBLE PERSON: S. Kilbey

19b. TELEPHONE NUMBER: 865-974-4303

Report Title

Final Report: STIR: Synthesis of Novel Purine-based Polymers

ABSTRACT

In this STIR project we have investigated the development of a new class of semi-rigid, highly-tailorable copolymeric materials based on purines. Synthetic efforts have been based on step-growth polymerization using Stille cross-couplings of halogenated purines and aryl-organotin reagents. These studies have demonstrated the first-ever synthesis of copolymers containing purine units as the chain backbone. With the feasibility of producing these novel materials demonstrated, a wide variety of efforts have been devoted to increasing the molecular weight of the copolymer through choice of solvent, catalyst, design of the monomeric building blocks, and reaction temperature. Thermal characteristics of the synthesized “poly(purines)” have been examined, and the high glass transition temperatures studies suggest that the resulting polymers are semi-rigid, tough materials. Outcomes from the project provide a launching point for subsequent studies aimed at understanding how chemical information and bonding arrangements affect chain properties and translate through macroscopic properties. These materials may have utility in optoelectronic applications and may possess useful coordination, recognition, sensing, or catalytic properties.

Enter List of papers submitted or published that acknowledge ARO support from the start of the project to the date of this printing. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

Received Paper

TOTAL:

Number of Papers published in peer-reviewed journals:

(b) Papers published in non-peer-reviewed journals (N/A for none)

Received Paper

TOTAL:

Number of Papers published in non peer-reviewed journals:

(c) Presentations

Given the novelty of the materials, we are holding publications until more thorough mechanistic studies can be completed. We anticipate at least 2 publications from this work.

Number of Presentations: 0.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Received	Paper

TOTAL:

Number of Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Peer-Reviewed Conference Proceeding publications (other than abstracts):

Received	Paper

TOTAL:

Number of Peer-Reviewed Conference Proceeding publications (other than abstracts):

(d) Manuscripts

Received	Paper

TOTAL:

Number of Manuscripts:

Books

Received Book

TOTAL:

Received Book Chapter

TOTAL:

Patents Submitted

Patents Awarded

Awards

co-PI Brian Long is the recipient of an ARO Young Investigator award (YIP) and the inaugural recipient of the Ffrancon Williams Endowed Faculty Award in Chemistry.

Graduate Students

NAME	PERCENT_SUPPORTED	Discipline
Kamlesh Bornani	0.20	
Jiadi Hou	0.16	
Rachel Ramirez	0.16	
W. Curtis Anderson	0.50	
Graham Collier	0.50	
FTE Equivalent:	**1.52**	
Total Number:	**5**	

Names of Post Doctorates

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Faculty Supported

NAME	PERCENT_SUPPORTED	National Academy Member
S. Michael Kilbey II	0.08	
Brian K. Long	0.05	
FTE Equivalent:	**0.13**	
Total Number:	**2**	

Names of Under Graduate students supported

NAME	PERCENT_SUPPORTED	Discipline
Evan Boone	0.00	Chemical Engineering
FTE Equivalent:	**0.00**	
Total Number:	**1**	

Student Metrics

This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period: 0.00

The number of undergraduates funded by this agreement who graduated during this period with a degree in science, mathematics, engineering, or technology fields:...... 0.00

The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields:...... 0.00

Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale):...... 0.00

Number of graduating undergraduates funded by a DoD funded Center of Excellence grant for Education, Research and Engineering:...... 0.00

The number of undergraduates funded by your agreement who graduated during this period and intend to work for the Department of Defense 0.00

The number of undergraduates funded by your agreement who graduated during this period and will receive scholarships or fellowships for further studies in science, mathematics, engineering or technology fields:...... 0.00

Names of Personnel receiving masters degrees

NAME

Total Number:

Names of personnel receiving PHDs

NAME

Total Number:

Names of other research staff

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Sub Contractors (DD882)

Inventions (DD882)

Scientific Progress

See attachment

Technology Transfer

We have collaborated with scientists at Army Research Laboratory on imaging polymeric materials by advanced transmission electron microscopy.

Statement of Problem Studied

The main aim of this short-term, exploratory STIR project was to assess the feasibility of synthesizing a new class of semi-rigid, highly-tailorable polymeric materials based on purines. The use of purines as monomer building blocks is compelling because of their remarkable monomeric properties that include: a) up to four independently addressable and spatially-defined positions on the fused bicyclic heterocyclic ring, three of which can participate in metal catalyzed carbon-carbon bond forming reactions; b) an enormous library of published synthetic transformations for peripheral and core functionalization; and c) availability from inexpensive, bio-derived precursors (e.g., guanine), a feature important for large scale and sustainable application.

While the idea of creating "poly(purine)s" is intrinsically novel, there are other reasons why this research is significant and stimulating. The fact that purines possess spatially-defined positions in their heterocyclic structure that participate in bond-forming reactions (C2, C6, C8, N7/N9, see structure in **Scheme 1**) provides a clear path to evaluate how chemical information and bonding arrangements affect chain properties, such as inherent stiffness and spatial extent. This also allows links to macroscopic properties, such as mechanical strength, thermal stability of the polymer, to be elucidated.

Summary of the Most Important Results

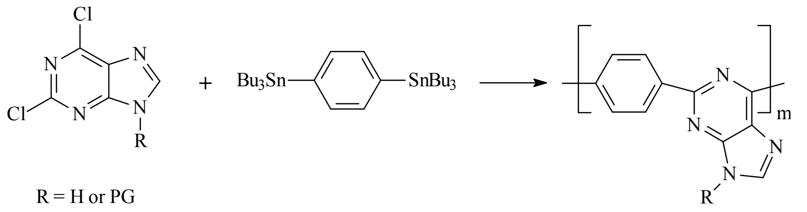
We undertook this effort with three specific goals in mind:

1. Demonstrate the feasibility of step-growth polymerization using Stille cross-coupling of 2,6-dichloropurine and 1,4-bis(tributylstannyl)benzene to create alternating "polypurine" copolymers;
2. Optimize conversion through the use of various electron-donating or electron-withdrawing ligand-based Pd catalysts and reaction conditions; and
3. Characterize basic macromolecular properties, including molecular weight and polydispersity, using a combination of NMR and size exclusion chromatography (SEC), as well as thermal properties, such as glass transition temperature, T_g, by DSC.

Our efforts, highlighted through key results described below, demonstrate that we accomplished these goals, at least in large part. It ***is*** possible to synthesize poly(purine)s. It is possible to tailor thermal properties by changing monomer design. We formed materials of modest molecular weight, but a variety of optimization efforts to drive the molecular weight higher were not successful. Nevertheless, having demonstrated the first-ever synthesis of poly(purine)s, we have opened a door to a new class of materials that appear to be thermally-stable and mechanically robust, and we are in a position to exploit further development of these new polymeric materials.

A. First Efforts and Test Reactions

Our first attempts we based on Stille coupling using the commercially available 2,6-dichloropurine and 1,4-bis(tributylstannyl)-benzene (**Scheme 1**). Small molecule coupling reactions using tributylstannyl-benzene were used to screen a variety of palladium catalysts, including Pd(0) and Pd(II) triphenylphosphines. These efforts to evaluate coupling efficiencies at the 2 and 6 positions determined that bis-(triphenylphosphine)palladium(II)dichloride produced the disubstituted product in highest relative abundance, and proved that Stille cross-coupling can be used to synthesize poly(purine)s. Although molecular weight ranges of 4kDa-10kDa were achieved, the resulting polymers suffered from solubility issues in common organic solvents; the polydispersity was broad and molar mass distributions were ill-defined. For these reasons, we began to use strategies that incorporated N9 protecting groups.

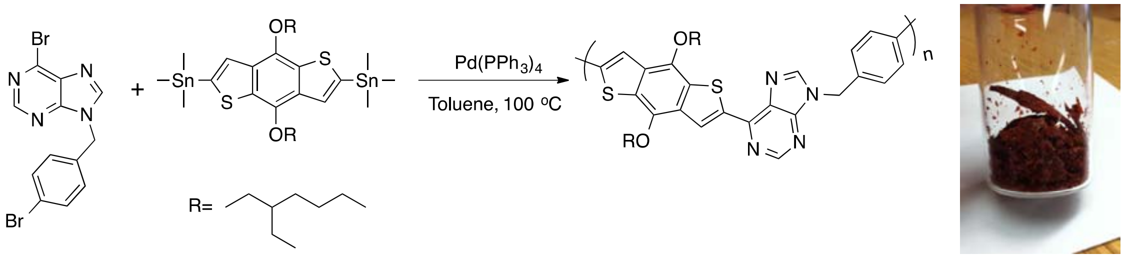


Scheme 1. Synthesis of purine-containing alternating copolymers by Stille cross-coupling. Initial efforts relied 2,6-dichloropurine with R = H at N9. Later efforts used an N9 protecting group (PG).

A variety of strategies of N9 protection, including trityl protection, were examined for their ability to affect polymerization (both by Stille and Suzuki cross-couplings) by enhancing solubility. During the course of this work, it was realized that it may be possible to enhance the coupling efficiency of the purine monomer by changing to bromopurine-based monomers. This precipitated an exploration of alkylation and Mitsunobu reactions to make new dibromopurine monomers. We found that 6-bromo-9-(4-bromophenyl)purine and 6-bromo-9-(3-bromophenyl)purine could be synthesized in yields ranging from 42%-55%. These new monomers (see **Scheme 2**) became the main building block for the poly(purine)s.

B. Synthesis and Optimization of Poly(purine)s

Initial attempts to polymerize the dibromo purine monomers (6-bromo-9-(3-bromophenyl)purine and 6-bromo-9-(4-bromophenyl)purine) using 1,4-bis(tributylstannyl)benzene in DMF and toluene were unsuccessful. As a result, Stille couplings with different stannyl monomers based on thiophene and benzodithiophene (BDT) were used. The latter set enabled greater tailorablity of the resulting poly(purine) through choice of solubilizing side chain on the BDT monomer. Traditional Stille-coupling conditions as well as syntheses using microwave irradiation were carried out. As a representative example, **Scheme 2** shows polymerization by Stille coupling of 6-bromo-9-(4-bromophenyl)purine and a stannylated ether-benzodithiophene comonomer. Polymerization was achieved using Pd(0) catalyst in toluene at 100 °C, with number average molecule weights (M_n) of roughly 7,000 Da (relative to PS standards).



Scheme 2. Synthesis of poly(purine) by Stille cross-coupling. The image at the right shows the purified polymer recovered as a reddish-powder.

The success of these reactions led to a broad and detailed suite of efforts to optimize the conversion, which would enable higher molecular weights to be achieved. According to the Carothers equation, high degrees of polymerization, X_n, (molecular weight) requires high conversion: $X_n \sim (1-\rho)^{-1}$, where ρ is the conversion. Efforts to increase conversion include screenings of 7 different catalysts and 4 different solvents. Polymerization was successful in all solvents studied and with 5 of the 7 catalysts, but in all cases, 5,500 Da < M_n < 8100 Da, which represents conversions up to ~90%.

We also examined 4 permutations of the side group on the BDT monomer and 2 different purine monomer designs: BDT monomers containing ethyl-hexyl and dodecyl side chains, linked wither through C-C bonds or by ether linkages were examined. 6-bromo-9-(3-bromophenyl)purine and 6-bromo-9-(4-bromophenyl)purine were used as well. (Here the design variation is 3-bromophenyl versus 4-bromophenyl – see structures shown in **Figure 1**, specifically the red bond.) These differences in monomer structure did little to alter the polymerization, but manifest in the thermal properties of the resultant poly(purine)s. The ether-linked side chains resulted in lower decomposition temperatures compared to the alkyl side chains, as shown in **Figure 1** (left); however these differences had a more dramatic effect on the glass transition temperature, T_g, as shown in **Figure 1** (right). Poly(purine)s having dodecyl side chains exhibited glass transition temperatures in the range of 95-110 °C, while those with ethylhexyloxy side chains (ether linked) had significantly higher T_g values.

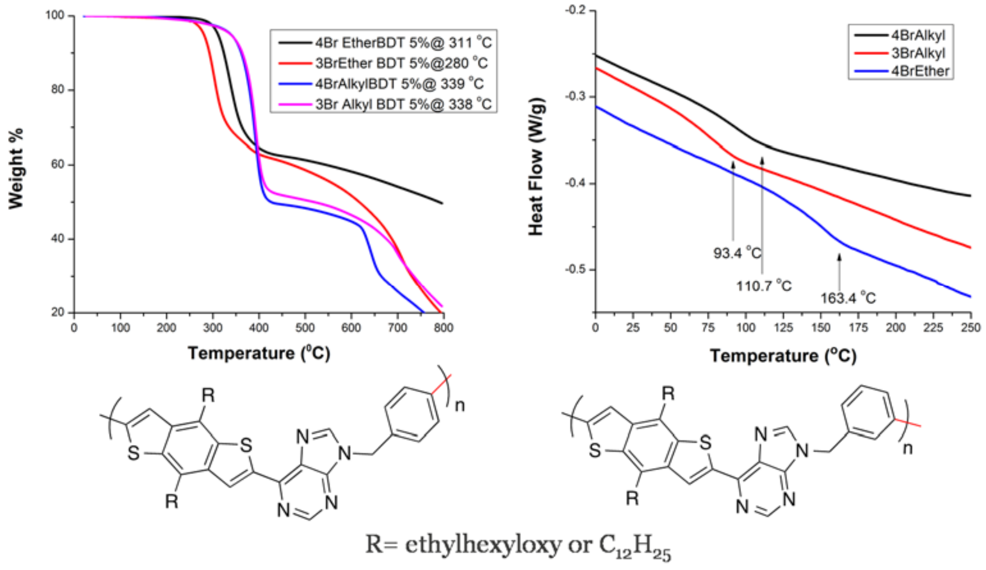


Figure 1. Characterizations of thermal properties of poly(purine)s differing in dibromopurine monomer design (red bond in structures) and side chains on benzodithiophene commoners (R groups).

C. Conclusions

We believe that the synthesis of poly(purine)s is a significant and signature accomplishment that is consistent with the high-risk/high-reward profile of the endeavor. In light of the large variation in thermal properties, we believe that the wide range of screening studies have positioned us to pursue follow-on studies to elucidate the role of monomer design on polymer properties. Multiple manuscripts based on this work are being developed, though these are being held pending a series of detailed follow-on studies using small molecule coupling reactions to assess the relative activity of the two halogenated sites on the purine monomer.