FINAL REPORT

Development of Novel Environmentally Sustainable Binders for Energetic Formulations

SERDP Project WP-2407

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Pascal Dubé
Nalas Engineering Services, Inc.

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14. ABSTRACT

The new binder system rests on the Diels-Alder cycloaddition reaction between previously undisclosed components. Our identification of a novel mode of reactivity offered by cyclooctynes in biological contexts paves the way for the development of a neutral, non-toxic binder system that could directly be implemented using existing equipment. The first phase of the program was aimed at the preparation of the new components of the binder system. The cyclooctyne component was dimerized using different linker units, following the hypothesis that the nature of the linker could modulate the physical and mechanical properties of the final polymer. The second reaction partner, a functionalized diene, was integrated to hydroxyl-terminated polybutadiene with the objective to again preserve the desirable physical properties of current formulations and impose only a minimal change to the system. A modified diene was produced using a new method developed at Nalas, and integrated onto commercial hydroxyl-terminated polybutadiene using mild and non-toxic conditions. A proof of concept for the binder system was obtained by the reaction of the cyclooctyne units with the functionalized polymer. This experiment led to the down selection of the linkers and identification of the optimal combination that provides a gum stock with ideal properties for use in formulations. The individual components of our new binder system are well-known for their compatibility with living organisms. Various functionalized cyclooctynes have been used as probes in living cells and animals without disrupting biological functions.

15. SUBJECT TERMS
Novel binder, non-toxic, new polymer ligation, cyclooctyne, isobenzofuran, HTPB

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List of Acronyms

AP	Ammonium perchlorate
ATP	Adenosine triphosphate
CJ pressure	Chapman-Jouguet pressure
DOA	Dioctyl adipate
DoD	Department of Defense
DoE	Department of Energy
ESOH	Environment, Safety and Occupational Health
HTPB	Hydroxy-terminated polybutadiene
MSDS	Material safety data sheet
NAWCWCLD	Naval Air Warfare Center Weapons China Lake Division
NFPA	National Fire Protection Association
R&D	Research and development
SEED	SERDP Exploratory Development
SERDP	Strategic Environmental Research and Development Program
US	United States

Keywords

Novel binder, non-toxic, new polymer ligation, cyclooctyne, isobenzofuran, HTPB

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ABSTRACT

Objectives

The objectives for this SEED effort were to establish the proof of concept for an entirely new class of binders for cross-linking polymeric formulations. The new binder system rests on the Diels-Alder cycloaddition reaction between previously undisclosed components. Our identification of a novel mode of reactivity offered by cyclooctynes in biological contexts paves the way for the development of a neutral, non-toxic binder system that could directly be implemented using existing equipment.

Besides its neutrality vs. living organisms, the binder system must operate under specifically defined thermal conditions in a reasonable time. While reactions occurring rapidly have been challenging for casting operations, reaction times too long are impractical for a variety of operations. The gum stock produced by the reaction of the binder system with the formulation's polymer also requires specific physical and mechanical properties. Most importantly, chemical compatibility with common formulation ingredients is fundamental for the establishment of a new binder system.

Technical Approach

The first phase of the program was aimed at the preparation of the new components of the binder system. The cyclooctyne component was dimerized using different linker units, following the hypothesis that the nature of the linker could modulate the physical and mechanical properties of the final polymer. The second reaction partner, a functionalized diene, was integrated to hydroxyl-terminated polybutadiene with the objective to again preserve the desirable physical properties of current formulations and impose only a minimal change to the system.

The stability of each component was evaluated by differential scanning calorimetry and thermogravimetric analyses and the key binding reaction was evaluated under thermal conditions. Finally, the new binder system was assessed in an actual formulation featuring ammonium perchlorate as energetic material and dioctyl adipate as plasticizer.

Results

After surmounting significant synthetic challenges, the cyclooctyne partner was produced by considerable modification of existing chemistry. Three dimeric cyclooctyne units were produced using different linkers. Following existing precedents for isocyanate binders, we elected to maintain a similar molecular arrangement of the linker. As such, the linkers chosen were the amine version of corresponding established isocyanates. The reactivity of the cyclooctyne towards Diels-Alder cycloaddition was assessed with a variety of dienes. This study led to the identification of isobenzofuran, which provided the desired reactivity at temperatures and timelines ideal for integration into current formulation workflows.

A modified diene was produced using a new method developed at Nalas, and integrated onto commercial hydroxyl-terminated polybutadiene using mild and non-toxic conditions. A proof of concept for the binder system was obtained by the reaction of the cyclooctyne units with the functionalized polymer. This experiment led to the down selection of the linkers and identification of the optimal combination that provides a gum stock with ideal properties for use in formulations.

The new binder components showed good stability towards energetic ingredients and good solubility with dioctyl adipate. An energetic formulation was tested and gave promising results.

Benefits

The individual components of our new binder system are well-known for their compatibility with living organisms. Various functionalized cyclooctynes have been used as probes in living cells and animals without disrupting biological functions.

The binder showed compatibility with energetic materials and common formulation ingredients while offering promising physical properties upon reaction. Moreover, upon further testing the new system could be directly integrated into current formulations with no or minimal change from the formulator’s perspective.

OBJECTIVES

Nalas and NAWCWCLD together seek to develop a long and sustainable solution to the toxicity of the binders currently utilized in energetic formulations. This solution can only occur via the identification and development of a novel binder system that relies on alternative chemistry to imbue energetic formulations with the desired energetic and physical properties.

Specifically, Nalas planned to develop a novel binder system based on the ligation of cyclooctyne and a functionalized diene to stabilize energetic formulations. In stark contrast with current systems relying on harsh curing, this system achieved smooth reaction under mild conditions, thus offering significant room for customization to various formulations with minimal requirements for equipment modification. Our technical objectives for this SEED program were the following:

1. Design and preparation of monomers
2. Proof of concept with energetic materials – assessment of compatibility
3. Application to existing formulation
4. Evaluation of sensitivity and performance
5. Preliminary assessment of environmental impact

Based on strong literature precedents, Nalas Engineering prepared diverse monomers of a new binder system based on the cycloaddition cyclooctyne with a functionalized diene. This approach offered a high chance of success by providing a rational platform towards the identification of a binder offering optimal properties in various formulations from physical, mechanical and energetic perspectives. These monomers would be produced and tested with individual energetic compounds to assess their compatibility prior to testing in formulations.

BACKGROUND

The formulation of energetics for applications in explosives, propellants and pyrotechnics is an important part of the DoD and DoE's scope. As these formulations find application every day across the globe, their preparation involves the use of multiple chemical ingredients in US-based facilities. These formulations owe their physical integrity to the use of binders, which provide structural stability and maintain energetic performance. The binder systems in current use are still based on old technology relying on the reactivity of toxic chemicals such as diisocyanates, phthalates and others. Diisocyanates are well-known for their ESOH risks and pose serious concerns for worker exposure due to their carcinogenic properties and extreme ability to sensitize operators. Diisocyanates are typically used as curing agents in a large number of applications, but using phthalates as plasticizer is equally dangerous given their reproductive toxicity.

The use of these compounds is restricted by many environmental agencies across the globe. Further regulation and restrictions of the key chemicals used as binder in almost all formulation systems in the US poses serious threat to our nation's security. The current stockpile of weapons, propellants and pyrotechnics composed of these binders poses a serious threat to the environment as well. The contamination of soils and groundwater by production waste or by leaching of chemicals from existing formulations can seriously damage wildlife and the ecosystem worldwide.

There is thus an urgent need to identify and develop novel binders that are based on alternative chemicals that are benign from an environmental and operational perspective. The toxicity of diisocyanates and phthalates are directly linked with their ability to act as binders through the reactivity of their functional groups (Figure 1). The toxicity of isocyanate functions is well-known due to the infamous Bhopal disaster that killed thousands of people in India. These compounds owe their toxicity to their ability to interrupt the electron transport chain that is known to regulate a plethora of processes across cellular membranes, including the production of adenosine triphosphate (ATP).

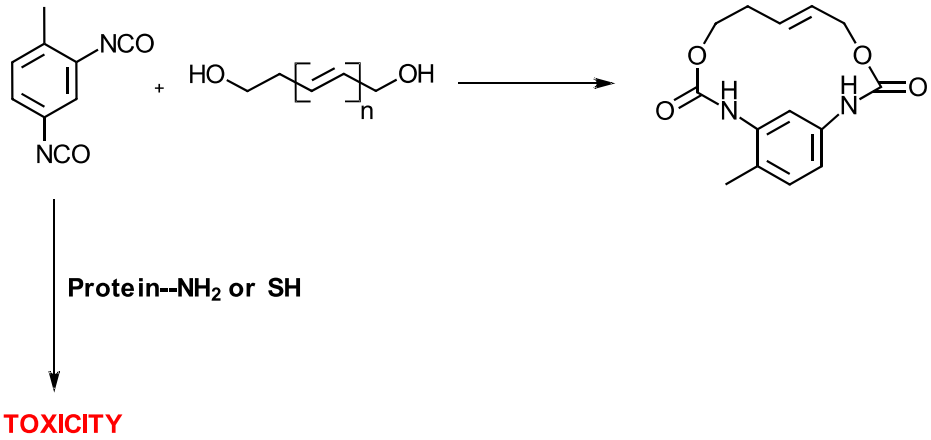

Figure 1. Mode of binding and toxicity of diisocyanates

The binders commonly utilized in the formulations relevant to our current effort all operate via the alkylation of highly reactive chemical functions, using the same mechanisms that interfere with biological systems. These chemical groups, typically classified as "alkylating agents," bind to proteins and disable them in a permanent way. Although short term solutions to the challenge could be found by chemically modifying existing binders to reduce their activity and thus toxicity, our team sought to develop a long and sustainable solution to this problem. This solution can only occur via the identification and development of novel binder systems that rely on alternative chemistry to imbue energetic formulations with the desired energetic and physical properties.

With the premise of using biorthogonal chemistry, Nalas has identified a novel class of chemicals that offer an alternative to traditional binders. The technology developed in this SERDP SEED relies on the chemoselective reactivity of non-toxic and mild chemicals under neutral conditions. This chemistry, based on the ligation of cyclooctynes, has been previously used in living cells and even animals without disrupting signaling functions, thus supporting their non-toxicity to biological systems (Figure 2).[1] Nalas plans to build on this strong precedent and develop an eco- and human-friendly system amenable to a variety of formulations to stabilize the energetic materials and minimize their impact on the environment.

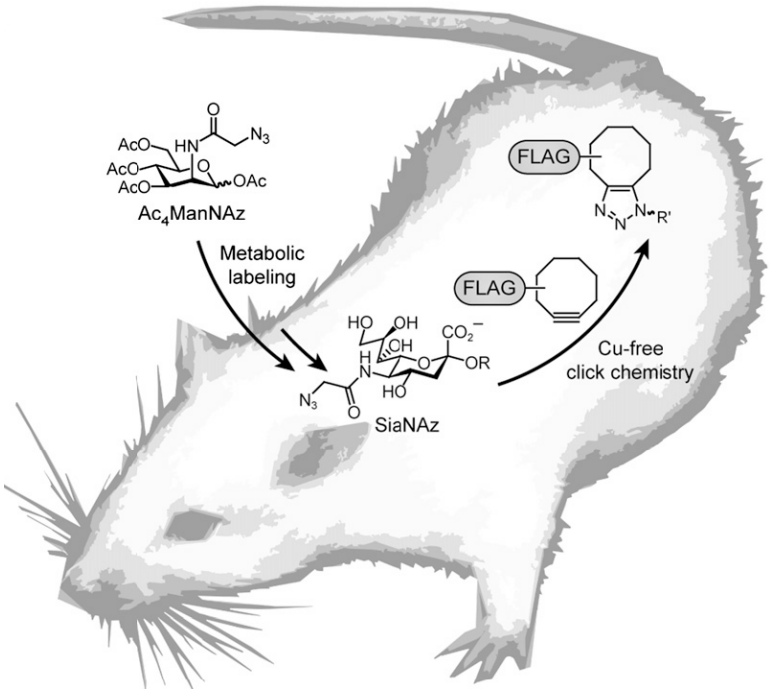

Figure 2. Technological inspiration for cyclooctyne ligation for formulations (taken from reference 1b)

Nalas and NAWCWCLD paved the way for a new binder system applicable to existing and future formulation systems based on the reaction of cyclooctynes and a suitable diene. As proof of concept was achieved, further development of this novel technology will offer the potential to revolutionize the field of energetic formulations but will also provide an entirely novel method to cross-link or polymerize new materials. The technology produced in this SEED effort will thus have a much broader impact with further investment in development. For example, the reactive system developed in this SEED effort has the potential to react in water, a feature that is impossible with current binder systems. These concepts and other opportunities are discussed later in this report.

MATERIALS & METHODS

The synthetic R&D efforts were conducted using the Mettler Toledo EasyMax™ reaction platform. This reactor system offers the opportunity to screen up to six different reactions in two defined temperature zones. It can be equipped with reaction vessels amenable to mechanical stirring and offers the control and recording of the temperature profile of the reaction. This allowed us to surpass significant synthetic challenges in our

preparation of the cyclooctyne units. A picture of the EasyMax™ system is presented in Figure 3.

Figure 3. Mettler Toledo EasyMax™ system

Using this reaction platform four different syntheses of cyclooctynes were evaluated at Nalas. These routes will be briefly discussed herein.

Route A

The first route was envisioned at Nalas and offered an unprecedented opportunity to rapidly access functionalized cyclooctynes. The strategy focused on a palladium-catalyzed reductive Heck reaction to functionalize cyclooctadiene in order to append the necessary handle to produce our oligomers for the binding reaction (Figure 4). This synthetic transformation has no precedent in the literature, but was deemed worthy of investigating. Initial screenings of this route using various reaction conditions showed mostly unreacted starting materials with a small amount of benzyl alcohol from proto-debromination. The reaction outcome was found to be independent of temperature, phosphine ligand and reaction solvent; all permutations provided only traces of the desired functionalized cyclooctene. This route was abandoned but could be reinvestigated further using various halogenated partners and different palladium or rhodium catalysts in the future. This sequence could offer a totally new avenue to functionalized cyclooctyne motifs.

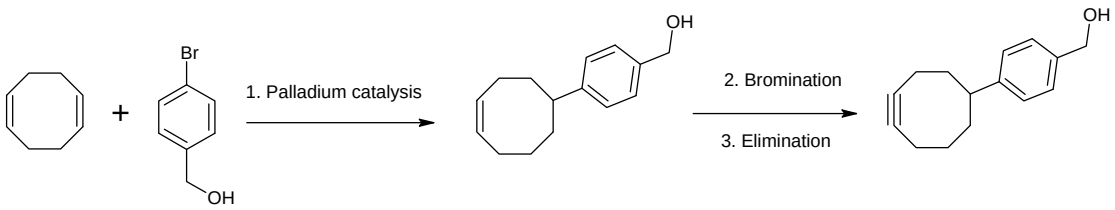

Figure 4. Route to a cyclooctyne monomer via reductive Heck coupling

Route B

The second route builds on the use of rhodium catalysis to functionalize cyclooctadiene via cyclopropanation following a sequence put forth by van Delft.[2] This chemistry was demonstrated on small-scale in the literature and the synthesis was carried through to the final cyclooctyne product at Nalas. As the first two steps proceed in ca. 80% yield, the bromination step occurred in quantitative yield. However, the elimination step provided a complex mixture from which the purification of the final cyclooctyne isomers from the reaction by-products using silica gel chromatography proved very difficult on small scale, forecasting a serious challenge on the multi-gram scale required under this effort. This route was thus not pursued further, as the purification and high cost of rhodium catalysts prevented a cost-effective binder system.

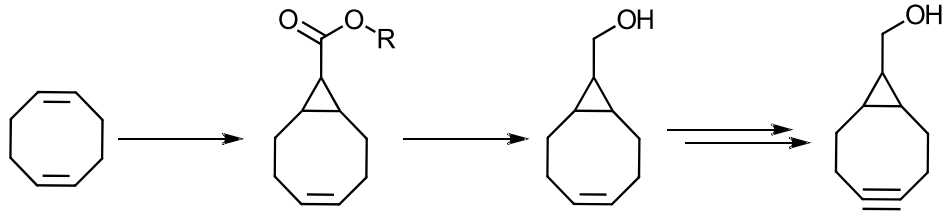

Figure 5. van Delft sequence to a cyclopropyl-derived cyclooctyne

Route C

Nalas also pursued the synthesis of an oxazoline functionalized cyclooctyne. This novel sequence was build on the precedent formation of the cyclooctadiene mono oxide in the chemical literature[3] and featured an unprecedented Lewis Acid-mediated opening of the oxirane with a nitrile. Specifically, our attention focused on using boron trifluoride as the acid with benzonitrile as model substrate. The desired reaction proceeded readily at sub-ambient temperatures and led to the formation of the target oxazoline which was readily isolated in high purity after an aqueous workup. This new oxazoline-functionalized cyclooctene was produced on gram scale. However, our extensive investigation of the following steps revealed that although the bromination seemed to proceed, subjecting the product to the elimination step produced a complex profile where the desired cyclooctyne could only be detected at low levels.

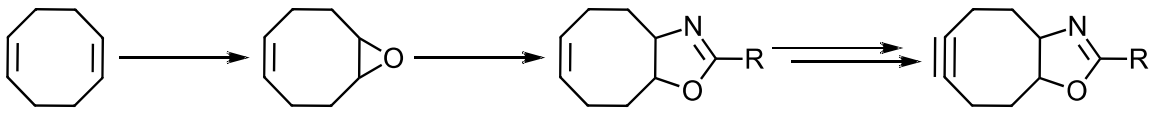

Figure 6. Synthetic route to oxazoline-functionalized cyclooctyne

Route D

Although a precedent existed for this sequence,[4] there is no report of this chemistry on quantities greater than a few hundred milligrams to our knowledge. Nonetheless we sought to evaluate the chemistry and perform the necessary process development to secure the multi-gram quantity of cyclooctyne necessary to support our work. As the published three step sequence starting from cycloheptene was investigated, our yields from the first two steps were similar to the reported values, but we were only able to obtain the target cyclooctyne in small quantity. This important step allowed us to validate the route and confirm that the desired functionalized cyclooctyne had indeed been produced. This step was accomplished by the use of our many analytical instruments, but also by growing single crystals of the cyclooctyne which were resolved with our in-house X-Ray diffraction expertise. It is noteworthy that the X-Ray structure of this compound had never been established.

With a confirmation of the sequence, Nalas optimized the conditions of each reaction and increased the yield of the overall sequence from ca. 20-30% to 70%. Specifically, the first improvement made was to replace the solvent of the reaction from toluene to dichloromethane. This modification was made because the $AgClO_4$/toluene complex is reported to be a sensitive explosive.[5] Moreover, a proper reaction quench was implemented to properly remove the silver salts by filtration and subsequently neutralize the perchloric acid byproduct with aqueous base. Finally, the chromatographic purification step, which was found to be ineffective at removing the problematic cis isomer, was bypassed entirely. The last step of the sequence benefited from an aqueous acid/base extraction, which gave a crude cyclooctyne that did not require further purification. The independent publication of this work is ongoing and will feature the relevant experimental details.

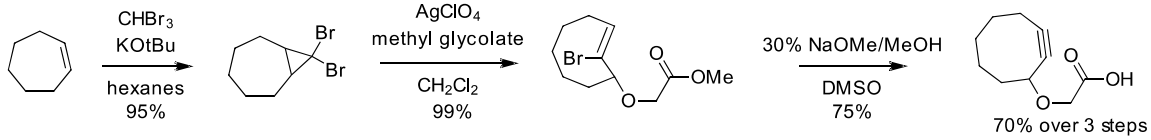

Figure 7. Nalas' optimized sequence to cyclooct-1-yn-3-glycolic acid

It is noteworthy that this material is of importance in other biological sciences for various uses including tagging proteins *in vivo* for spectroscopic analyses. Our production of the largest quantity of this cyclooctyne has set a new ground that will impact other branches of science.

This important work, preceding our official Task 1, was found to be significantly more challenging than expected. Prior to our work, the chemistry of cyclooctyne had been limited to milligram quantities and was not amenable to the multi-gram scale required by our current effort. These challenges forced us to shift our schedule and

impacted our ability to complete all Tasks as planned. Nonetheless, we were able to gather key data that warrants further assessment of our binder system (*vide infra*). Moreover, the synthetic work developed in this effort will pave new ground for many chemical fields.

RESULTS & DISCUSSION

TASK 1 – DESIGN AND PREPARATION OF MONOMERS

Task 1.1 – Preparation of cyclooctyne dimers with different linkers

After preparing gram quantities of the cyclooctyne partner, we took advantage of the glycolic acid moiety to introduce the necessary linker. Although the standard isocyanates-based reagents induce significant toxicity, the isocyanate function allows for the formation of amide bonds which provided highly desirable physical and mechanical properties to the formulations. In order to retain these properties in our novel binder system, we selected our linkers to ensure they would provide the same structural motif and amide bonds. As such, we identified hexamethylene diamine, 2,4-diaminotoluene and 5-amino-1,3,3-trimethyl-cyclohexanemethylamine (isophorone diamine) as suitable linkers for our binder system based on structural analogy to commonly used the diisocyanate curing agents toluene-diisocyanate, hexamethylene diisocyanate and isophorone diisocyanate.[6]

The desired linkers were thus functionalized with our cyclooctyne unit at both terminuses by standard amide coupling technology,[7] thus providing three different partners for the key binding reaction with the functionalized HTPB (Figure 8).

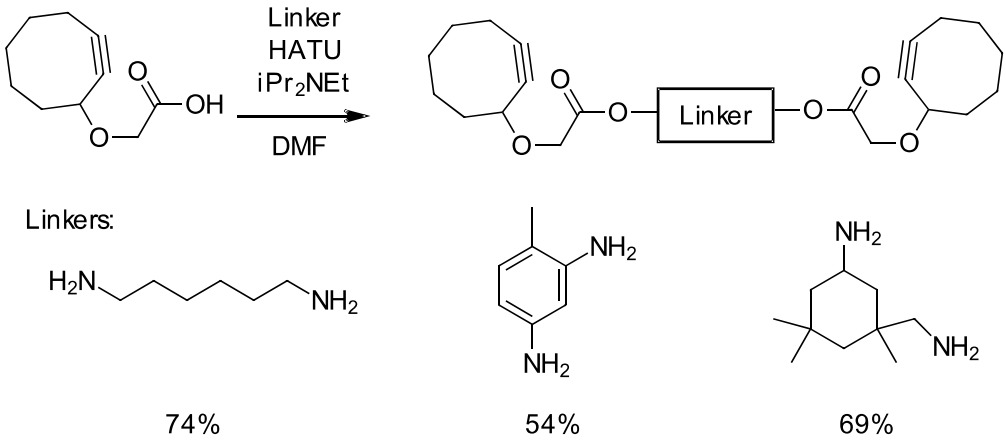

Figure 8. Top: General dimerization of glycolic acid cyclooctyne by amide formation. Bottom: linker motifs, hexadiamine (left), toluenediamine (center) and isophorone diamine (right)

It is noteworthy that these amine motifs are structurally related to different isocyanates used as curing agents. By preserving both the amide functions and their hydrogen bonding potential along with the same carbon backbone of current binders, we hoped to also preserve physical properties of current formulations while offering a new non-toxic alternative bonding event. The preparation of gram quantities of each cyclooctyne dimer thus concluded Task 1.1 of our work plan.

Task 1.2 – Preparation of diene unit

In parallel to Task 1.1, we set out to evaluate the reactivity of the cyclooctyne unit to determine the structural requirements of the diene partner for the desired reaction to occur. Based on discussions with China Lake, it was determined that the coupling reaction should occur in at least several hours at temperatures around 50°C.

The screen of dienes was thus performed using cyclooctyne glycolic acid based on its reactivity in Diels-Alder reactions with a range of dienes. We postulated that the carboxylic acid moiety would not interfere with the desired reaction and should provide a similar reactivity to the amide-linked dimers prepared in Task 1 based on electronic properties and no proximal steric bias. As such, we initially focused on evaluating the reactivity of isoprene, cyclohexadiene, methyl sorbate, *trans, trans*-2,4-hexadien-1-ol and *trans, trans*-mucconic acid at temperatures of 23-80°C (Figure 9). These dienes showed no reaction with the cyclooctyne under any of the conditions tested. After 24-48 hours at 80°C, a new set of signals was observed by ^{1}H NMR in the reaction of *trans, trans*-mucconic acid with the cyclooctyne glycolic acid. This may represent the desired Diels-Alder reactivity; however, it is well outside of the desired temperature envelope for binder curing.

A second series of dienes (anthracene, 2-cyanoanthracene, furan and 1,3-diphenylisobenzofuran) were evaluated for reactivity at temperatures ranging between 23-60°C. The first three remained intact, but the Diels-Alder reaction of 1,3-diphenylisobenzofuran with cyclooctyne glycolic acid was found to be complete within five hours at ambient temperature. The resulting adduct was isolated by precipitation of the water-insoluble sodium salt and characterized by NMR (^{1}H, ^{13}C, COSY, HSQC, HMBC) as the free acid to confirm its identity. The identification of this diene is noteworthy, as the reactivity observed falls exactly in the temperature range and timeline required for its implementation in formulations.

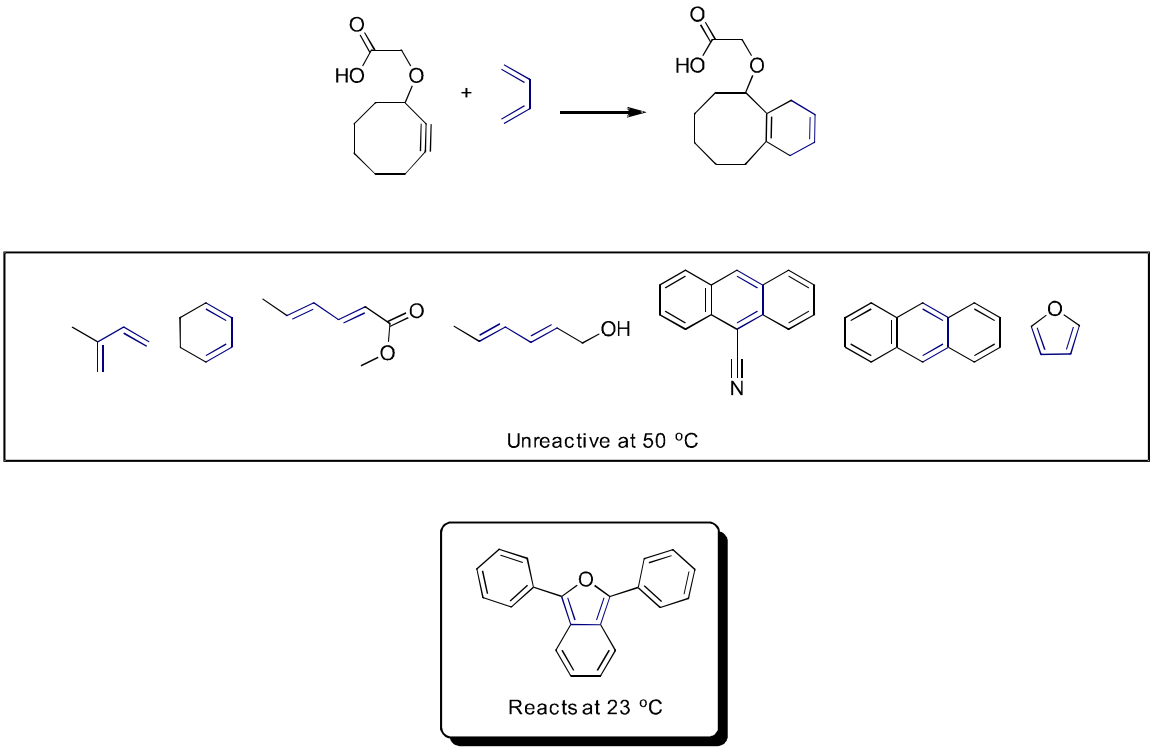

Figure 9. Screen of dienes for the coupling of cyclooctyne glycolic acid via Diels-Alder cycloaddition

The identification of 1,3-diphenylisobenzofuran as suitable diene prompted us to reevaluate our strategy for the incorporation of the new binder into formulations. We sought to attach the diene unit to the hydroxyl functions of HTPB via non-toxic covalent chemistry. This would allow for the incorporation of this new polymer into various HTPB-based formulations, which would be subjected to cross-linking/curing by the addition of the cyclooctyne dimeric units currently under preparation. This strategy would allow potentially preservation of the formulation properties provided by the HTPB while using the same equipment and process as currently in function.

The identification of a diene unit offering the desired reactivity prompted synthetic efforts towards the preparation of an analog possessing a synthetic handle that would allow its incorporation onto HTPB. Although simple in concept, this task ended up being another significant problem albeit successfully solved. Isobenzofurans seemed a likely candidate since they are commonly used in biological systems due to their high fluorescence, but we rapidly realized that the literature had very few reliable precedents for such an endeavor. In addition to very toxic reagents being used, low yielding lengthy sequences plagued the production of functionalized isobenzofurans.

After considering various synthetic targets and routes, it was discovered that the best position for the necessary synthetic handle was on one of the pendant phenyl rings. Based on literature precedents, a route based on a chemoselective Grignard addition was evaluated (Figure 10). Unfortunately, the key Grignard addition did not work as disclosed despite repeated attempts. Moreover, experimentation with alternative conditions was also met with failure.[8] It was determined that the close proximity of the ketone was the root cause the problem, and that this arrangement of functional groups had to be avoided.[9]

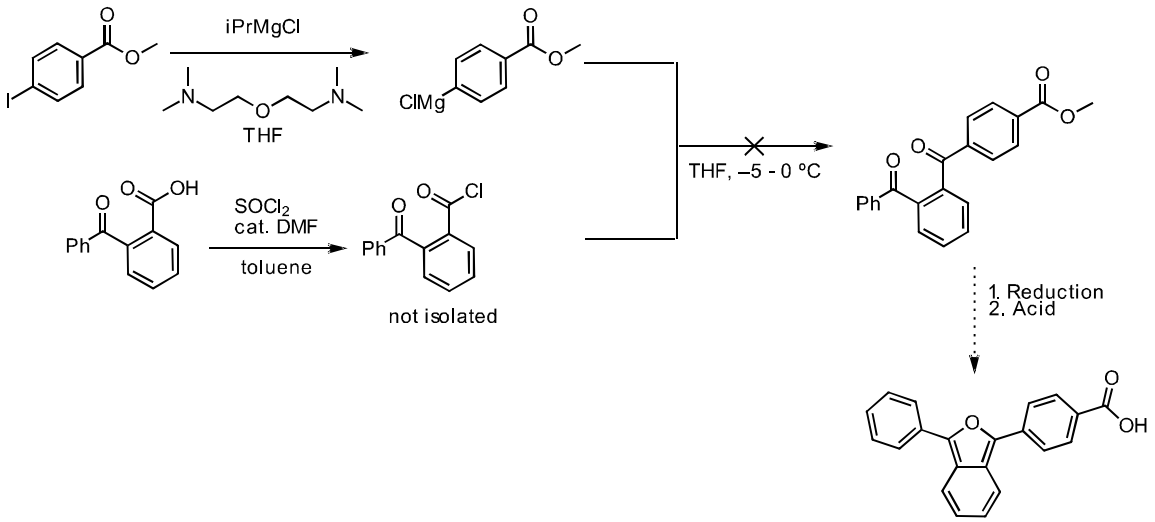

Figure 10. Unsuccessful strategy for the preparation of the functionalized isobenzofuran

After unsuccessfully assessing multiple published sequences, we decided to invent a novel method to produce these compounds. Our efforts led to the establishment of a novel high yielding 3-step route to these materials from 4-iodo methylbenzoate (Figure 11). At this point, we are applying for a patent for this new technology, which will be followed by a publication in an international peer-reviewed journal.

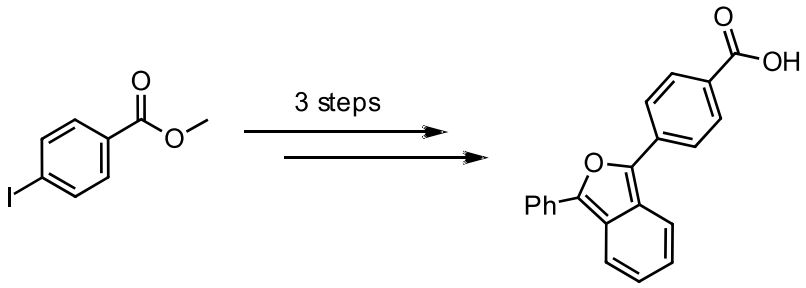

Figure 11. New method for the 3-step production of the desired functionalized isobenzofuran

Due to the significant challenges associated with the preparation of the requisite diene unit and the pressing schedule for our efforts under this SEED, about one gram of the desired diene was preliminarily produced using our novel protocol.

Following its preparation, many conditions were examined for its incorporation onto HTPB. It was found that the derivatization of the carboxylic acid moiety as an acyl chloride was necessary to obtain any functionalization. Moreover, using oxalyl chloride

at reduced temperature was the only effective activation method that would not degrade the isobenzofuran unit. The corresponding acyl chloride was thus coupled to the terminal hydroxyl functions of HTPB under standard conditions (Figure 12).

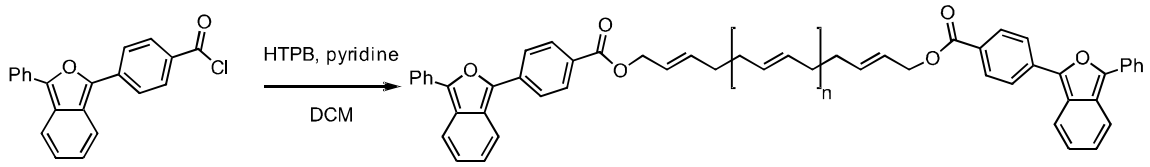

Figure 12. Incorporation of the isobenzofuran motif onto HTPB

It is noteworthy that this functionalization step was not fully optimized due to time restrictions. Characterization of the new HTPB to determine loading levels was also challenging and will have to be addressed during future scale-up efforts. Nonetheless, multi-gram quantities of diene-functionalized HTPB were produced. The evaluation of the reactivity of this new HTPB is presented in Task 2.3.

Task 1.3 – Identification of optimal operation conditions for polymerization

During ongoing efforts at preparing a functionalized isobenzofuran (Task 1.2), we sought to confirm the reactivity of the linked-cyclooctyne with the isobenzofuran. We believed that the Diels-Alder reaction (i.e. binding reaction) between these two components would also establish a proof of concept for the real reaction between functionalized-HTPB and a cyclooctyne dimer.

For this reason, we subjected the hexamethylene diamine cyclooctyne dimer to a reaction with commercial diphenylisobenzofuran (Figure 12). The desired reaction was found to occur over several hours when using an organic solvent at ambient temperature, thus confirming our hypothesis and further establishing the validity of our binding strategy. The product of the reaction was isolated by flash chromatography and fully characterized to confirm the results.

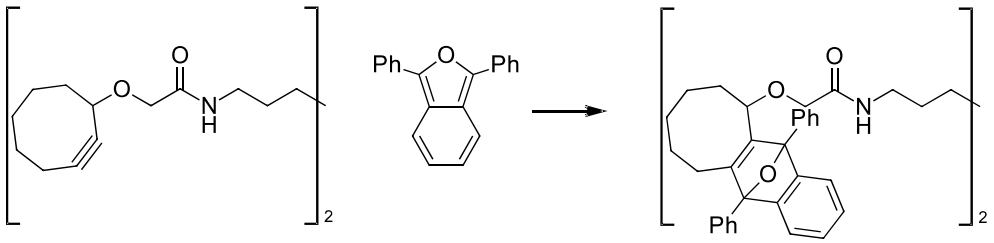

Figure 13. Proof of concept for the reaction of a cyclooctyne dimer bearing hexamethylene diamine as linker

The observed reactivity suggested that the desired binding of the cyclooctyne dimer with the diene-functionalized HTPB should again occur within the current operating conditions used by formulators (i.e., 50°C over a few hours). This result thus allowed us to conclude our efforts on Task 1.3 with the intent to determine the optimal linker in Task 2.3.

Task 1.4 – Evaluation of glass transition temperature

The glass transition temperature (Tg) of the functionalized HTPB is of significant importance for the low temperature performance of energetic formulations. Maintaining elastic mechanical response at low temperatures is particularly critical for rocket propellant applications since fixed and rotational wing aircraft often require operation at -65 °F (-54 °C) and -45 °F (-43°C), respectively. While commercially available R45M HTPB from Cray Valley has a glass transition of -75 °C, the isobenzofuran-functionalized HTPB produced at Nalas was found to have a Tg of -70.1 °C. This slight variation of the glass transition is in line with our expectations, and still within the desirable range for use in formulations.

TASK 2 – PROOF OF CONCEPT WITH ENERGETIC MATERIALS – ASSESSMENT OF COMPATIBILITY

Task 2.1 – Evaluation of compatibility of binder system with formulation materials

With all components in hand we have evaluated their compatibility with common formulation ingredients. This was accomplished by separately analyzing the new binder components, namely the cyclooctyne dimer and the diene-tagged HTPB, with representative ingredients by DSC and TGA. Following the recommendation of our expert collaborators at China Lake, these tests featured ammonium perchlorate (AP) as the energetic material and dioctyl adipate (DOA) as the plasticizer component. The analyses were designed to test the thermal compatibility by separately mixing components in pairs. Accordingly, hexamethylene linker on the cyclooctyne and diene-

functionalized HTPB were found to produce stable mixtures with DOA, and AP. Interestingly, DSC tests of our new cyclooctyne and HTPB with AP actually shifted the decomposition of AP to higher temperatures (Figures 14-15). This very interesting feature is at odds with the effect of standard binders, which typically shift the decomposition to lower temperatures.

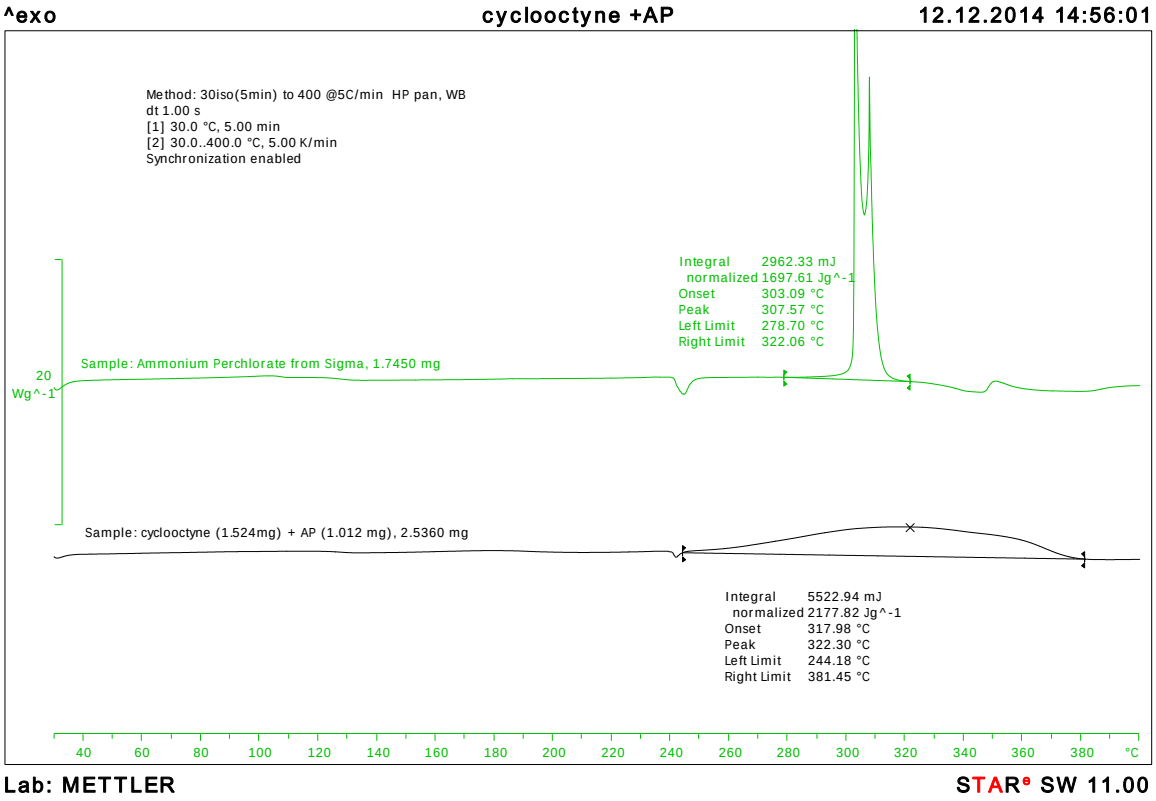

Figure 14. DSCs in gold pans of an AP standard (top) and cyclooctyne-AP mixture (bottom) at 5°C/min.

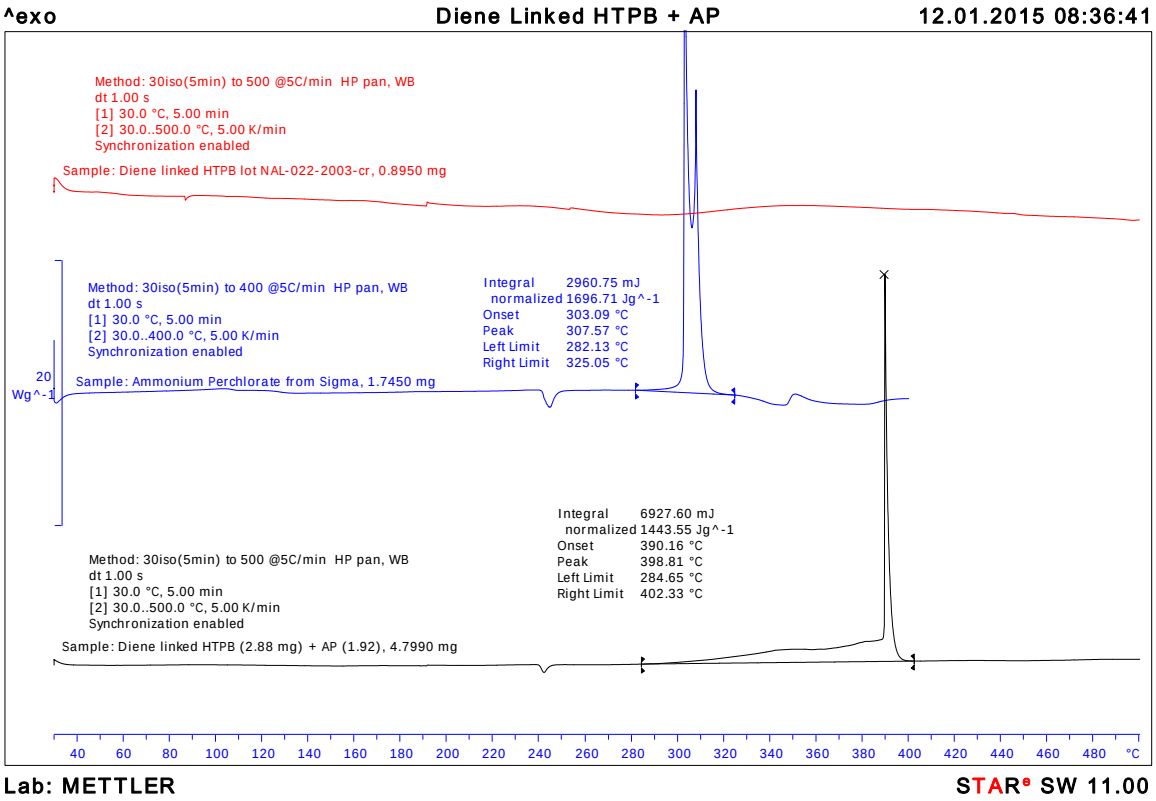

Figure 15. DSCs in gold pans of the diene-HTPB (top), AP standard (middle) and diene-HTPB/AP mixture (bottom) at 5°C/min.

Although the DSC of the cyclooctyne with AP showed a broadening of the decomposition, this behavior is not atypical and our experts at China Lake concluded in a stable system. Accordingly, this behavior is fairly common when performing a first analysis of novel AP mixtures at this scale using DSC. Such a behavior is not expected with a more uniformly mixed sample. Complementary data for these studies is presented in the Appendix.

Task 2.2 – Determination of binder solubility

The solubility of our binder system was evaluated at Nalas following recommendations by China Lake. Accordingly, it was determined that a full quantitative solubility study was unnecessary at this point. The evaluation of the component's solubility in DOA was the key point deserving evaluation, as insoluble components would force the use of co-solvents in the testing of the formulation planned in Task 3.

Following proportions recommended by China Lake, the functionalized HTPB was found to fully dissolve in DOA at ambient temperature, reminiscent of commercial

HTPB. The addition of isophorone-linked cyclooctyne as model cyclooctyne to this mixture led to a homogenous phase in which all components were fully dissolved (Figure 16).

Figure 16. Solution obtained with 48% wt functionalized HTPB, 45% wt DOA and 7% wt isophorone cyclooctyne at ambient temperature

The conclusion of this test is that the components of our new binder system display suitable solubility in DOA and should be tested in a formulation. As a more extensive solubility study will be part of future work, the data gathered in this test was sufficient to pursue our formulation studies given the limited supplies of material at hand.

Task 2.3 – Determination of optimal linker for use in formulation

As three different linkers were incorporated with the cyclooctyne unit, we sought to evaluate their respective reactivity with the functionalized HTPB. Such a test constituted the final validation of our new binder system prior to its evaluation in a real formulation. Following our original hypothesis, we envisioned that the nature of the linker would imbue the polymer with different physical and mechanical properties after reaction. Interestingly, the incorporation of the isobenzofuran motif into HTPB also resulted in a drastic change of color due to fluorescent properties of the functional group. The diene component thus provides a convenient indicator of the reaction progress, as the disappearance of the yellow tinge correlates with the consumption of the isobenzofuran through binding. Comparative reactions were thus performed with the three cyclooctyne analogs and the diene-functionalized HTPB. Both components were put in contact neat and heated to 50 °C overnight. While toluene diamine and isophorone diamine linkers both gave putty-like consistency, the hexamethylene diamine linker was observed to give

a more liquid aspect (Figure 17). This is consistent with the longer chain of this linker, which possesses a greater degree of movement even after cross-linking.

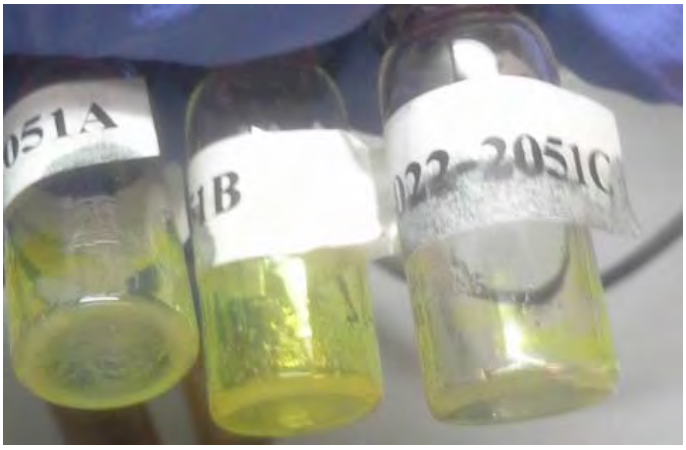

Figure 17. Picture of polymerization reactions of the different linked cyclooctynes with the functionalized HTPB after 16h at 50°C. Toluene diamine linker (left), hexamethylene diamine linker (middle) and isophorone diamine linker (right)

The samples were further kept at temperature for a week, following standard formulation protocols, and re-analyzed visually (Figure 18). The polymer with the hexamethylene diamine linker remained a sticky oily solid with a very soft consistency. The properties of the material featuring a toluene diamine linker were better, where a sticky elastic gum was formed. Finally, cross-linking with the isophorone diamine-substituted cyclooctyne gave a malleable rubbery elastic material. The gum was not very sticky, which is a desirable property.

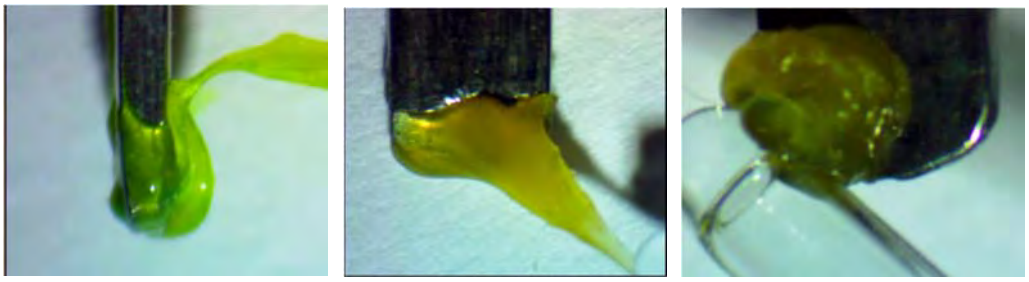

Figure 18. Pictures of the gum stocks after curing for one week at 50°C. Hexamethylene linker (left), toluene diamine linker (middle), isophorone linker (right)

The gum stock obtained from the reaction of the functionalized HTPB with the isophorone-linked cyclooctyne displayed very promising physical properties for rocket

propellant formulations. These experiments further confirmed our hypothesis regarding the influence of the linker on the physical properties of the polymer. Interestingly, this simple study opened up new opportunity for the application of the binder in various scenarios depending on the properties desired. The isophorone-cyclooctyne unit was thus selected as the leading candidate for testing in a real propellant formulation. It is noteworthy that the cross-linking of our novel binder system occurred at the desired temperature range and timeline, and provided a polymer with the desired consistency. We believe this validation constitutes a major step forward for our strategy aimed at integrating this new binding mode into various formulations.

TASK 3 – APPLICATION OF BINDER TO EXISTING FORMULATION

The limited supplies of our binder partners and delays in R&D timelines occasioned by synthetic challenges have limited our China Lake team in their ability to fully assess the binder system.

Task 3.1 – Small scale formulation conducted by RAM

Nonetheless, the binder system was evaluated for the preparation of a 5-gram AP-based rocket propellant formulation. Towards this end, a formulation with AP of different particle sizes (200 μm and 20 μm) was tested with a composition comprised of 80% by weight AP with a 2:1 ratio of coarse to fine particles, 12% functionalized HTPB and 6% biscyclooctyne isophoronediamine. The formulation was plasticized with 6% DOA for a total plasticizer-to-polymer ratio of 0.5. The propellant formulation was mixed using a LabRAM mixer (Figure 19), and was found to have great flowing properties when compared with other standard formulations performed in the same equipment at China Lake.

Figure 19. Picture of Resodyn LabRAM benchtop resonant mixer (left) and resulting propellant formulation with new binder system (right)

The mixture was then set to cure at 60°C for a few days; however, the mixture failed to completely cure into a stiff rubber-like composite after several days at temperature. In light of our small scale assessments, we attribute this result to an incomplete functionalization of the HTPB, which led to a lower degree of cross-linking and thus lower rigidity after curing. Nonetheless, the preliminary results for the application of our new binder system in this formulation looks so far very promising, as the problems obtained could be easily solved in our next scale up of the functionalized HTPB.

Task 3.2 – Vacuum thermal stability test

This Task was not undertaken due to the incomplete binding observed in Task 3.1.

Task 3.3 – Mechanical properties evaluation/comparison to baseline formulation

This Task was not undertaken due to the incomplete binding observed in Task 3.1.

TASK 4 – EVALUATION OF SENSITIVITY & PERFORMANCE

The bulk of this Task was not completed due to limited supplies of binders and delay in our timelines. A full evaluation of the sensitivity and performance of a formulation is planned for the next phase of this program.

Task 4.1 – Small scale safety testing (impact, friction, ESD)

The impact, friction and electrostatic discharge sensitivity of a formulation was not completed due to the incomplete binding observed in Task 3.1.

Task 4.2 – Determination of theoretical performance by thermochemical calculations

This Task was not undertaken due to the incomplete binding observed in Task 3.1.

Task 4.3 – Evaluation of rheological properties

This Task was not undertaken due to the incomplete binding observed in Task 3.1.

TASK 5 – PRELIMINARY ASSESSMENT OF ENVIRONMENTAL IMPACT

As discussed in the Background section, the components of our new binder system have already demonstrated their benign nature to living systems. Key for this Task is the consideration of both reaction partners for their impact on the environment and human toxicity. The individual assessment of the toxicity of both the functionalized HTPB and cyclooctyne unit is discussed.

The toxicological profile of our functionalized HTPB can be broken down to its components: the activated diene unit and HTPB itself. Isobenzofurans are routinely used as fluorescence probes in cell assays without the disruption of biological functions.[10] Phenyl-derived isobenzofurans, as developed in our work, are considered non-toxic based on their MSDS.[11] However, as this component is only a small fraction of the functionalized HTPB, the toxicological profile of HTPB itself is more relevant. Accordingly, HTPB is categorized as non-toxic to humans and to the environment, with an NFPA health rating of 0.[12] This analysis thus supports that the functionalized HTPB partner is innocuous to living organisms.

A plethora of cyclooctyne analogs have been extensively studied in the context of copper-free click chemistry. The various cyclooctyne cores have thus been adapted to amide linkers, such as in our system, for their use as fluorescence probes in a series of animal cells and organisms. These cyclooctyne derivatives were found to be stable in aqueous solutions and in the presence of 2-mercaptoethanol, suggesting that these cyclooctyne motifs will not cross-react with biological functions.[1a] When injected directly into cells at biologically high concentrations, such probes demonstrated no cellular toxicity in the various models studied at all concentrations.[13] These findings were confirmed by the thorough evaluation of cell morphologies and by propidium iodide

staining, a well-accepted viability assay used to differentiate necrotic, apoptotic and normal cells.[14] The results for one of the cyclooctyne probes tested is presented in Figure 20, where the emission of fluorescence confirms the normal activity of the cell two days after the injection of a 10 mM solution of a cyclooctyne analog. These previously conducted tests thus lead to the conclusion that cyclooctyne analogs demonstrate no apparent toxicity.

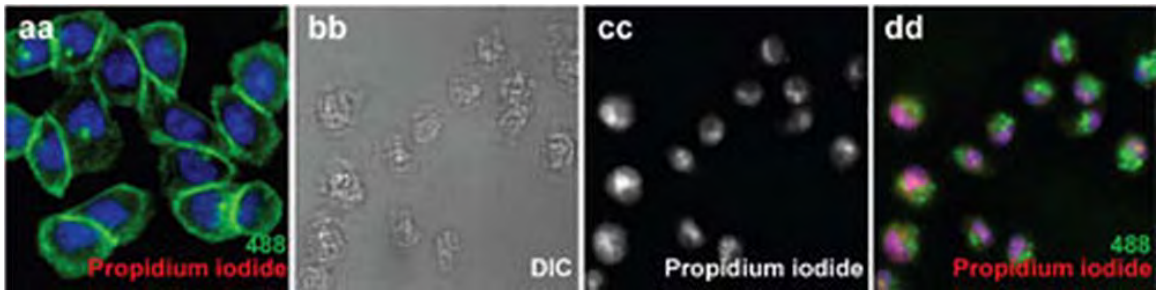

Figure 20. Propidium iodide test of different strands of live cells incubated with a functionalized cyclooctyne. Data taken from reference 1a.

Both the functionalized HTPB and the cyclooctyne dimers are highly lipophilic, further limiting their potential absorption in biological systems. Accordingly, similar cyclooctynes have been calculated to have considerable hydrophobicities, a property that compromises their bioavailability.[15]

Experimental testing of the binder system was not evaluated as we originally planned, due to material restrictions consequent to the synthetic challenges that were surmounted. Nonetheless, the strong precedents and established non-toxicity profiles suggest that our binder system can be considered compatible with the environment and living organisms. Further toxicity testing should be performed in the next phase of this research to quantify compatibility with biological functions.

CONCLUSIONS & IMPLICATIONS FOR FUTURE RESEARCH

A new binder system was produced and successfully tested under this SEED effort. As Nalas was forced to innovate to produce the requisite components, we developed the chemistry to the cyclooctyne and produced it on gram scale. This unprecedented feat will most certainly have an impact on many fields, including cell biology. Innovation was also required for the preparation of the functionalized isobenzofuran, and our efforts have led to an entirely novel method to produce these compounds. Given their significance as fluorescence and peroxide probes, Nalas is envisioning patenting the technology. This diene was attached to HTPB currently used in formulations using mild conditions.

The components displayed stability vs. AP and DOA along with good solubility in the latter. Beyond showing compatibility with energetic materials and common formulation ingredients, we confirmed our hypothesis that the linker unit can influence the physical properties of the final cross-linked polymer. An isophorone-cyclooctyne unit was identified to provide the desired physical properties as gum stock after curing under standard conditions.

The individual components of our new binder system are well-known for their compatibility with living organisms. Various functionalized cyclooctynes have even been used as probes in living cells and animals without disrupting biological functions. Our results support reaching a proof of concept for the establishment of a new non-toxic binder system for propellant formulations. Because challenges with the initial synthesis had to be overcome, we were forced to abbreviate our evaluation efforts.

As this program constitutes a great success for a SEED effort, we propose to transition to a full scale effort focused on producing significant quantities of the new binder and thoroughly testing formulations. This effort would allow the comparison of our new binder with existing systems and clear demonstration of its advantages and potential limitations.

Specifically, the production of larger quantities of the binder system will require the optimization of the chemistry and development of processes. For example, the preparation of the necessary quantities of cyclooctyne will require the replacement of the expensive silver salt with a more practical reagent. Such technology is already disclosed in the literature and can be applied directly to our system.[16] Another important parameter to optimize is the functionalization of HTPB with our isobenzofuran motif. As our ability to optimize this reaction was limited during the SEED effort, a complete optimization and quantification of the functionalization will be performed in the next phase of this program.

The optimization of the chemistry will enable the production of larger quantities of material through the development of processes to these materials. The successful, safe and environmentally conscious production of our binder system will require the evaluation of each step from an engineering perspective to evaluate the heat of reaction amongst other parameters necessary for transitioning these reactions to a larger scale. This type of development effort is at the core of Nalas' expertise.

The production of multi-gram quantities of the key ingredients will enable the evaluation of formulations featuring our binder system and comparison of them to baseline formulations. A thorough evaluation of the binder will require the completion of the previously planned tasks. These important studies are summarized below, with many of them potentially accomplished with a single batch of propellant.

The vacuum thermal stability of the propellant will be assessed in order to predict the performance in different launch scenarios. Dynamic Mechanical Analysis (DMA) will be used to determine the Tg of the composite formulation. These studies will be performed in parallel with sensitivity studies, which will determine the impact of the new binder on the sensitivity of the formulation to stimuli. Next, we plan to proceed to tensile testing of "dog bone" samples. A variety of sizes of dogbone tensile test specimens are possible, but the best size to use for a rocket propellant that incorporates large particles (100 – 400 µm) of oxidizer, such as our current study, is the full size JANNAF C specimen. China Lake's LabRAM II mixer will be used to produce approximately 1 kg of propellant per batch, each of which would yield 9-10 full size JANNAF C dogbones. For a tactical rocket propellant, hot, cold and ambient temperatures are tested at three different strain rates (0.2, 2.0 and 20 in/min). A complete study would require running each sample in triplicate to ensure accuracy.

The theoretical performance of the energetic formulations will be determined by thermochemical calculations using the Cheetah or Propellant Evaluation Program at China Lake. The density and heat of formulation of these compounds will be measured with helium pycnometry and bomb calorimetry and will be input into the thermochemical codes. Experimental performance testing will require additional resources that could be allocated if follow-on research continues under SERDP. The experimental performance testing could be conducted specific to typical tests for either the propellant or explosive formulation of interest. For example, window bomb and small-scale motor firing could be conducted on a propellant formulation, while detonation velocity and CJ pressure could be conducted for an explosive formulation.

The rheological properties of the binder pre-polymers, which determine the processability of energetic mixtures formulated with the new binder system, need to be fully evaluated at China Lake by rotational viscometer measurements. The initial quantity available evaluated at China Lake was too small to get an accurate measurement of material viscosity, but our team has estimated the material's viscosity at around 10 kilo poise at approximately 110 °F by visual inspection and based on their extensive experience. Once more material is made available, we will test the material viscosity as a function of time at the curing temperature to determine the working time or "pot life" of the new propellant.

Further work could also feature combustion analysis performance testing. Initially, this task would start with strand burner analysis of a 500-gram batch of propellant cut into multiple strands that are burned at pressures ranging from 500 psi up to 5000 psi. The combustion analysis could culminate in a series of small rocket motor firings at the

same pressures as those tested using the strand burner. China Lake is equipped with a small rocket motor that has been used in the past as a lot acceptance test (LAT) for large strategic systems. Each test uses about 70 grams of propellant per motor, and we would want to cast and fire at least 7-8 motors at pressures ranging from 500 psi up to around 3000 psi to collect the data necessary to compare propellant formulations with our new binder.

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NALAS Engineering Services, Inc.

85 Westbrook Road
Centerbrook, CT 06409
860-581-8477
www.nalasengineering.com

APPENDIX

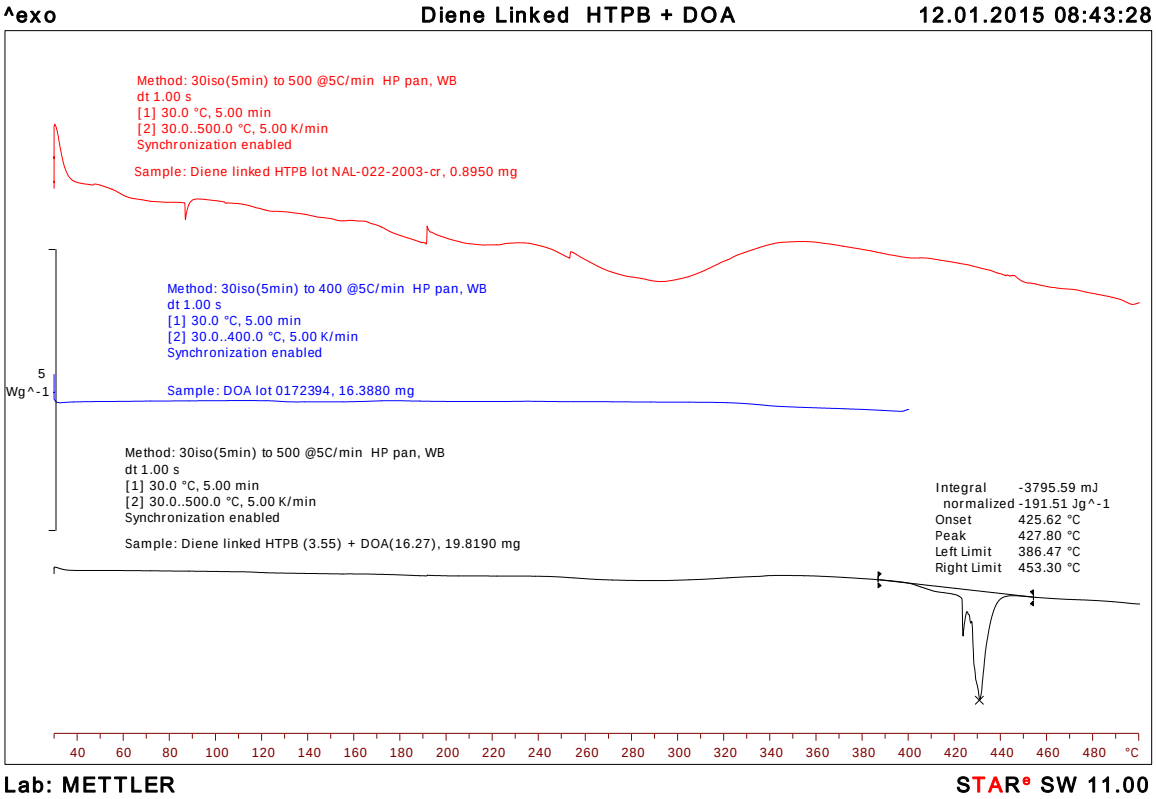

Figure 21. DSCs in gold pans of the diene-HTPB (top), DOA standard (middle) and diene-HTPB/DOA mixture (bottom) at 5°C/min

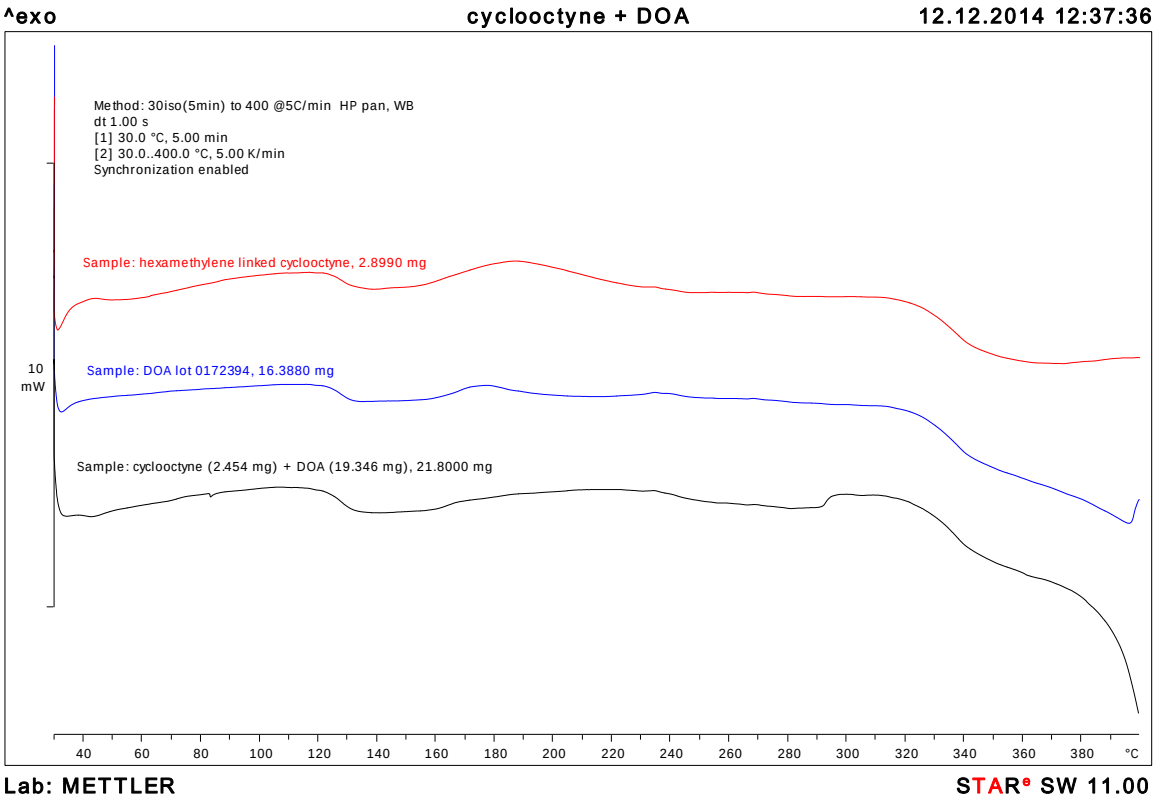

Figure 22. DSCs in gold pans of the cyclooctyne (top), DOA standard (middle) and cyclooctyne/DOA mixture (bottom) at 5°C/min

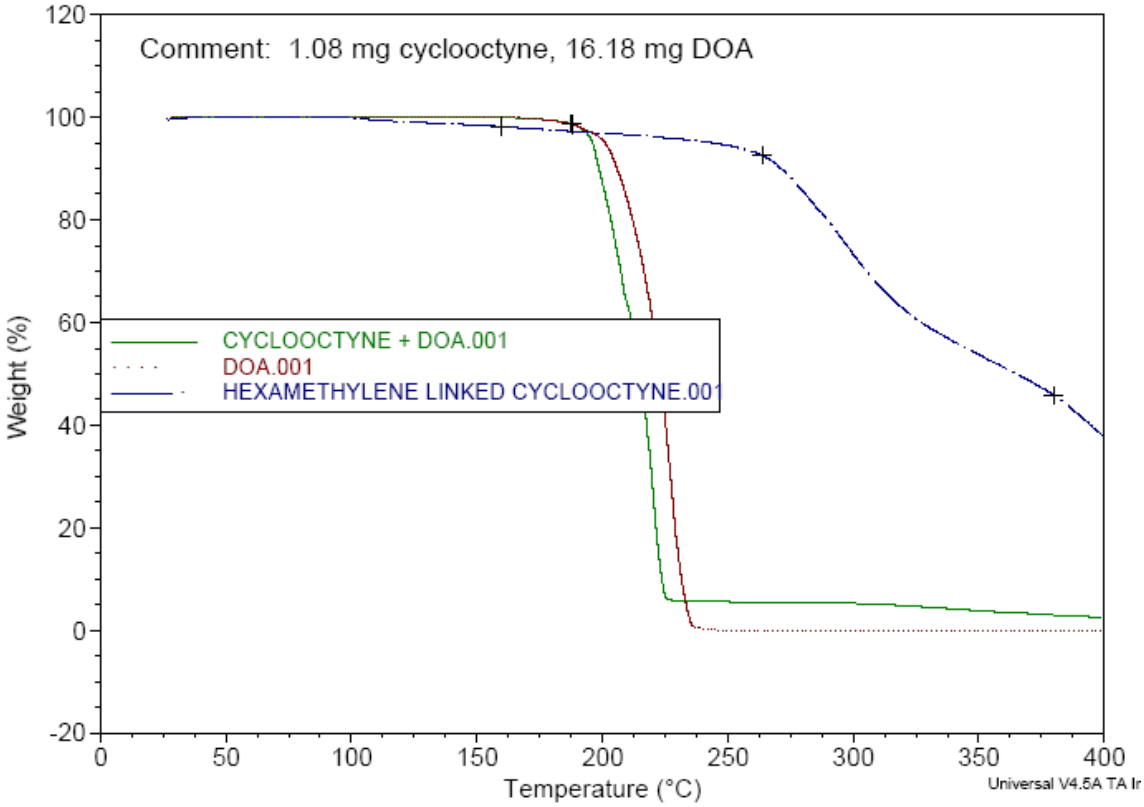

Figure 23. TGA of cyclooctyne/DOA mixture (green), DOA (red) and cyclooctyne (blue) at 5°C/min

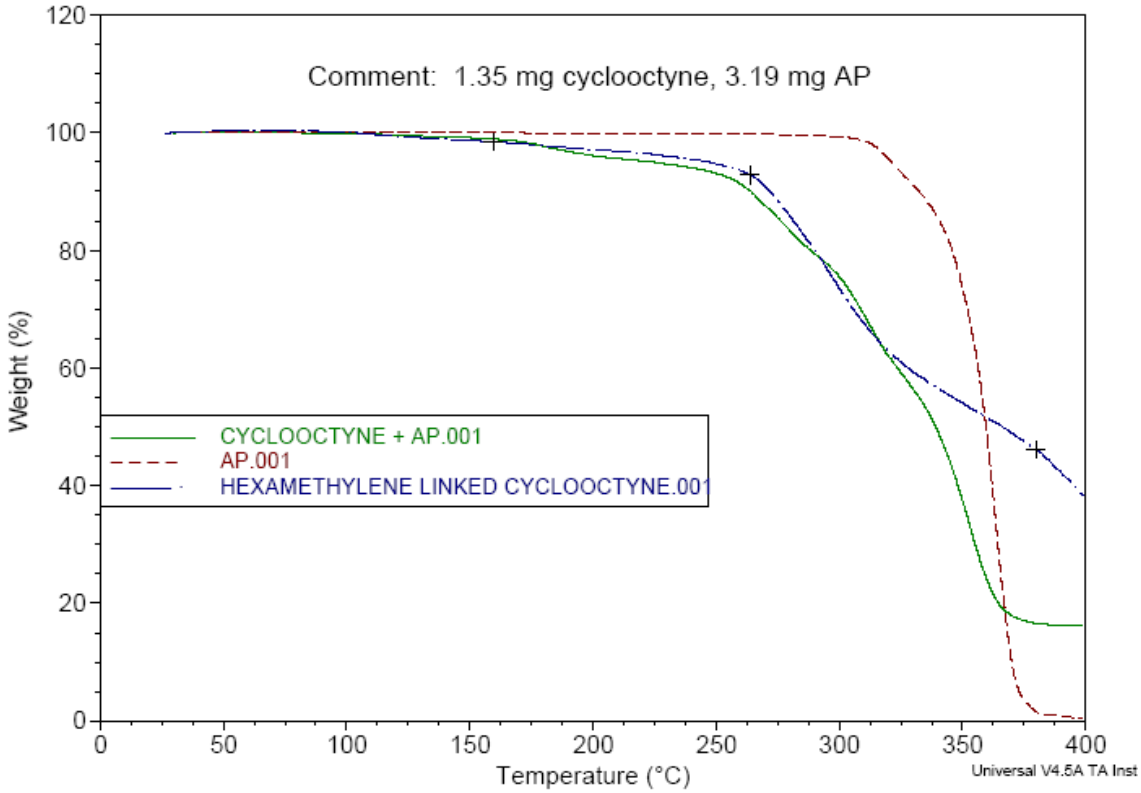

Figure 24. TGA of cyclooctyne/AP mixture (green), AP (red) and cyclooctyne (blue) at 5°C/min