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"Metafining" of Nerolidol with a Grubbs-Hoveyda Catalyst to Generate High-Performance Sustainable Aviation Fuels

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Abstract

trans-Nerolidol was quantitatively converted into a stoichiometric mixture of 2-methyl-cyclopentene-1-ol and 2,6-dimethyl-1,5-heptadiene via ring-closing metathesis with a 2nd generation Grubbs-Hoveyda catalyst at 0.03 mol% loading. The alcohol was then converted into tetrahydrodimethyldicyclopentadiene isomers (THDMDCPD) by dehydration, Diels-Alder cycloaddition, and hydrogenation. In parallel, 2,6-dimethyl-1,5-heptadiene was hydrogenated to generate 2,6-dimethylheptane (DMH). A stoichiometric mixture of THDMDCPD and DMH (F1) exhibited outstanding fuel properties including density, gravimetric heat of combustion, and viscosity measurements that met the requirements for Jet-A. In addition, hydrogenation of 2,6-dimethyl-1,5-heptadiene in the presence of a heterogeneous acid catalyst resulted in partial cyclization followed by hydrogenation to yield a mixture containing 70% 2,6-dimethylheptane and 30% 1,1,3-trimethylcyclohexane (F2). F2 exhibited an outstanding gravimetric net heat of combustion of 43.69 MJ/kg and a kinematic viscosity of only 1.75 mm^2s^{-1} at -20 °C. The remarkable fuel properties of F1 and F2 suggest that they have applications as sustainable aviation fuels or blendstocks with conventional jet fuel.

Introduction

As the impacts of global warming worsen, researchers around the globe are focused on developing sustainable pathways to fuels and materials that will enable stable economic development while curtailing carbon emissions.[1] Sustainable aviation fuels (SAFs) are a key target in the transportation sector due to difficulties in decarbonizing the airline industry through a transition to electric motors.[2] HEFA-Jet is currently the most widely used sustainable SAF with worldwide production of HEFA-type fuels (much of it diesel) of approximately five billion liters in 2021.[3] HEFA-Jet is derived from fatty acids by a top-down hydrogenation/hydroisomerization process (**Figure 1**) along with thermal cracking to convert the long-chain fatty acids into shorter jet fuel range hydrocarbons (C_9-C_{16}).[4] The resulting blend is a complex mixture of lightly branched alkanes, which exhibits an outstanding gravimetric net heat of combustion and meets many of the performance requirements of Jet-A. A number of commercial and military flights have been conducted with HEFA-Jet and it is certified as a blendstock with Jet-A at up to 50 volume %.[5]

In parallel with the expansion of HEFA-Jet as a viable sustainable aviation fuel, a number of research groups have explored alternative top-down approaches for the conversion of fatty acids and other mid to long-chain unsaturated hydrocarbons into jet fuels. For example, linoleic acid can be cleaved to generate 1-octen-3-ol, which can then be dehydrated to a mixture of octadienes and thermally dimerized to generate jet and diesel fuel blendstocks.[6] Other researchers have leveraged olefin metathesis chemistry to generate alternative fuels. For example, Harvey et al. developed a process to convert linalool, a terpene alcohol, into tetrahydrodimethyldicyclopenatediene isomers (THDMDCPD),[7] which is a high-density fuel blend that has been produced from a number of bio-based sources.[8,9,10] This process was further supplemented with dehydration/cyclization reactions to generate additional fuel components.[11,12] Other researchers have focused on the use of

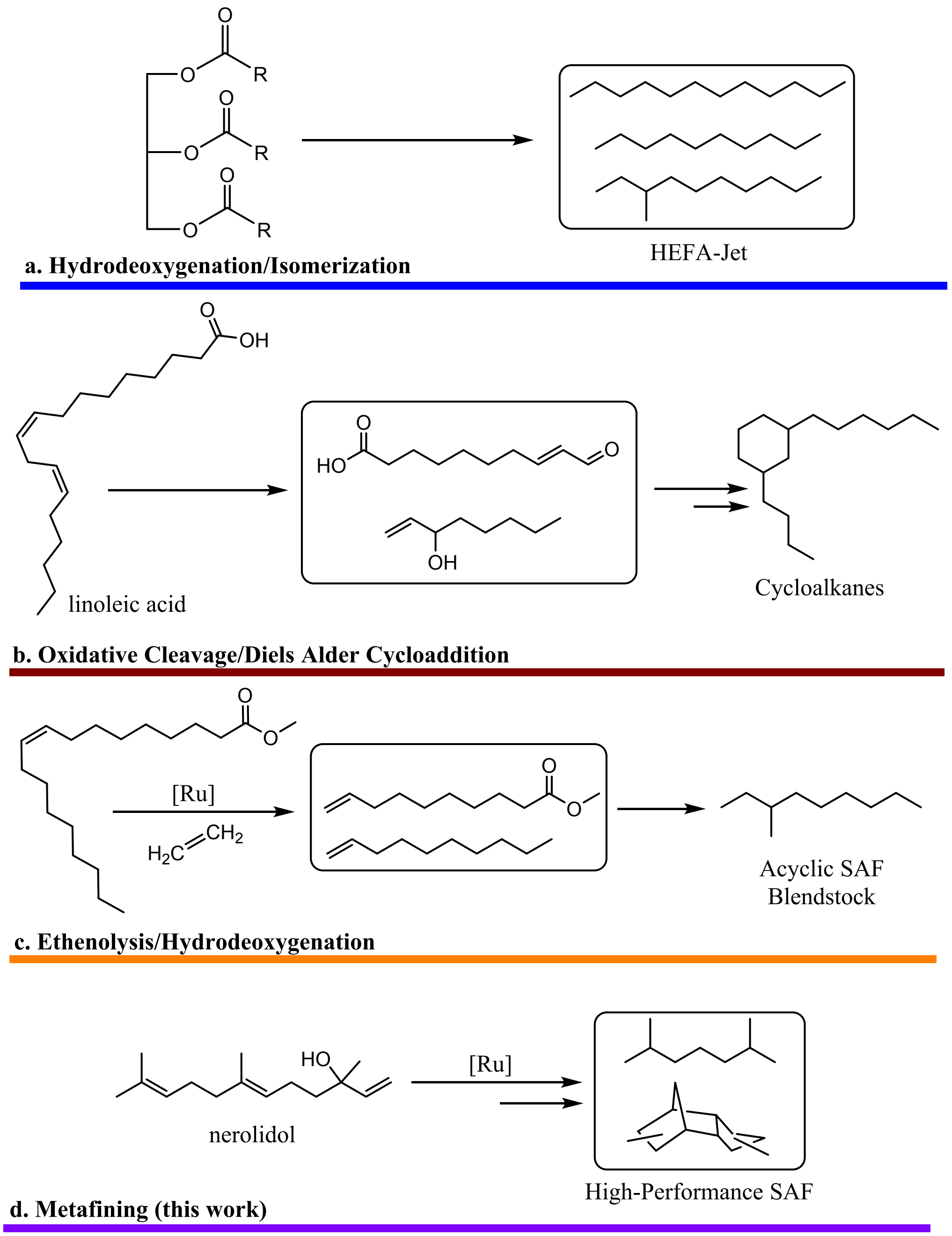


Figure 1. Examples of "top-down" approaches for the synthesis of SAF from lipids. a. Triglycerides or fatty acids are converted to a mixture of acyclic alkanes (HEFA-Jet) by a combination of hydrodeoxygenation and isomerization. b. Linoleic acid is oxidatively cleaved by an enzyme and the resulting 1-octen-3-ol is converted to a complex mixture of cycloalkanes by dehydration, Diels-Alder cycloaddition, and hydrogenation. c. Unsaturated fatty acids are cleaved by ethenolysis followed by hydrodeoxygenation to generate a SAF blendstock. d. trans-Nerolidol is converted to a high-performance SAF through "metafining", which consists of ring-closing metathesis followed by dehydration, Diels-Alder cycloaddition, and hydrogenation.

unsaturated oils derived from crops like camelina[13] and *Amygdalus Pedunculata*[14] or from microbes.[15] Ethenolysis of the oils with metathesis catalysts can efficiently break down the longer hydrocarbon chains into jet fuel range hydrocarbons. Whereas HEFA-Jet, and other sustainable aviation fuels (e.g. hydrotreated pyrolysis oils) are synthesized through traditional refining routes with steps that include hydrodeoxygenation, cracking, and isomerization, the use of well-defined metathesis catalysts or "metafining" approaches (**Figure 1**) hold great promise for the efficient and targeted synthesis of unique fuel blends.

Most conventional approaches to SAF focus on the synthesis of lightly branched alkanes, which provide advantages including low viscosity and high gravimetric heat of combustion. However, these approaches often neglect the synthesis of cycloalkanes, a hydrocarbon class that provides a number of advantages including high density, low to moderate viscosity, high heat of combustion, and a greater ability to swell O-rings compared to acyclic hydrocarbons.[16,17] Cyclic hydrocarbons can be readily synthesized through a number of pathways including catalytic cycloaddition of small molecules,[18,19,20] aldol coupling,[21,22,23] Diels-Alder chemistry.[6,24,25] and electrochemistry.[26] Alternatively, naturally occurring cyclic molecules can be utilized as substrates for the preparation of high performance fuels. In particular, several groups have explored cyclic monoterpenes[27,28,29,30,31,32,33,34,35] and sesquiterpenes[36,37,38,39,40,41] as fuel precursors. Conveniently, many of these molecules can be made via a synthetic biology approach in which metabolically engineered organisms produce the desired molecules from biomass sugars.

trans-Nerolidol is an acyclic sesquiterpene alcohol that is widely used in perfumery and has also been tested as a transdermal delivery system for therapeutic drugs.[42] It has a chemical structure similar to that of the monoterpenoid linalool, which can be readily cyclized via transition metal catalyzed ring-closing metathesis (RCM).[7] This similarity suggests that nerolidol can be readily transformed to a well-defined hydrocarbon fuel mixture through a similar approach. Nerolidol is typically isolated from the essential oils of various plants, but can also be produced biosynthetically from biomass sugars through a fermentation process. For example, Zhang et al. obtained a titer as high as 16 g/L of trans-nerolidol in two-phase extractive fed-batch fermentation.[43] Similarly, Qiao et al. obtained titers as high as 7.01 g/L using a recombinant yeast strain and fed-batch fermentation.[44] Although these results are promising, much higher titers will likely be required for a commercial process. For example, farnesene, an acyclic sesquiterpene useful as a precursor to diesel and jet fuel blendstocks, has been produced at titers up to 130 g/L.[45] In addition, to make biosynthetic fuels more competitive with petroleum it will be necessary to utilize crude biomass sources (e.g. lignocellulose) as feedstocks.

To explore the use of nerolidol as a substrate for the production of high-performance fuel blends, we studied the RCM of the sesquiterpene alcohol to generate unsaturated intermediates that were then converted to jet fuel range hydrocarbons by dehydration and hydrogenation reactions. The fuel properties of these blendstocks were then evaluated and compared to conventional jet fuel.

Experimental

General. All glassware was dried in an oven at 140 °C prior to use. Amberlyst-15 H^+ form, trans-nerolidol, glacial acetic acid, and 10% Pd/C were obtained from Sigma-Aldrich. Hoveyda-Grubbs M720 was obtained from Sigma Aldrich, stored in a nitrogen-filled glovebox, and used as received. Magnesium sulfate was purchased from Fisher Scientific. Aluminum phosphate was synthesized by a literature procedure[7] and the nerolidol was distilled prior to use. Sonication reactions were performed on a Branson M3800 sonicator. ^1H NMR spectra were recorded on a Jeol ECZ400S spectrometer at 25 °C, operating at 400 MHz. Proton-decoupled $^{13}C\{^1H\}$ NMR spectra were recorded with the same instrument at 25 °C, operating at 100 MHz. Chemical shifts are reported in parts per million downfield from tetramethylsilane and are referenced relative to the NMR solvent ($CDCl_3$) according to the literature values–$\delta(^{1}H) = 7.26$, $\delta(^{13}C) = 77.16$. All product distributions were quantified by GC-FID.

RCM of nerolidol. Hoveyda-Grubbs M720 catalyst (.139 g, 0.223 mmol) was weighed out in the glovebox and added to a 500 mL Schlenk flask. The flask was removed from the glovebox and trans-nerolidol (156.74 g, 0.705 mol) was added under nitrogen. The reaction mixture was stirred for 20 seconds to disperse the catalyst and then sonicated until the catalyst dissolved (~10 min), followed by sonication for an additional 20 min. ^{1}H NMR spectroscopy showed complete conversion to the ring closing products, 2,6-dimethyl-1,5-heptadiene and 1-methylcyclopent-2-enol. Trace amounts of the dehydration product, 2-methylcyclopentadiene, were also observed. The product mixture was used without further purification in the next step. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81, (m, 1H), 5.71, (m, 1H), 5.11, (m, 1H), 4.68, (m, 2H), 2.53-2.46, (m, 1H), 2.35-2.28, (m, 1H), 2.12-1.90, (m, 6H), 1.72, (s, 3H), 1.68, (s, 3H), 1.61, (s, 3H), 1.39, (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 138.0, 132.8, 131.6, 124.3, 109.9, 83.6, 39.8, 38.0, 31.2, 27.6, 26.8, 26.4, 25.7, 22.6, 17.8.

Dehydration. The RCM product was added to a 500 mL round bottom flask. Anhydrous $MgSO_4$ (15.15 g) and $AlPO_4$ (8.97 g) were added to the flask, and the reaction mixture was stirred at ambient temperature for 10 min. The pressure was reduced to 182 mmHg and the reaction was heated to 80 °C to initiate distillation. Over the next two hours, the pressure was gradually reduced to 149 mmHg. The distillate was collected in two fractions. Fraction 1 (14.37 g) was collected under the following conditions: T_{head} (55 ˚C), T_{bath} (81 ˚C), $p = 182.0$ mmHg and was a mixture of 41.3% 2-methylcyclopentadiene, 38.1% 2,6-dimethyl-1,5-heptadiene and 20.6%

dimethyldicyclopentadiene. Fraction 2 (101.16 g) was collected under the following conditions: T_{head} (80 ˚C), T_{bath} (100 ˚C), p = 148.8 mmHg and was a mixture of 20.2% 2-methylcyclopentadiene, 64.8% 2,6-dimethyl-1,5-heptadiene and 15.0% dimethyldicyclopentadiene. The total amount of distilled product was 115.53 g, representing an 80.2% carbon yield.

Diels-Alder Cycloaddition. Fractions 1 and 2 from the dehydration step were combined and added to a 500 mL round bottom flask. $AlPO_4$ (5.15 g) was added and the flask was fitted with a water-cooled condenser. The reaction mixture was then stirred and heated to 70 ˚C for 72 h. The supernatant was isolated by filtration and the resulting solution was fractionally distilled under partial vacuum. 4.76 g of residual 2-methylcyclopentadiene was obtained at 132.1 mmHg and a head temperature of 29 °C. The pressure was then reduced to 97.5 mmHg and a second fraction (57.53 g) was distilled at a head temperature of 76 ˚C. This fraction contained pure 2,6-dimethyl-1,5-heptadiene. A third fraction (9.54 g) was distilled under similar conditions compared to fraction 2 and found to be mostly 2,6-dimethyl-1,5-heptadiene, with a trace of methylcyclopentadiene dimers. A fourth fraction (10.53 g) was distilled at 24.8 mmHg and a head temperature of 92 °C. This fraction was composed of dimethyldicyclopentadiene isomers. A fifth fraction (23.16 g) was then distilled under full vacuum (~0.1 mmHg, T_{Head} = 55 °C), and was composed of methylcyclopentadiene dimers. The overall distillate mass was 105.52 g, representing recovery of 91.3% of the carbon obtained after the dehydration step. The overall yield of 2,6-dimethyl-1,5-heptadiene from nerolidol was 76.6% while the overall yield for dimethyldicyclopentadiene from nerolidol was 59.6%. If desired, residual methylcyclopentadiene can be recycled for subsequent fuel synthesis.

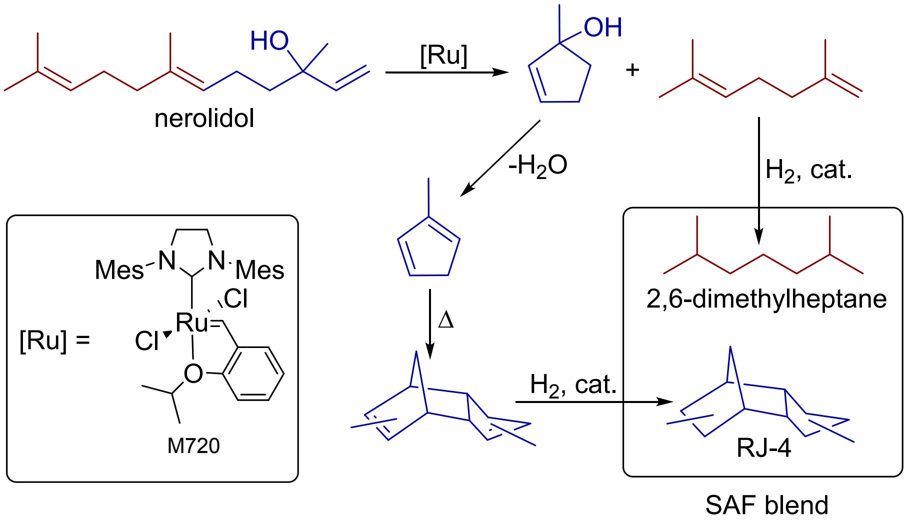
Hydrogenation of 2,6-dimethyl-1,5-heptadiene. Fractions 2 and 3 from the step above (67.07 g) along with 10% Pd/C (0.72 g, 6.76 mmol) were added to a Parr reactor. The reactor was evacuated/refilled with hydrogen three times and the pressure was then increased to 500 psi. The reactor was heated to 150 °C over the course of ~ one h and vigorously stirred. After 24 h, the reaction had ceased uptaking hydrogen and was shown by NMR analysis to be complete. The mixture was then filtered over Celite to yield 62.48 g of crude 2,6-dimethylheptane. The product was distilled from calcium hydride via short path distillation under the following conditions: p = 97.9 mmHg, T_{head} (70˚C), T_{bath} (95˚C). to obtain 60.11 g of distillate (86.8% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51 (sept, J = 6.8 Hz), 1.31-1.21 (m), 1.17-1.09 (m), 0.85 (d, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 39.4, 28.1, 25.2, 22.7.

Hydrogenation of methylcyclopentadiene dimers. The combined fractions 4 and 5 from the Diels Alder cycloaddition step described above (32.73 g) and 10% Pd/C (0.43 g, 4.04 mmol) were added to a Parr reactor. The reactor was evacuated/refilled with hydrogen three times, the pressure was then increased to 500 psi and the reactor heated to 50 ˚C for 24 hours followed by an additional four hours at 75 °C. The reactor was then cooled and the product was filtered through Celite, using diethyl ether to rinse out the reactor. The filtrate was fractionally distilled under reduced pressure to yield a mixture of hydrogenated methylcyclopentadiene dimers.

Cyclization and hydrogenation of 2,6-dimethyl-1,5-heptadiene. 2,6-dimethyl-1,5-heptadiene (39.00 g) was added to a 100 mL Parr Reactor, along with Amberlyst-15 (3.93 g) and 10% Pd/C (0.46 g). The reactor was evacuated/refilled with hydrogen three times and the pressure was then increased to 750 psi. The reactor was heated to 100 ˚C with rapid stirring for four hours, cooled to ambient temperature and opened. Additional 10% Pd/C was added (0.42 g), the reactor was subjected to another three evacuation/refill cycles, and the pressure was then increased to 750 psi.

The reactor was heated to 150˚C and stirred overnight. The reactor was then cooled and the product was filtered over Celite. The filtrate was distilled from calcium hydride via short path distillation under the following conditions: p = 12.6 mmHg, T_{bath} (45 ˚C), T_{head} (34 ˚C). ^{13}C NMR spectrum for 1,1,3-trimethylcyclohexane (100 MHz, $CDCl_3$): δ 48.8, 39.2, 35.4, 33.6, 31.0, 28.4, 24.9, 23.2

Results and Discussion



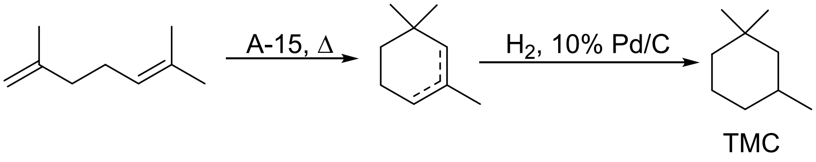
Scheme 1. Synthesis of jet fuel blendstocks from nerolidol.

trans-Nerolidol was readily converted to an equimolar mixture of 1-methylcyclopent-2-en-1-ol (MCP) and 2,6-dimethylhepta-1,5-diene by a facile ring-closing metathesis reaction using a 0.03 mol% loading of Grubbs-Hoveyda 2nd Generation catalyst (**Scheme 1**). Conveniently, the reaction was conducted neat, which greatly enhanced the sustainability of the process. The catalyst had only moderate solubility in nerolidol. However, this limitation was easily overcome through the use of sonication, which accelerated the initiation and rate of the reaction. Once activated, the catalyst was soluble in the reaction mixture. The reaction was complete after 20 minutes of sonication and the conversion was quantitative by NMR spectroscopy. A similarly facile reaction was previously observed starting from the structurally similar molecule linalool.[7] However, in that case, the RCM reaction generated isobutylene as a byproduct, which was rapidly removed from the reaction mixture as a gas at ambient temperature. In contrast, for nerolidol, the alkene byproduct formed was a C_9 hydrocarbon (2,6-dimethylhepta-1,5-diene) which stayed in the reaction mixture, reducing the entropic driving force for the reaction. In addition, there were initial concerns that 2,6-dimethylhepta-1,5-diene could inhibit the RCM reaction by coordinating to the metal center. These concerns turned out to be unfounded.

The catalyst loading used for the ring-closing metathesis reaction was 0.03 mol%, which equates to an impressive TON of >3333. The use of a homogenous Ru-based catalyst may be considered a drawback due to the scarcity and high cost of ruthenium coupled with perceived challenges with recycling. However, the chelating alkylidene ligand in M720 is remarkably stable and Hoveyda demonstrated that a catalyst similar to M720 could be easily recycled in high yield by column chromatography.[46] Other approaches to reduce overall catalyst costs and enhance sustainability could focus on the use of bespoke [Ru]-catalysts with higher TONs or supported [Ru]-catalysts that can be recycled by simple decantation.[47] Beyond [Ru]-based catalysts, there have been significant advances in alcohol-tolerant [Mo]-based metathesis catalysts.[48] If this class of materials offered similar activity and stability, the lower cost and greater abundance of molybdenum could enable a more sustainable route to large-scale production.

After the RCM reaction was complete, MCP was dehydrated with a method similar to that used in our work with linalool.[7] The use of a weak Lewis acid ($AlPO_4$) and a desicant ($MgSO_4$) allowed for dehydration under modest conditions (80-100 °C; 149 mmHg). The distillate was composed primarily of 2-methylcyclopentadiene along with 2,6-dimethylhepta-1,5-diene. This mixture was then thermally dimerized in the presence of $AlPO_4$. The Diels-Alder cycloaddition of methylcyclopentadiene proceeded in the presence of the acyclic diene without any discernible formation of cross-products. After the cycloaddition was complete the product mixture was purified by vacuum distillation to yield pure fractions of 2,6-dimethylhepta-1,5-diene and dimethyldicyclopentadienes.

2,6-dimethylhepta-1,5-diene was readily converted to 2,6-dimethylheptane (DMH) by hydrogenation under moderate conditions (10% Pd/C, 500 psi, 150 °C). In parallel, the dimethyldicyclopentadiene was hydrogenated with the same catalyst to generate tetrahydrodimethyldicyclopentadiene isomers (THDMDCPD). DMH and THDMDCPD were then blended to form an equimolar mixture designated as F1. In preliminary work on the Diels-Alder cycloaddition of methylcyclopentadiene we explored Amberlyst-15 as an alternate catalyst to $AlPO_4$. During this work we observed partial conversion of 2,6-dimethylhepta-1,5-diene to trimethylcyclohexene intermediates that were subsequently hydrogenated to generate 1,1,3-trimethylcyclohexane (TMC) (**Scheme 2**). We therefore conducted a hydrogenation reaction in the presence of Amberlyst-15 and generated a 70:30 mixture of DMH and TMC designated as F2.



Scheme 2. Conversion of 2,6-dimethylhepta-1,5-diene to 1,1,3-trimethylcyclohexane (TMC).

The basic fuel properties of DMH including density, viscosity, and heat of combustion were measured to understand its utility as a SAF component (**Table 1**). The density of DMH at 15 °C was 0.714 g mL^{-1}, which is 8% lower than that required for Jet-A (>0.775 g mL^{-1}). This low density is due to the acyclic nature and low molecular weight of DMH. As expected, DMH had a remarkably low kinematic viscosity of 1.66 and 2.55 mm^2s^{-1} at -20 and -40 °C, respectively. These values are 79% lower than the maximum values for Jet-A at these temperatures. The gravimetric net heat of combustion of DMH was 44.07 MJ kg^{-1}, which is 3.0% higher than the lower limit for Jet-A. The extremely low viscosity and high gravimetric heat of combustion of DMH make it a valuable SAF blendstock to mitigate the high viscosities of higher molecular weight components while simultaneously increasing the energy density on a mass basis.

After studying the fuel properties of DMH we explored the stoichiometric blend of DMH and THDMDCPD designated F1. The density of F1 at 15 °C was 0.783 g mL^{-1} which is above the minimum requirement for Jet-A (> 0.775 g mL^{-1}). The high density of the THDMDCPD isomers at this temperature (~0.925 g mL^{-1}) increase the density, balancing out DMH. Serendipitously, the combination of these hydrocarbons in a 1:1 mole ratio based on the reaction chemistry, resulted in a blend with a density that meets specifications. The kinematic viscosity of the blend at -20 °C was only 2.87 mm^{2}s^{-1}, which is 64% lower than the upper limit for Jet-A (**Figure 2**). This remarkably low viscosity is due to the DMH. In contrast, commercial THDMDCPD isomers have an unacceptably high viscosity of 18.31 mm^{2}s^{-1} at the same temperature (**Table 1**). Thus, a non-linear order of magnitude decrease in the viscosity is observed in the blend, similar to previous studies conducted with high viscosity terpene dimers and various C_{10} hydrocarbons.[49] This effect was maintained even at -40 °C at which the blend had a viscosity of 5.02 mm^{2}s^{-1}, 58% lower than the limit. The gravimetric NHOC of the blend was 43.27 MJ kg^{-1}, which is ~1% higher than the lower

Table 1. Fuel properties of fuels studied in this work

Fuel	**NHOC (MJ kg^{-1})**	**NHOC (MJ L^{-1})**	**ρ [15 °C, g mL $^{-1}$]**	**η [-20 °C, mm^2 s^{-1}]**	**η [-40 °C, mm^2 s^{-1}]**
Jet-A	>42.80	>33.17	>0.775	<8.0	<12.0
2,6-DMH	44.07	31.46	0.714	1.66	2.55
RJ-4	42.21	39.03	0.925	18.31	49.86
F1	43.27	33.88	0.783	2.87	5.02
F2	43.69	31.87	0.729	1.75	2.71

limit required for Jet-A. The gravimetric NHOC of THDMDCPD has previously been reported as 42.21 MJ kg^{-1}, which is 1.4% lower than the required minimum for Jet-A. However, the exceptional gravimetric NHOC of DMH (44.04 MJ kg^{-1}) increased the value for F1 to a level where it met the specification.

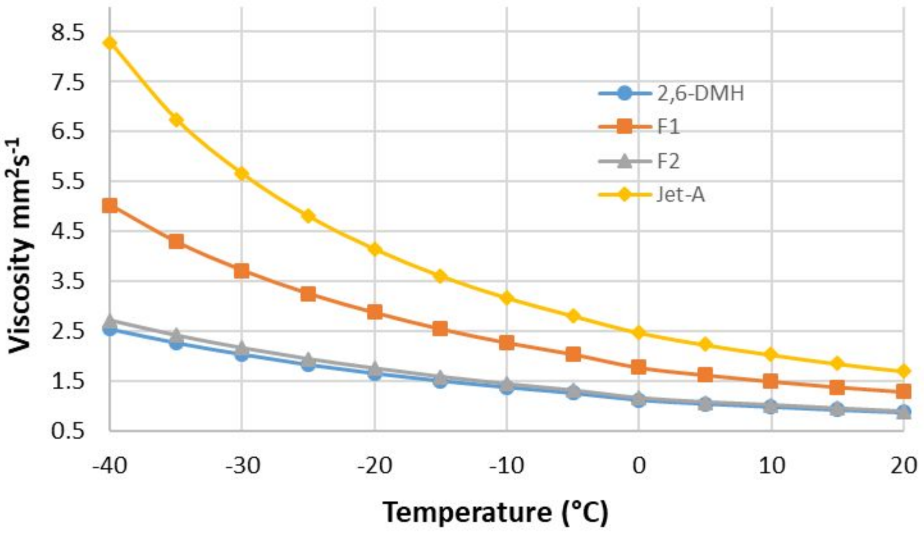


Figure 2. Kinematic viscosity of 2,6-DMH, F1, F2, and Jet-A from -40–20 °C

In a similar fashion, we explored the fuel properties of F2, which can be found in **Table 1**. F2 exhibited a gravimetric NHOC 2.1% higher than the lower limit for Jet-A and a -20 °C kinematic viscosity 78% lower than the upper limit for Jet-A. The inclusion of TMC in the blend slightly increased the viscosity of F2 compared to pure 2,6-DMH, but also increased the density by 1.4%, which brings F2 into the lower range of synthetic paraffinic kerosenes that have been certified for blending with conventional jet fuel.

Conclusions

In this work we demonstrated a novel approach for the synthesis of sustainable aviation fuel blendstocks from the sesquiterpenoid, nerolidol. Our approach, coined as "metafining", utilizes olefin metathesis to convert a C_{15} lipid into a blend of C_9 and C_{12} hydrocarbons with outstanding fuel properties including low viscosities and high heats of combustion. Some of the advantages of this approach include outstanding atom economy, production of a well-defined and predictable fuel mixture, and a final fuel product with properties that exceed those of conventional jet fuel. To realize the promise of metafining for the development of SAF, it will be necessary to produce nerolidol biosynthetically on a commercially relevant scale. Future work should focus on increasing nerolidol titers and the carbon efficiency of the fermentation process. In parallel, additional work will need to be conducted on low-cost and energy-efficient pathways for the valorization of crude biomass sources. Utilization of lignocellulose and other waste biomass sources as feedstocks will be required for the production of sustainable aviation fuels on a relevant scale at prices competitive with petroleum.

In addition to commercial production of nerolidol, improvements in the catalytic conversion of nerolidol to fuels will be required. As described above, very low loadings of a Grubbs-Hoveyda catalyst were utilized to catalyze the ring-closing metathesis of nerolidol. However, to improve the sustainability of the process and mitigate the high cost and scarcity of ruthenium, further research on reducing catalyst loadings through the design of more robust systems may be warranted. Alternative approaches might include recycling the homogenous catalyst for subsequent runs, utilizing supported [Ru]-based catalysts, or transitioning to alcohol-tolerant metathesis catalysts based on molybdenum or tungsten. Catalytic studies along these lines with nerolidol and related substrates are ongoing in our laboratory.

Conflicts of Interest

There are no conflicts of interest to declare.

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