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Flexible polyurethanes, renewable fuels, and flavorings from a microalgae oil waste stream

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Renewable polymers have become an important focus in next-generation materials, and algae biomass offers an environmentally low-impact feedstock that can serve multiple uses. This study aims to develop a scalable methodology for production of microalgae-based polyols for polyurethane synthesis from waste oils derived from algae biomass. Following separation of omega-3 fatty acids from algae oil, residual oils can offer valuable building blocks for petrochemical replacements. However, unlike vegetable oils, algae oils contain organic contaminants, including photosynthetic pigments and hydrophobic cofactors that can complicate preparative methodologies. Here we convert and purify waste streams from omega-3 depleted *Nannochloropsis salina* algae oil, with major components consisting of palmitic and palmitoleic acid, into azelaic acid (AA) as a building block for flexible polyurethanes, with a simultaneous production of heptanoic acid that was subsequently converted to flavor and fragrance. Conversion of free fatty acid mixtures into a soft soap allows extraction of organic contaminants, and urea complexation provides isolated palmitoleic acid, which was subsequently ozonolyzed to produce AA and heptanoic acid. Bio-based polyester diols were prepared from AA via esterification to a provide polyol as a monomer for flexible polyurethane foam applications. The heptanoic acid co-product was used to produce the flavoring agent methyl heptanoate and decarboxylated to produce hexane as a renewable solvent. This scalable process can be performed on oils from multiple algal species, offering valuable monomers from a highly sustainable source.

To avoid fossil carbon use, renewable resources that offer the next generation of transportation fuels and chemical feedstocks have been studied in recent years [1,2]. Although plant oils are known for low toxicity, renewability, and biodegradable properties [3,4], use of food crops poses other problems, including high arable land, water, and nutrient use. They also present a competition between biofuel feedstocks and food production [5]. Algae biomass has experienced growing interest as a future source for producing sustainable fuels and materials due to fast growth rate, flexible habitat preferences, and substantial yield [6]. Algae produce more unsaturated fatty acids compared to conventional vegetable oils, which have useful applications to high-value products[7]. In addition, residual microalgae biomass, such as proteins, can be extracted and transformed to high-value biobased products, such as polymers [8]. Algae can be rapidly cultivated on large scales and need not consume arable land or fresh water [9]. One of the major challenges of algae production has been to identify strains with the highest growth rate, lipid content, and lipid productivity for scalable production [10]. Identifying the highest and best use of algae oils will be important to ensure sustainability of the market, and omega-3 fatty acids from microalgae currently offer a high-value product within a growing nutraceutical market [11]. *Nannochloropsis* strains of green algae offer high titers of eicosapentaenoic acid (EPA, C20:5), roughly 25% of total lipid content, and we reasoned that other high value applications could be explored with the 75% of residual fatty acids. As an application, we identified polyurethane (PU) foam to offer a promising market that is predicted to show continuous growth in coming years, from a USD 54.2 billion in 2018 to over USD 79.8 billion predicted by 2023[12]. Without fundamental change, this rapid upward trend of global plastic demand is predicted to offset or reverse any decrease in petroleum demand from the use of renewable energies by 2050[13]. Additional co-products from this process, which include renewable fuels and fragrances, have significant market value [14].

We previously established and developed a large-scale production system for cultivation of a variety of microalgae strains to produce biomass in both photobioractors and open ponds[15], and the resulting algae oils have recently been applied to both biofuel production and for polymeric material synthesis[1]. The most abundant components in algae oil are triacylglycerides (TAGs) which can be easily hydrolyzed into saturated and unsaturated free fatty acids, including palmitic acid (C16:0), palmitoleic acid (C16:1), oleic acid (C18:1), and linoleic acid (C18:2). Unsaturations within these fatty acids can be converted into oxygenated functional groups (carboxyl or hydroxyl)[16], which can be valuable for a variety of chemical uses.

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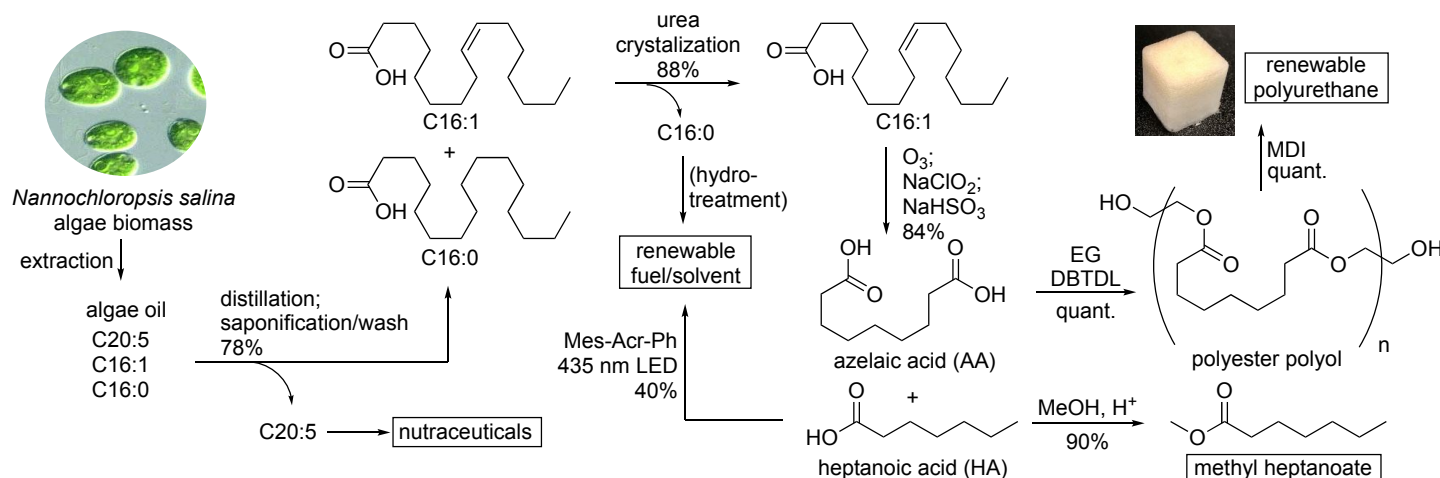
Scheme 1. Pathway to renewable polyurethane, *n*-hexane and methyl heptanoate synthesis from algae biomass.

The oxidative cleavage of olefins of unsaturated fatty acids is industrially carried out by ozonolysis[17] for production of mono- and dicarboxylic acids, which play an important role in a variety of chemical applications including polyesters, polyamides, plasticizers, and pharmaceuticals [18, 19]. The ozonolysis of oleic acid has been shown to be a rapid source of AA and nonanoic acid[18, 19], both of which have applications in polymer manufacturing.

As monomers with multiple hydroxyl group within their structures, polyols serve as precursors for production of polyurethane products, such as flexible and rigid PU foams [20]. Recently, bio-based polyols have emerged as renewable and sustainable monomers for the production of PU products. Previous publications showed the syntheses of several bio-polyols from palm, soya, corn, and castor oils [21, 22], however vegetable oils offer comparatively pure source of TAGs. Algae biomass, by contrast, may be extracted to provide "green crude," which contains significant photosynthetic pigments and other small organic molecules. In order to prepare homogenously pure feedstock for polymer synthesis, we have developed new methodologies for isolation and conversion of algae fatty acids into PU monomers.

Here we demonstrate a scalable approach to synthesize flexible PUs from omega-3 depleted algae biomass through the preparation of polyester polyols (Scheme 1). The procedure requires five stages: purification of fatty acids from omega-3 depleted algae oil; isolation of palmitoleic acid (C16:1) from free fatty acids; synthesis of azelaic acid (AA, C9-dicarboxylic acid) from C16:1; polycondensation of ethylene glycol and AA for polyester polyol synthesis; and polymerization with methylenediphenyl diisocyanate (MDI).

We chose the *N. salina* as a strain for growing algae in large scale because of its established high production of EPA and our ability to grow this strain for high biomass content[23,15]. Following separation of the low boiling point fractions from the omega-3 fatty acids by distillation, the composition of the resulting mixture was identified by GC-MS by converting free fatty acids into fatty acid methyl esters (FAMEs). These peaks were identified using retention time and mass spectral matching from the NIST reference library. The composition of the fatty acids is listed in Figure S3 and Table S1: 8.3% myristic acid (C14:0), 28.9% palmitic acid (C16:0), 58.7% palmitoleic acid (C16:1), 2.3% oleic acid (C18:1), and 1.8% linoleic acid (C18:2). The major constituents are palmitoleic acid (C16:1) and palmitic acid (C16:0). Importantly, the high percentage of palmitoleic acid is advantageous as a rich source of monounsaturated fatty acids. Due to the presence of palmitic acid, with melting point of 62.9 °C, the raw oil is a solid at room temperature that quickly melts to liquid when it reaches temperature of 70 °C (Figure S4a).

In addition to these fatty acids, multiple contaminants, including chlorophyll fragments and carotenoids, were identified in the sample, as evidenced by ^{1}H-NMR (Figure S5)[1, 24-26]. Unlike seed plants, which store primarily triacylglyceride small molecules, organic extracts from microalgae contain a variety of metabolic components that are insoluble in water but freely soluble in organic solvents such as acetone, diethyl ether, tetrahydrofuran and chloroform [27, 28]. The presence of these pigments with conjugated pi systems may decrease downstream reaction efficiency, therefore their removal is a key process in the production renewable chemicals from algae oil. Multiple studies have described elimination of chlorophylls and carotenoids, which include physical absorption, oxidative treatment, phosphoric acid degumming, precipitation, and bleaching, but are not practical for large scale applications[29-33]. Recently, Li et al., published a two-step process that includes bleaching combined with saponification to remove chlorophylls from oil, however a large proportion of oil was also lost [34].

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In this study, we found a practical pathway to not only improve the purity of the algae oil but also to obtain high purified yield with a simple, cost-effective step through saponification. After forming the carboxylate salts of free fatty acids, the obtained soap was washed several times with acetone until the observed filtrate turned from an orange to colorless solution with no UV absorption, indicating that a removal of the pigments was complete. After elimination of pigments, the resulting fatty acids were collected by acidification with aqueous hydrochloric acid. Two classes of soaps could be prepared depending on the cation used. Potassium hydroxide forms a soft soap, retaining a liquid form that is more amenable to large scale acetone extraction. Sodium hydroxide forms a hard soap that requires more solvent and time to remove pigments due to the solid, waxy state.

Treatment of washed soft soap with aqueous hydrochloric acid recovered a mixture of fatty acids with a 85% yield. As shown in Figure S6, the ^{1}H-NMR of purified oil indicated that pigment impurities were eliminated. These pigments can be also accurately detected by fluorescence measurement down to parts per million [35, 36]. As shown in Figure S7, the raw oil displayed a strong emission peak at 668 nm, indicative of π-π^* transition [35, 36], while the purified oil exhibited no emission peak. These color differences between raw oil (Figure S4a) and purified oil (Figure S4b) could also be clearly visualized by eye.

In the next step, we employed a practical method to isolate palmitoleic acid (C16:1) from the purified oil mixture. A variety of reported methods for separation of saturated and unsaturated fatty acids have been published, such as urea inclusion complexation [37, 38], nanoporous membranes [39, 40], ion-liquid solvent extraction[41], molecular distillation[42], chromatography[43], supercritical fluid extraction[44], and lipase concentration[45]. In many of the above-mentioned methods, urea complexation has proven to be a favorable technique for large-scale isolation of mono-unsaturated fatty acids due to its high separation capacity and simple process. Urea and thiourea are well known to form crystalline complexes with hydrocarbons, saturated fatty acids and other straight-chain molecules[46]. This is made possible by a crystalline tube structure formed by urea that creates an inclusion site for linear compounds when packed densely with the guest molecule [47]. Therefore, the straight-chained palmitic acid and other saturated fatty acids within mixtures crystallize with urea, while the presence of *cis*-double bonds in unsaturated fatty acids results in a kinked molecular structure [48, 49], and consequently they cannot enter the hexagonal crystal channel and remain in the solvent. In addition, the urea complexation procedure shown in Figure S2 benefits from facile recycling of solvents (methanol and hexane) and urea using only physical methods (evaporation and crystallization)[37, 38, 49]. Table S1 summarizes the compositions of the initial fatty acid mixture, as well as those of the palmitic and palmitoleic acid after separation by urea complexation.

As can be seen from Table S1, palmitoleic acid content of 86% ,with a yield of 80%, was obtained from the liquid phase of urea complexation, while the palmitic acid content of 85.9% was recovered from the solid phase. Importantly, most of saturated palmitic acid was removed from the unsaturated fatty acid fraction (Figures S8-S9). The palmitic acid is a white solid that melts at 62.9 °C, while palimitoleic acid is yellow liquid at room temperature with a melting point of -0.1 °C. Figure S10 shows the ^{1}H-NMR spectra of the isolated palmitoleic acid C16:1 and palmitic acid C16-0.

We next produced AA through oxidative cleavage of palmitoleic acid with ozonolysis. Ozonolysis is well known to offer excellent selectivity through a simple procedure that avoids toxic waste products from oxidants such as nitric acid, permanganate, or dichromate [17]. The three-step mechanism for ozonolysis of mono-unsaturated fatty acid has been reported [17, 18]. A green, sustainable oxidizing agent, ozone is preferred as a safe alternative to most other oxidants and catalysts [17, 50]. It is important to note that a continuous flow process with ozone have been developed for industrial applications, enabling conversions on the ton scale of product per day[50]. Despite the advantages of ozonolysis, the process can suffer from sub-optimal yields, reported at around 70% for oleic acid [17, 19]. Published procedures report AAs yield of only 20%, although the ozonolysis of oleic acid has been optimized by high temperatures of up to 150 °C for 2h[19]. Most published ozonolysis procedures quench the intermediate ozonide using 30-60% aqueous H_2O_2 [19, 51], initially producing aldehyde and carboxylic acid as products [51], and can result in low yields of mono and di carboxylic acid products[19, 52].

To optimize the quench step, we evaluated a variety of methods, with the goal of complete conversion to carboxylic acid. The combination ozonolysis with oxidation using phosphotungstic acid or tungstic acid and quaternary ammonium salts were found to produce AA at around 70%[53-55]. The obtained yield of AA was identical when ozonolysis was combined with metal oxidation catalysts such as Mo-, V-, Mn-, Co-, Fe-, and Pb- oxides and tungstic acid[56, 57]. Ackman, et al., used *in situ* formed performic acid from H_2O_2 and formic acid incorporation in methanol with oleic acid. Although this approach increased the yield of AA to 95%[58], it is only suitable for small laboratory scale due to safety concerns. Here, instead of quenching with oxidative cleavage once completing ozonolysis, solvent was first removed under vacuum, followed by addition of H_2O_2 and HCO_2H [58]. As the formed ozonides or peroxides are potentially explosive, further workup raised safety concerns.

Recently, a mild one-pot ozonolysis oxidation process of olefins was reported to synthesize carboxylic acids with yields of up to 98%[59]. This process, which employs sodium chlorite as an oxidant, is reported to be a scalable procedure, safely converting over 20 kg of an alkene starting material in a high yield and purity [59]. Therefore, we chose ozonolysis in combination with oxidative cleavage using sodium chlorite to prepare AA from palimitoleic acid C16:1. Here we report a mild one-pot, metal-free process to oxidatively cleave palmitoleic acid to AA and heptanoic acid[59]. Ozonolysis was conducted in an

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aqueous organic solvent (10%H_2O-MeCN), and the generated intermediates were converted to desired carboxylic acids by oxidation with sodium chlorite, which was then followed by a reductive quench with sodium bisulfite. AA was extracted away from heptanoic acid byproduct and hexane solvent with hot water, followed by recrystallization. This ozonolysis - oxidation procedure obtained AA and heptanoic acid in yields of 83%. For mass production of HA and AA on kg scale, a continuous-flow ozonolysis process can be implemented to improve safety through high transfer rates and small reaction volumes[50, 51].

A linear polyester with an average molecular weight of 4000 and a weight average molecular weight of 10,600 was prepared through acid-catalyzed polycondensation of AA with ethylene glycol. A detailed procedure is described in supporting information. The acid number of the polyester polyol was in the range of 1-3, indicating near-completeness of the polymerization reaction. The structure of polyester polyol was characterized by ^{1}H-NMR spectroscopy (Figure S14) and FT-IR (Figure S15). The IR spectrum displayed characteristic polyester polyol peaks at 3500 cm^{-1} and 1730 cm^{-1}, showing OH and C=O stretching from the hydroxyl and ester carbonyl groups, respectively. The double peaks at 2927 and 2852 cm^{-1} were consistent with C-H stretching from hydrocarbons, and the large peak at 1160 cm^{-1} in the fingerprint region was also identified as ester C-O stretching. The broader OH peak in the algae-based polyol maybe because of a combination of lower hydroxyl number and/or residual acid content. H^{1}-NMR indicated the existence of both terminal alcohols and ester groups in the obtained polyol sample. The molecular weight, OH number and acid number are summarized in Table S2.

As illustrated in Figure 1a, the obtained polyol shows a melting point of 25 °C and glass transition temperature (Tg) within the range of -25 to -16.5 °C. A broad and weak endothermic above Tg is due to the crystallization of a short chain in the polyol structure. The polyol exhibits a Tg below room temperature, a characteristic property which indicates its elastomer behavior. A high mobility of short chains in the polyol results in the elasticity at temperature above the Tg[60].

The flexible polyurethanes synthesized here can be described as a low density water-blown foam, similar to those commonly made in the molded and slabstock industries. The foam formulation (Table S3) was chosen to represent a basic flexible polyurethane that can be used in a variety of applications ranging from furniture to automotive cushioning. Resultant polyurethane cubes were fabricated using a stainless steel mold, as described in the supporting information. This allows for standard compression and hardness tests to be done with accuracy and reproducibility. We used a compression-decompression cycle (ASTM D3574-C) to determine how quickly the foam cubes can respond to stress, as well as their load-bearing capacity. This allowed us to understand whether the foam is springy, and returns quickly to its original shape, or exhibits viscoelastic behavior, i.e., 'memory effect'. By measuring the force relative to displacement, integrating the compression curve, subtracting the same integral for decompression, we determined

energy loss. We found that our synthesized polyurethanes gave 51% energy loss, indicating that that they deform easily and cannot quickly revert to their native state, and exhibited a pronounced memory effect. The nine-carbon AA chain could be responsible for this; relative to polyols based on shorter diacids, AA-based polyols have more bonds capable of free rotation and fewer rigid ester bonds. It is important to note that high energy loss is not an indicator of poor performance. In fact, in certain products such as mattresses, this effect is desirable.
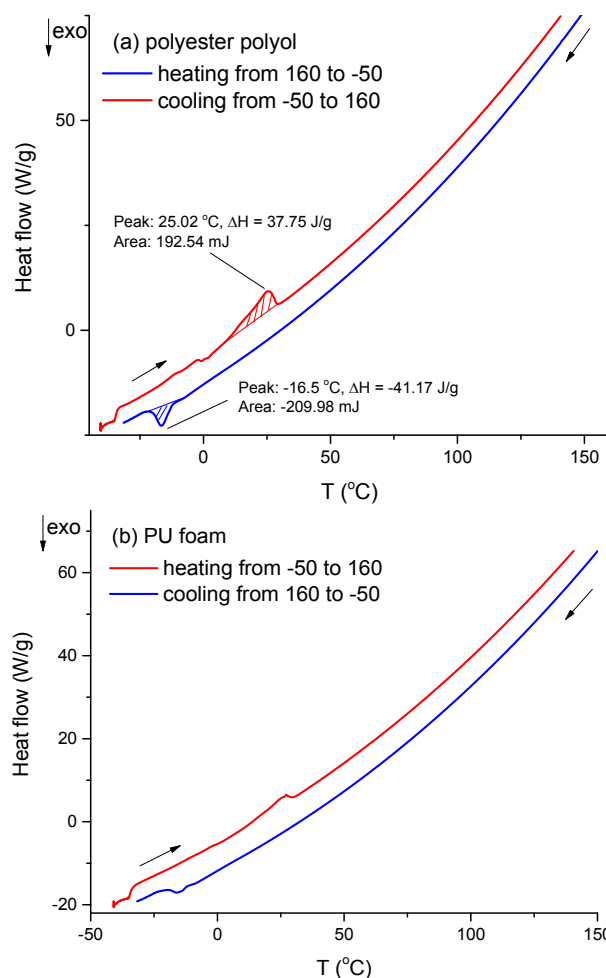

Figure 1. DSC of (a) polyester polyol and (b) polyurethane foam

The DSC curve of resulting algae-derived PU foam is presented in Figure 1b. The curve shows a glass transition temperature of 26.5 °C in a heating scan of PU foam. PU foam is a 3D network structure of mobile soft segments (polyol) and rigid hard segments (MDI). The PU matrix itself is highly cross-linked[61]. Therefore, the flexibility of polyol chains lead to good elasticity of PU foam at room temperature.

The properties of resulting algae-based PU cubes are shown in Table 1. Mechanical properties strongly depend on the degree of crosslinking and network structure of the PU foam. The diisocyanate

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react with algae polyol leads to urethane linkage which generates the hard domain of PU foam because of the possibility of association by hydrogen bond while the high molecular weight and mobility of algae polyol represent the soft domain, resulting in superior mechanical properties. The hysteresis and peak force values trend well with shore hardness, and the more rigid algae PU cubes demonstrate lower energy loss and higher peak force as is expected.

Table 1. Azelaic Polyol Foam Cube Properties

Formula	Avg. Density (kg/m^3)	Avg. Hardness (Shore A)	Avg. Hysteresis (%)	Avg. Peak Force (N)
Photosynthetic PU foam	297 ± 4	30 ± 3	51 ± 3	217 ± 17

The other ozonolysis co-product was heptanoic acid. Methyl heptanoate, an ester from the condensation of heptanoic acid and methanol, is widely used in the flavor and fragrance industry, with a fruity, green aroma and flavor [62-64]. We prepared methyl heptanoate from our algae based heptanoic acid via esterification with a 90% yield (Schemes 2 and S4 and Figure S18). Methyl heptanoate can be applied in a broad range of consumer products, including food, beverages, fragrances, cosmetics, personal care and household products.[63]
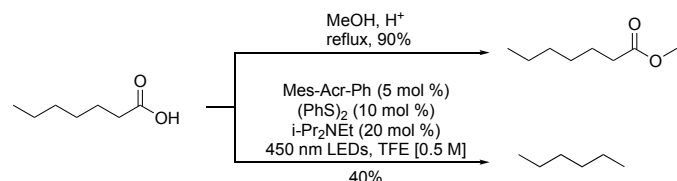
Scheme 2. Synthesis of methyl heptanoate and hexane from heptanoic acid.

In addition, carboxylic acids can be converted to hydrocarbons and other chemicals by decarbonylation, decarboxylation, and deoxygenation [65-68]. These conversion can be challenging due to the requirement for higher temperatures (300-400 ^{o}C) [66], nobel metal catalysts (Pd, Pt), low reaction rates[65] and rapid catalyst deactivation[69]. In recent years, photoredox catalysis have emerged at the forefront of synthetic organic chemistry for decarboxylative functionalizations[70], including decarboxylative alkylation[71], decarboxylative vinylation[72] and decarboxylative arylation[73]. Photoredox catalysis utilizes the energy of light to accelerate a chemical reaction via single electron transfer[74], which avoids the use of traditional chemical reagents that are often toxic or hazardous. A direct organocatalytic protocol for the decarboxylation of carboxylic acids to alkanes has been reported[70]. We applied this procedure with algae-based heptanoic acid (Schemes 2 and S3 and Figure S17). The procedure produced renewable hexane at 40% yield by treatment with 450 nm light and a photocatalyst. Hexane has

innumerable uses, including edible oil extraction, degreasing agents, and as fuel additives. We note, however, in this photoredox catalyst, catalyst is expensive, and the methodology would require significant optimization for further exploration.

To explore the economic value of this process, we can provide a conservative estimate based on the market value of AA and methyl heptanoate. Assuming theoretical (quantitative) yields, palmitoleic acid (16:1) represents ~50% of crude fatty acid waste stream mass, and the ozonolysis process provides 70% AA (by molecular weight). Taking into account our 58% overall yield to prepare AA (over 3 steps), and that we purchase the crude algae fatty acid waste stream for $1/kg (~$0.25/mol), our cost to produce AA is $1.22/mol ($6.48/kg). The bulk price of AA is currently $8.85/mol ($47/kg), which is 7.25-fold value increase. We did not estimate the value of final PU products, given the size and complexity of the PU market. Using similar metrics, our cost to produce methyl heptanoate is $2.02/mol ($14.00/g), and bulk price is currently $72.10/mol ($500/kg). This is a 36-fold value increase, although there is a limited market for these flavors/fragrances.

In summary, AA and HA were successfully prepared from an algae oil waste stream and converted into a flexible PU foam, a bio-based flavoring, and renewable solvent (Scheme 1). After separating EPA for nutraceutical uses from algae oil, the resulting waste stream consists of a mixture of fatty acids is purified and separated into C16-1 and C16-0 in at yield of 85-88% by urea complexation. Subsequent ozonolysis cleavage results in AA and HA, both in 84% yield. This study indicates that AA derived from an algae-sourced waste stream has the potential to support material production of polyester polyols, a precursor for polyurethane synthesis, and renewable solvents. Valorizing a waste stream from omega-3 fatty acid production in this manner, which would otherwise be converted into liquid fuels, provides added cost benefits for algae biomass production. Heptanoic acid co-product can be converted into methyl heptanoate (90% yield), a valuable product for the flavors and fragrances industry, and renewable hexane (40% yield). We plan to optimize and scale these procedures to enable large scale production of AA and HA, where continuous flow ozonolysis will allow achievement of large-scale capacities. The exploration and utilization of algae biomass to prepare high value products offers tools to sustainably transition from petrochemicals to renewable chemical feedstocks.

Conflict of Interest

M.D.B., S.P.M. and R.P. are founders and advisors to Algenesis Materials, a biotechnology company interested in developing renewable materials.

Author Contributions

T.A.P.H., N.N., R.P., S.P.M., and M.D.B. designed the research. N.N. prepared the polyol. S.D.S. and G.G. prepared the PU material. M.T.

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