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Separation of *cis*-Fatty Acids from Saturated and *trans*-Fatty Acids by Nanoporous Polydicyclopentadiene Membranes

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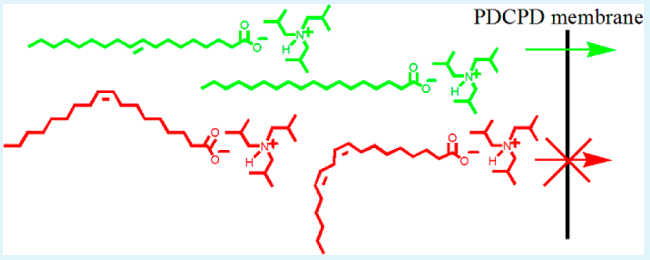
Supporting Information

ABSTRACT: This article describes the separation of mixtures of fatty acid salts using a new organic solvent nanofiltration membrane based on polydicyclopentadiene (PDCPD). Mixtures of free fatty acids could not be separated by the membranes because they permeated at similar rates. When triisobutylamine was added to the fatty acids, the *cis*-fatty acid salts (oleic, petroselinic, vaccenic, linoleic, and linolenic acid) had slower permeation though the membranes than saturated (stearic acid) and *trans*-fatty acid (elaidic acid) salts. The reason for the difference in permeation was due to the formation of stable salt pairs between the amine and fatty acids that increased their cross-sectional areas. The fatty acid salts derived from saturated and *trans*-fatty acids were smaller than the critical area cutoff for the PDCPD membranes, so they readily permeated. In contrast, the fatty acid salts derived from the *cis*-fatty acids had critical areas larger than critical area cutoff of the PDPCD membranes and had slowed permeation. The partitioning coefficients of fatty acids and fatty acid salts were investigated to demonstrate that they were not responsible for the difference in permeation. The use of pressure was investigated to greatly accelerate the permeation through the membranes. For a solvent mixture of 35/65 (v/v) toluene/hexanes, the permeation of solvent was approximately 39 L m^{-2} h^{-1}. This value is similar to values reported for permeation through membranes used in industry. The separation of a mixture of fatty acids based on the composition of soybean oil was investigated using pressure. The saturated fatty acid salts were almost completely removed from the *cis*-fatty acid salts when iBu$_3$N was used as the amine to form the salt pairs. The separation of the *cis*-fatty acids found in soybean oil was investigated with Pr$_3$N as the amine. The oleic acid salt (oleic acid has one cis double bond) preferentially permeated the membrane while the linoleic (two cis double bonds) and linolenic (three cis double bonds) salts were partly retained. The separation of fatty acids using membranes may have real applications in industry to purify fatty acids on a large scale.



KEYWORDS: *polydicyclopentadiene, organic solvent nanofiltration, fatty acid, vegetable oil, size-selective*

INTRODUCTION

Over 140 million tons of vegetable oils are produced in the United States each year, and this value has been increasing by 5% a year since 2000. The quantity of oils is expected to greatly increase if biodiesels from algae are produced in significant quantities as some believe will happen.[1−7] Vegetable oils are triesters of glycerol ($HOCH_2CHOHCH_2OH$) and three fatty acids; each fatty acid contains 16, 18, 20, or 22 carbon atoms and zero, one, or more carbon−carbon double bonds depending on their source (Figure 1).[8−12] For example, over 35 million tons of soybean oil are produced each year, and it has a composition of 10% palmitic acid, 4% stearic acid, 18% oleic acid, 55% linoleic acid, and 13% linolenic acid (palmitic acid is a 16 carbon saturated fatty acid).[1] Despite the large scale production of vegetable oils and the fact that they are a critical biorenewable source of starting materials, both the oils and their fatty acids are used only in small quantities in industrial applications. Over 96% of vegetable oils are "burned" by humans or animals after being consumed or in engines when used as biodiesel. A critical reason for the lack of applications of fatty acids as a starting material for industrial applications is that it is not possible to separate a mixture of fatty acids into individual components on a scale of millions of tons per year. Fatty acids isolated from vegetable oils are a mixture of five or more different fatty acids with different reactivities and that will yield different products after a reaction. Simply, when a mixture of five fatty acids derived from soybean oil are used as starting materials in an industrial process, many different products are obtained. The challenge of utilizing a mixture of fatty acids as starting materials limits their broader transformations into more valuable commercial products.

In this article we describe a method to purify fatty acids using an organic solvent nanofiltration membrane based on polydicyclopentadiene (PDCPD). This is the first report of the use of a membrane to separate fatty acids from one another and represents an important advance in this field. This method may allow the purification of a mixture of fatty acids into single fatty acids such that they could be used in more industrial

Received: November 5, 2012
Accepted: January 2, 2013
Published: January 2, 2013

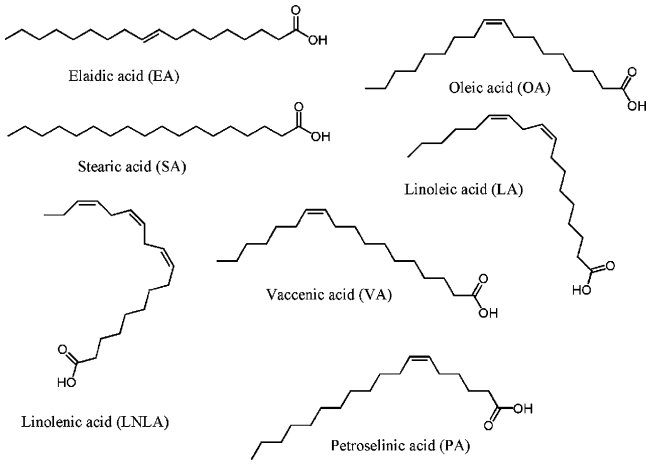


Figure 1. Structures of the fatty acids used in this study.

applications. Other methods to purify fatty acids include selective precipitation, distillation of esters of fatty acids, liquid chromatography, or selective hydrolysis of *trans*-fatty acids from glycerol.[13−20] Although each method has found applications on small batches of fatty acids, none of them can separate complex mixtures of fatty acids into individual components on the scale of millions of tons per year that is required for widespread applications.

Membranes are commonly used in industry to remove impurities from a mixture of molecules. Separations using membranes are a preferred method for large industrial applications because they are one of the simplest and least energy intensive methods of purification. Unfortunately, membranes do not readily separate fatty acids from each other because they are similar in size and polarity. Although cis and trans double bonds confer differences in overall shape to fatty acids, the ease of rotation about the numerous carbon−carbon sigma bonds leads to a large number of conformations for each fatty acid which increases the complexity of separating them with membranes.

We recently developed size-selective membranes based on highly cross-linked polydicyclopentadiene (PDCPD).[21,22] These membranes were fabricated by polymerizing 5000 mol equiv of dicyclopentadiene with 1 mol equiv of the Grubbs first generation catalyst to yield solid, dense membranes. These membranes do not have well-defined pores such as zeolites; rather, when they are swollen in organic solvents, they possess openings between the polymer chains that small molecules may diffuse through. The distribution in size of the openings is polydisperse and on the nanometer to subnanometer size scale. We investigated the flux of a large number of molecules through PDCPD membranes and discovered that the membranes were highly selective to retain molecules with cross-sectional areas above 0.50 nm^2 as shown in Figure 2, but molecules with cross-sectional areas below 0.38 nm^2 permeated the membranes.[22] The cross-sectional areas were the smallest, rectangular cross-sectional area of each molecule as measured in silico.[22] The molecules that were retained had values for their flux that were at least 4−5 orders of magnitude lower than those for molecules that did permeate. These membranes did a poor job of separating molecules based on their molecular weights as shown in Figure 2a, but when the smallest cross-sectional area for each molecule was plotted against retention a clear difference was observed. PDCPD membranes are a new

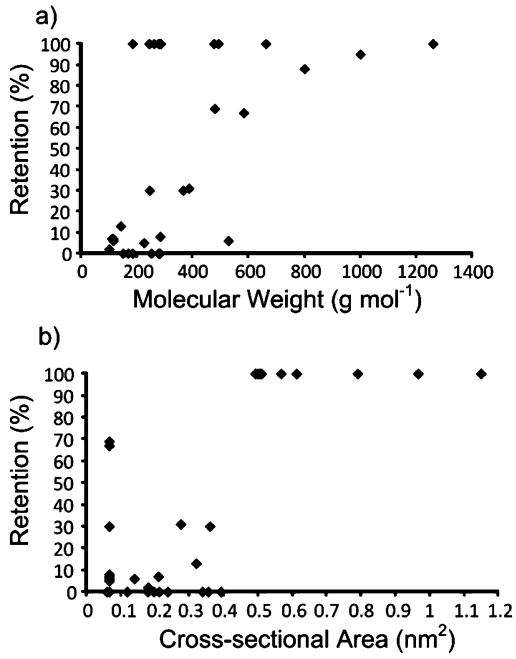


Figure 2. Retention of 100% indicating that the molecule did not permeate the membrane at any level and a retention of 0% indicating that the molecule readily permeated the membrane and was not retained. (a) Plot of retention versus molecular weight for 35 samples. (b) Plot of retention versus smallest cross-sectional area for the molecules in part a.

type of size-selective membrane that separates organic molecules with molecular weights up to 600 g mol^{-1} based on their cross-sectional areas.

Membranes have been used to remove other impurities (i.e., proteins and glycerols) from fatty acids, but they had never been used to separate the individual components of fatty acids from one another. In this article, we show that fatty acids are too small to be separated using PDCPD membranes, but when they are coordinated with amines that increase their sizes, *cis*-fatty acid salts are selectively retained by PDCPD membranes. In contrast, saturated and *trans*-fatty acid salts readily permeated the membranes and were not retained. This is the first example of the separation of fatty acids using membranes and a significant new method to isolate *cis*-fatty acids.

EXPERIMENTAL PROCEDURES

Materials. Dicyclopentadiene, elaidic acid, oleic acid, stearic acid, linoleic acid, linolenic acid, vaccenic acid, petroselinic acid, triethylamine, tripropylamine, triisobutylamine, tributylamine, *p*-nitrobenzaldehyde, and solvents were purchased at their highest purity from Aldrich and Acros and used as received.

Characterization. ^{1}H NMR spectra were acquired using a Bruker DPX-500 at 500 MHz and referenced to TMS.

Measurement of Concentrations of Fatty Acid Salts. In the experiments that follow, the concentration of fatty acid salts were found by extracting 1.0 mL of solvent that contained unknown amounts of fatty acid salts. A known and small amount of tetraethylene glycol (toluene was used in some instances) was added to each aliquot and then the solvent was evaporated. A ^{1}H NMR spectrum was acquired of the residue. The concentrations of the fatty acid salts were determined by comparison to the known concentration of tetraethylene glycol in the ^{1}H NMR spectrum.

Fabrication of PDCPD Membranes. A 20 mg mL^{-1} solution of Grubbs first generation catalyst was made using 1,2-dichloroethane. A sample of this solution (0.72 mL, 6.0 × 10^{-3} mmol of catalyst) was

dx.doi.org/10.1021/am3025867 | ACS Appl. Mater. Interfaces 2013, 5, 924−933

added to 12 mL of dicyclopentadiene heated to 40 °C. Heat was used to keep dicyclopentadiene (melting point 33 °C) a liquid. This solution was immediately placed between two glass slides with 100 μm thick paper as spacers along the edges. The sample was heated to 50 °C for 2 h and then removed from the glass slides. Due to the low boiling point of methylene chloride (bp = 40 °C), very little methylene chloride was expected to remain in the membranes at the completion of their fabrication. All PDCPD membranes used in this project were fabricated according to this method.

Permeation of Oleic Acid and Elaidic Acid with Different Amines. A PDCPD membrane was placed between two glass vessels to study permeation. CH_2Cl_2:MeOH (v/v, 75:25, 25 mL) was added to the downstream side of the membrane, and 25 mL of the same solvent was added to the upstream side of the membrane with 0.426 mmol (0.120 g) of oleic acid, 0.426 mmol (0.120 g) of elaidic acid, 0.852 mmol (0.158 g of triisobutylamine) of amine, and 0.426 mmol (0.064 g) of *p*-nitrobenzaldehyde as an internal standard. Solvent on both sides of the membrane was stirred continuously at room temperature. At 24, 48, and 72 h, a 1 mL aliquot of solvent was removed from solvent on both sides of the membrane. The aliquots were used to determine the concentration and the absolute amounts of the oleic acid salt, elaidic acid salt, and *p*-nitrobenzaldehyde by ^{1}H NMR spectroscopy after the addition of toluene as an internal standard.

Partition Coefficients of Molecules in PDCPD. A PDCPD slab was cut into small rectangular pieces. A typical value for the dimension of the slab was 2.5 cm × 0.9 cm × 0.3 cm, and the weight was approximately 0.800 g. A fatty acid (0.213 mmol) and triisobutylamine (0.213 mmol; 0.039 g) was dissolved in 12.5 mL of CH_2Cl_2:MeOH (v/v, 75:25) solution. The weight of the PDCPD slab was measured, and it was immersed in the solution. The solution was stirred for 96 h, and then, the PDCPD slab was removed from the solution. The solvent was removed in vacuo, and the weight of the slab was measured. The amount of molecule that partitioned into the slab was calculated based on the difference in weight of the slab before and after being swollen. The volume of the solvent was measured prior to removing it in vacuo. An aliquot of the residue was added to an NMR tube. The absolute amount of the fatty acid in the solvent was determined by ^{1}H NMR spectroscopy by the addition of known amounts of tetraethylene glycol. The partition coefficient of the molecule was calculated by dividing the concentration of the molecule in PDCPD by the concentration of the molecule in the solvent.

Separation of a Mixture of Four Fatty Acids Using Multiple Extractions. A PDCPD membrane was placed between two glass vessels to study permeation. CH_2Cl_2 (25 mL) was added to the downstream side of the membrane and 25 mL of the same solvent was added to the upstream side of the membrane with 0.426 mmol of stearic acid, 0.426 mmol of oleic acid, 0.426 mmol of linoleic acid, 0.426 mmol of linolenic acid, and 1.704 mmol of triisobutylamine. Solvent on both sides of the membrane were stirred continuously at room temperature. After 24, 48, and 72 h, the downstream solvent was removed and replaced with fresh 25 mL CH_2Cl_2. After 96 h, the downstream solvent was combined with the previous solvent removed from the downstream side of the membrane. After 96 h, the upstream solvent was removed and replaced with 25 mL of CH_2Cl_2 and 1.278 mmol of triethylamine to extract any fatty acid retained in the membrane. After 45 h, the solvent was replaced with 25 mL of CH_2Cl_2 for a second recovery cycle. The downstream and upstream solvents were combined separately to determine the absolute amounts of stearic acid salt, oleic acid salt, linoleic acid salt, and linolenic acid salt by ^{1}H NMR spectroscopy. The absolute amounts of each fatty acid were found by the addition of known amounts of tetraethylene glycol to each aliquot.

Use of Pressure to Increase the Flux through PDCPD Membranes. A PDCPD membrane was immersed in 30 mL of CH_2Cl_2:MeOH (v/v, 90:10, 75:25, or 60:40) for 15 min. Next, the membrane was added to a metal vessel to study flux. CH_2Cl_2:MeOH at the same v/v ratio (100 mL) was added to the upstream side of the membrane with 0.426 mmol (0.121 g) of stearic acid, 0.426 mmol (0.120 g) of oleic acid, and 0.852 mmol (0.157 g) of triisobutylamine. The valve on the downstream side was opened. A valve on the upstream side was attached to a tank of N_2. The pressure was increased to 90 psi in 10 min using N_2. At lower pressures no solvent permeated. Higher pressures were not investigated. The pressure was constant at 90 psi during an induction period of a few hours where no solution permeated to the downstream side. After this induction period, the solution was collected on the downstream side in 15−20 min. A 1 mL aliquot of solvent was removed and a known amount of tetraethylene glycol was added. The absolute amounts of stearic acid and oleic acid salts were found by ^{1}H NMR spectroscopy. The same experiment was repeated with mixtures of toluene:hexane (v/v, 40:60, 35:65, or 30:70).

RESULTS AND DISCUSSION

Choice of Fatty Acids and How the Experiments Were Completed. The fatty acids shown in Figure 1 were used in this study. These fatty acids all possessed 18 carbon atoms and represented some of the most common fatty acids found in vegetable oils. Included in this study were linolenic acid and linoleic acid which are two essential fatty acids that are needed within the body but that humans are not able to synthesize.

PDCPD membranes were fabricated as described in the Experimental Procedures section (Figure 3). These membranes

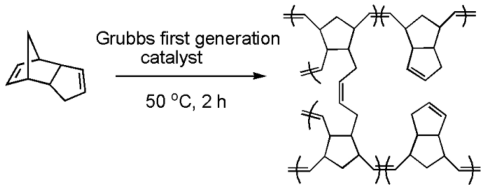


Figure 3. Polymerization of dicyclopentadiene by the Grubbs first generation catalyst yielded a highly cross-linked solid polymeric slab.

were highly cross-linked by the Grubbs catalyst. Dicyclopentadiene has two carbon−carbon π bonds; one is highly strained (approximately 25 kcal/mol of ring strain), and the other is less strained (approximately 7 kcal/mol of ring strain). The ring-opening metathesis polymerization of the highly strained π bond yielded polymer, and the ring-opening of the less strained ring yielded cross-links.[21−28] In prior work, it was shown that 83% of the less strained π bond was ring opened which led to a highly cross-linked matrix.[21,22]

The experimental apparatus for studying the permeation of fatty acids is shown in Figure 4. A 100 μm-thick PDCPD membrane was fabricated and placed between two glass

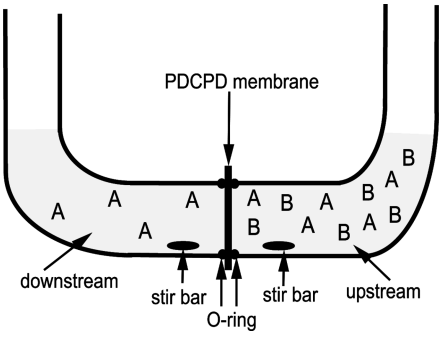


Figure 4. A scheme of the apparatus that was used in these experiments. Molecules A and B were initially added to the solvent upstream of the membrane and only molecule A permeated to the downstream solvent.

dx.doi.org/10.1021/am3025867 | ACS Appl. Mater. Interfaces 2013, 5, 924−933

Table 1. Permeation of Oleic Acid and Elaidic Acid with Different Amines through PDCPD Membranes

		oleic acid (S_d/S_u)			elaidic acid (S_d/S_u)		
entry	salt	24 h	48 h	72 h	24 h	48 h	72 h
1	no salt	0.26	0.72	1.04	0.27	0.73	1.08
2	triethylamine	0.09	0.36	1.03	0.11	0.34	1.08
3	tripropylamine	0.01	0.09	0.17	0.13	0.58	1.08
4	triisobutylamine	0.017	0.05	0.07	0.20	0.68	1.01
5	tributylamine	0.0	0.0	0.0	0.0	0.0	0.0

reservoirs. Solvent was added to either side of the membrane. On the upsteam side of the membrane molecules (i.e., the fatty acids and amines) that were to be studied were added with the solvent. Only solvent was added on the downstream side. The molecules diffused from the upstream to the downstream solvent. Two stir bars were added to constantly mix the solvent to ensure uniform concentrations on each side of the membrane. After a period of time, typically 24 h, well-defined aliquots of downstream and upstream solvent were removed. An internal standard of toluene or tetraethylene glycol was added prior to analysis by ^{1}H NMR spectroscopy to allow the concentrations of each fatty acid in solvent downstream and upstream of the membranes to be measured.

Separation of Oleic Acid and Elaidic Acid. The separation of oleic acid from elaidic acid was chosen as an initial test due to the similarities of these fatty acids. They possess identical molecular formulas and the double bond is located at the same position, but oleic acid is the cis isomer and elaidic acid is the trans isomer. A 75/25 (v/v) mixture of CH_2Cl_2/MeOH was used because all fatty acids dissolved in this solvent and reasonable flux values were obtained.

A mixture of oleic acid, elaidic acid, and *p*-nitrobenzaldehyde were added to solvent on the upstream side of the membrane. The permeation of *p*-nitrobenzaldehyde was known from prior work, so it provided an internal standard for the physical properties of the membranes.[21,22] It readily fluxed through all of the membranes at similar rates which provided evidence that the membranes did not possess any holes and that they had similar properties. The fabrication of the membranes was very reproducible and the permeation of *p*-nitrobenzaldehyde was similar in all experiments. The ratio of the concentration of each molecule (i.e., the fatty acids, amines, and *p*-nitrobenzyaldehyde) in the solvent on the downstream side (S_d) to the upstream side (S_u) was measured every 24 h as reported in the Experimental Procedures section. The S_d/S_u ratio was zero at the beginning of the experiment because the molecules were only added to the upstream side of the membrane. The S_d/S_u ratio was equal to one when the concentration of a substrate was the same on both sides of the membrane. Both oleic and elaidic acid readily permeated the PDCPD membrane at similar rates and were fully equilibrated after 72 h (entry 1 in Table 1). This result was expected based on the small cross-sectional areas of these fatty acids.

A series of trisubstituted amines were added to the fatty acids to investigate their effect on the observed permeation. From prior work by our group, it was known that triethylamine, tripropylamine, and triisobutylamine readily permeated the membranes but that tributylamine did not permeate at any detectable level.[21] The difference in permeation between triisobutylamine and tributylamine was surprising because these two molecules are constitutional isomers; yet, their flux differed by at least 4−5 orders of magnitude. The difference in flux was due to the smaller, compact shape of triisobutylamine (critical area of 0.38 nm^2) compared to tributylamine (critical area of 0.50 nm^2). Critical area is defined as the smallest, rectangular cross-sectional area of a molecule. To find these values, the energy of a molecule was minimized in silico and the smallest cross-sectional area of a two-dimensional projection was measured as described in the Supporting Information. These values are expected to be similar to the smallest size of a pore that a molecule may permeate through.

An amine was added to solvent on the upstream side of the membrane with the fatty acids to form a noncovalent bond (Figure 5). The fatty acid and the amine formed a salt pair by

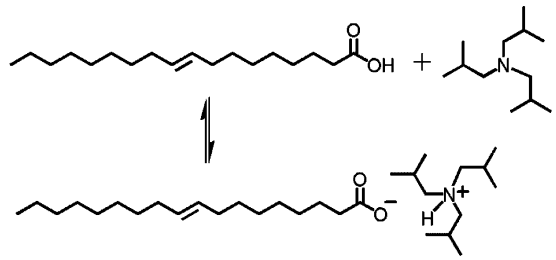


Figure 5. Addition of triisobutylamine led to formation of a stable salt with the fatty acids.

transfer of a proton from the acid to the nitrogen. These salts were stable and persistent in a variety of organic solvents. The amines had compact shapes and larger cross-sectional areas than the fatty acids, so their addition increased the critical area of each fatty acid. It was hypothesized that the curvature of the *cis*-fatty acids would lead to a larger increase in their critical areas when compared to the saturated and *trans*-fatty acids. It was also hypothesized that the amine would increase the cross-sectional area of the fatty acids to reach the size range where PDCPD membranes were effective at separating molecules. The critical areas of each fatty acid and fatty acid salt are reported later in this article.

The results for the flux when a 1:1:2 molar ratio of oleic acid:elaidic acid:amine was added to the solvent on the upstream side of the membrane was shown in Table 1. Not surprisingly, the addition of triethylamine (critical area = 0.18 nm^2) had little impact on the flux of oleic and elaidic acid; both fatty acid salts equilibrated after 72 h. When tripropylamine (critical area = 0.32 nm^2) was added, the flux of oleic acid was slowed but elaidic acid equilibrated after 72 h. Better results were obtained when triisobutylamine (critical area = 0.38 nm^2) was used. The value for S_d/S_u of oleic acid was only 0.07 after 72 h, but the elaidic acid was fully equilibrated.

Not surprisingly, the use of tributylamine (critical area = 0.50 nm^2) kept both oleic and elaidic acid from permeating the membrane. Prior work showed that tributylamine did not permeate these membranes at any detectable level, so it was expected that the salts would not permeate.[21] This experiment

dx.doi.org/10.1021/am3025867 | ACS Appl. Mater. Interfaces 2013, 5, 924−933

with tributylamine demonstrated that the fatty acids coordinated strongly to the amines because if the fatty acids dissociated from tributylamine, they would have readily permeated the membranes.

Separation of *cis*-, *trans*-, and Saturated Fatty Acids. Five additional fatty acids were studied for their ability to permeate PDCPD membranes. Stearic, linoleic, vaccenic, petroselinic, and linolenic acid all readily permeated the membranes and fully equilibrated within 72 h (Figure 6).

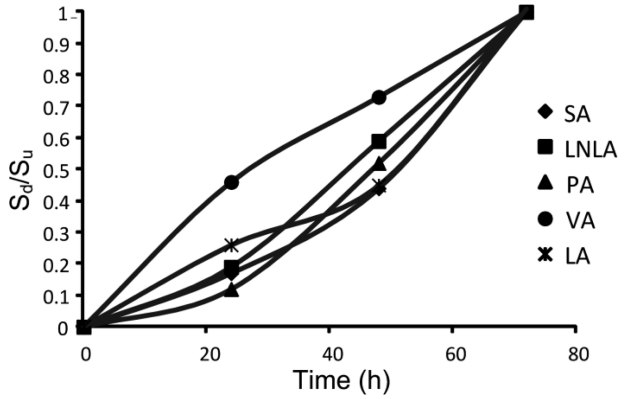


Figure 6. Values for S_d/S_u at 24, 48, and 72 h for stearic (SA), linoleic (LA), vaccenic (VA), petroselinic (PA), and linolenic (LNLA) acid are shown. The lines are meant for ease of viewing the data and do not represent a fit to any equation.

The results for the permeation of these five fatty acids were remarkably different when triisobutylamine was added to the solvent on the upstream side of the membrane (Table 2).

Table 2. Permeation of *cis*-Fatty Acid Salts with Triisobutylamine through PDCPD Membranes

		stearic acid (S_d/S_u)			unsaturated acid (S_d/S_u)		
entry	fatty acids[a]	24 h	48 h	72 h	24 h	48 h	72 h
1	stearic acid and linoleic acid	0.24	0.67	1.04	0.00	0.00	0.035
2	stearic acid and linolenic acid	0.21	0.78	1.04	0.00	0.00	0.00
3	stearic acid and petroselinic acid	0.15	0.62	0.83	0.02	0.06	0.10
4	stearic acid and vaccenic acid	0.40	0.65	1.00	0.03	0.07	0.11

[a]1 mol equiv of triisobutylamine to fatty acid was added to each experiment.

When triisobutylamine was used, stearic acid readily permeated the membranes but the other four fatty acids had greatly reduced permeation. To ensure that the diminished permeation of the *cis*-fatty acids was due to their structures rather than another effect, the flux of each *cis*-fatty acid was studied in the presence of both stearic acid and *p*-nitrobenzaldehyde. In these experiments, both *p*-nitrobenzaldehyde and the stearic acid salt with triisobutylamine readily permeated the membranes. Thus, the diminished permeation of the *cis*-fatty acid salts was not due to the membranes, but rather it was due to their structures.

Two interesting sets of *cis*-fatty acids were studied in these experiments. Petroselinic, oleic, and vaccenic acid all possessed 18 carbon atoms and one cis double bond, but they differed in the location of the double bond (see Figure 1). Petroselinic, oleic, and vaccenic acid had respectively 11, 8, and 6 sp^3 hybridized carbons after the double bond. The saturated ends of the fatty acids represented the "hooks" of the *cis*-fatty acids that led to their diminished flux through the membranes. All three of these fatty acids had similar flux through the membranes despite the difference in location of the cis bonds (entries 3 and 4 of Table 2 and entry 4 of Table 1).

In a second set of *cis*-fatty acids, the number of cis bonds differed. Oleic, linoleic, and linolenic acids all possessed one cis bond at the 9 carbon, but linoleic acid had a second cis bond at the 12 carbon and linolenic acid had two additional cis bonds at the 12 and 15 carbons. The number of cis bonds had a small effect on the flux of a fatty acid, but all of the *cis*-fatty acids were retained by the PDCPD membrane (entries 1 and 2 in Table 2 and entry 4 of Table 1).

In all prior experiments, a mixture of 75/25 (v/v) of CH_2Cl_2/MeOH was used as the solvent. To investigate if the difference in flux for *cis*-fatty acids resulted in part from a choice of solvent, chloroform, and toluene were studied (Table 3). In these experiments the permeation of stearic acid and oleic acid salts were examined to investigate how rapidly the stearic acid salt permeated and whether the oleic acid salt permeated. In both experiments, the stearic acid salt readily permeated the membranes but the oleic acid salt did not permeate. The flux of the stearic acid salt was faster when toluene and chloroform were used as solvent than with the CH_2Cl_2/MeOH mixture. In the CH_2Cl_2/MeOH mixture, the value for S_d/S_u was 0.68 after 48 h (this value was the average of the four experiments shown in Table 2), but the value for S_d/S_u after 48 h was 0.98 and 0.92 in toluene and chloroform, respectively.

Table 3. Permeation of Stearic Acid and Oleic Acid As Triisobutylamine Salts through PDCPD Membranes in Different Solvents

	stearic acid (S_d/S_u)			oleic acid (S_d/S_u)		
solvent	24 h	48 h	72 h	24 h	48 h	72 h
toluene	0.32	0.98	1.00	0.03	0.06	0.05
chloroform	0.34	0.92	1.00	0.03	0.06	0.07

Partitioning Coefficients for Fatty Acids and Fatty Acid Salts. The equations that describe permeation can be complex, but the main concepts are straightforward.[29−37] To permeate a membrane, a molecule must partition into it and have a nonzero rate of diffusion inside the membrane. The well-known equation $P = DS$ describes this relationship (P is the permeability, D is the rate of diffusion, and S is the solubility of a molecule in the membrane). The partitioning coefficient, PC (unitless), is defined as the ratio of the concentration of a molecule in a membrane divided by its concentration in solvent when a system is at equilibrium. The partitioning coefficients for every fatty acid salt with triisobutylamine were investigated for their ability to permeate into PDCPD slabs as described in the Supporting Information.

The partitioning coefficients of oleic and elaidic acid in the absence of any amine were almost identical (entries 1 and 2 in Table 4). This result was expected based on the similarities of these fatty acids. Interestingly, the partitioning coefficients of all seven fatty acids with triisobutylamine were also nearly identical (entries 3−9 in Table 4). This result was due to the similarities in size and composition of the fatty acid salts and that the charged parts of the salts were encapsulated by the isobutyl groups and the hydrophobic tails of the fatty acids. The

dx.doi.org/10.1021/am3025867 | ACS Appl. Mater. Interfaces 2013, 5, 924−933

Table 4. Partitioning Coefficients of Fatty Acids and Fatty Acid Salts into PDCPD

entry	fatty acid	PC
1[a]	oleic acid	1.07
2[a]	elaidic acid	0.997
3	elaidic acid salt	0.999
4	oleic acid salt	1.00
5	stearic acid salt	1.00
6	linoleic acid salt	0.999
7	linolenic acid salt	1.00
8	petroselinic acid salt	1.00
9	vaccenic acid salt	1.00

[a]The first two entries were measured as free acids without triisobutylamine. Entries 3–9 were measured with 1 mol equiv of triisobutylamine present.

difference in permeation of the *cis*-fatty acid salts compared to the saturated and *trans*-fatty acid salts was not due to their partitioning coefficients; rather, the differences were due to their rates of diffusion within the PDCPD matrix.

Measurement and Comparison of Critical Areas. Differences in partitioning coefficients do not explain the differences in permeation of the fatty acid salts, so the differences in permeation must have been due to the differences in diffusion. In cross-linked polymer matrixes the diffusion, D, of a molecule depends exponentially on the energy of activation, E_a (kcal mol^{-1}) according to the equation $D = D_o \exp(-E_a/RT)$.[31] Molecules that are much smaller than the pores in a matrix can diffuse rapidly because the polymer matrix does not have to rearrange to allow them to diffuse. Molecules that are on the same size as the pores or larger than the pores diffuse slowly because the polymer matrix must deform and the value for E_a is large. In practice, the rate of diffusion in cross-linked polymers has been shown to be heavily dependent on the cross-sectional areas of molecules. For instance, in 1982 Berens and Hopfenberg plotted the log of diffusion versus the square of diameter for 18 molecules that permeated poly(vinyl chloride), polystyrene, and poly(methyl methacrylate).[38] The diffusion of He (diameter squared = 6.66×10^{-2} nm^2) was 10 orders of magnitude faster than the diffusion of neopentane (diameter squared = 3.36×10^{-1} nm^2). PDCPD was a highly cross-linked polymer matrix, and the rate of diffusion of molecule was expected to depend on their critical areas. In prior work it was shown that molecules above a critical area of 0.50 nm^2 did not permeate PDCPD membranes, but molecules with critical areas below 0.38 nm^2 did permeate.[21]

One challenge in the field of size-selective membranes is defining the critical area of a molecule. This is usually not attempted; rather, membranes are described as possessing a "molecular weight cutoff" that is used to determine whether a new molecule will permeate.[39−45] The molecular weight cutoff is used although it is not meant to be a good predictor of what will permeate (see Figure 2a). It is well understood that molecular weight does not have a strong correlation with cross-sectional area. Rather, a molecular weight cutoff provides a simple, unambiguous method to suggest which molecules may permeate a membrane. The molecular weight of a molecule can be determined within minutes, but the critical area is much harder to determine and dependent on the method used.

The critical areas for the molecules in this study were found using Spartan '08 V1.2.0. The free fatty acids were constructed and their energies were minimized in Spartan. Not surprising, the fatty acids were in the all-trans conformations. The fatty acids were rotated until the smallest rectangular cross-sectional area was found, and this value was labeled the critical area and reported in Table 5. The critical area was measured because this

Table 5. Critical Areas of Fatty Acids

molecule	critical area of free fatty acid (nm^2)	critical area of fatty acid salt (nm^2)
elaidic acid	0.12	0.38
stearic acid	0.067	0.38
oleic acid	0.21	0.95
linoleic acid	0.34	0.97
linolenic acid	0.36	0.74
petroselinic acid	0.20	1.27
vaccenic acid	0.24	0.47

area was the smallest size for the pore that each molecule may diffuse through. The procedure to find the critical areas for the fatty acids salts was similar. The energy of triisobutylamine was first minimized such that it could be docked in the same conformation with each fatty acid. Next, the energy of the fatty acid with the amine was minimized. The critical areas of the salts were found as described before.

In Figure 7, the seven fatty acids and fatty acid salts are shown in their energy minimized structures. The view on the left shows a side view of the fatty acids in the absence of amine to emphasize the curved structures of the *cis*-fatty acids. The view on the right shows the orientation of the fatty acid salts that was used to find their critical areas. The saturated and *trans*-fatty acids were completely eclipsed by triisobutylamine. In contrast, the *cis*-fatty acid salts were not completely eclipsed by triisobutylamine due to the omega ends of the *cis*-fatty acids. These ends were "hooks" that increased the critical areas of the *cis*-fatty acid salts.

It is important to note that there are other methods to measure critical areas. For instance, we defined the critical area as possessing a rectangular shape, but other shapes (i.e., sphere, square, oval, etc) can also be used and will give different values for the critical areas. The variation of the critical area depending on the method of its measurement is an important reason why many nanofiltration membranes use a molecular weight cutoff rather than a critical area cutoff. Although the absolute value for the critical areas may be debatable, it was clear from Figure 7 that *cis*-fatty acid salts had larger critical areas than the saturated and *trans*-fatty acid salts.

Separation and Isolation of *cis*-Fatty Acids from Saturated and *trans*-Fatty Acids. The saturated and *trans*-fatty acids equilibrated between the solvent upstream and downstream of the membranes; at the end of the separations approximately 50% of these fatty acids were found in the upstream solvent with the *cis*-fatty acids. In contrast, the *cis*-fatty acids were selectively retained by the membranes, so their concentration was low in the downstream solvent but still relatively high in the upstream solvent. Thus, the downstream solvent was highly enriched in saturated or *trans*-fatty acids, but the upstream solvent had significant quantities of all fatty acids. Approximately only half of the saturated and *trans*-fatty acids were removed from the *cis*-fatty acids.

A series of separations were completed using CH_2Cl_2 as the solvent to decrease the concentration of saturated fatty acids in the upstream solvent. CH_2Cl_2 was chosen rather than the CH_2Cl_2/MeOH mixture due to the faster flux for fatty acid salts

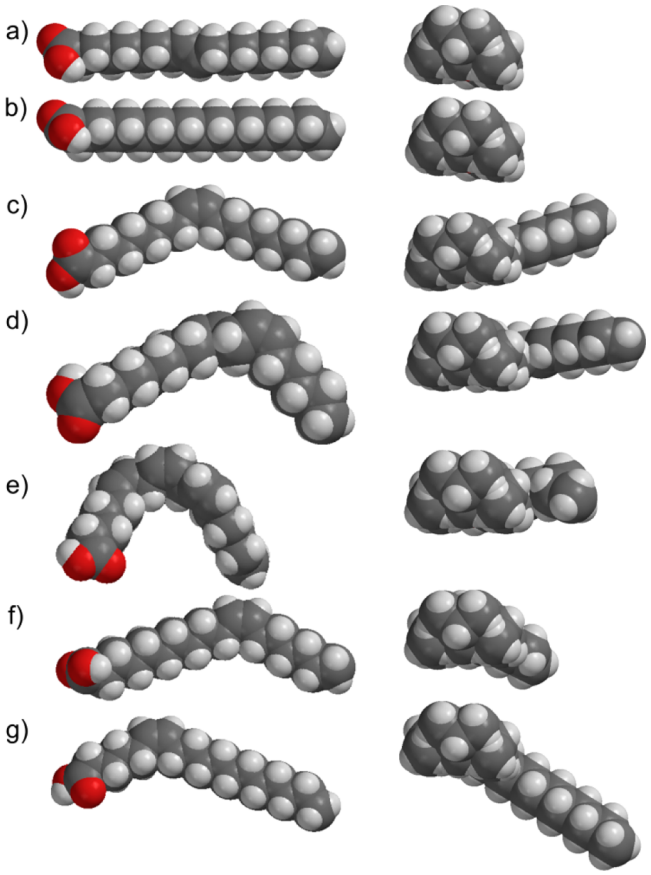


Figure 7. Energy-minimized space filling models for each fatty acid and fatty acid salt with triisobutylamine. One image shows the fatty acid to emphasize any curvature. The other image shows a view of the critical area of each fatty acid salt. These images for (a) elaidic acid, (b) stearic acid, (c) oleic acid, (d) linoleic acid, (e) linolenic acid, (f) vaccenic acid, and (g) petroselinic acid are shown.

in CH_2Cl_2. In these experiments, the downstream solvent was periodically removed and replaced with fresh solvent. Replacing the downstream solvent lowered the concentration of the fatty acids in it which lowered the amount of fatty acid that permeated from the downstream solvent to the upstream solvent. This experiment was similar to a continuous extraction that is common in industrial applications.

In one experiment, a 1:1:2 mixture of stearic acid:oleic acid:triisobutylamine was added to 25 mL of CH_2Cl_2 upstream of the membrane. On the downstream side 25 mL of CH_2Cl_2 was added. The upstream and downstream solvents were stirred for 24 h, and then, the downstream solvent was removed and a fresh 25 mL of CH_2Cl_2 was added. The solvents were stirred for an additional 24 h, and then, the downstream solvent was removed and replaced with fresh 25 mL of CH_2Cl_2. The solvents were stirred for 24 h, and then, the upstream and downstream solvents were removed. All of the downstream solvents were combined, the solvent evaporated, and the residual was analyzed by ^{1}H NMR spectroscopy. To remove any fatty acid within the PDCPD matrix, the membrane was extracted with CH_2Cl_2 and Et_3N twice as described in the Experimental Procedures section. This solvent was combined with the upstream solvent and analyzed by ^{1}H NMR spectroscopy.

In this experiment, 90% of the stearic acid and only 13% of the oleic acid that were originally added to the apparatus were found in the downstream solvent. In contrast, 5% of the stearic acid and 86% of the oleic acid were found in the upstream solvent and membrane. For many applications purification of the *cis*-fatty acids is desired, and this experiment took a 1:1 molar ratio of stearic acid:oleic acid to yield an isolated ratio of 1:17. Notably, 97% of the fatty acids that were added to the apparatus were isolated at the end of the experiment. The fatty acids were not permanently trapped within the PDPCD membrane.

This experiment was repeated with four extractions rather than three as before, and the results were similar. Stearic acid (94%) and oleic acid (17%) were isolated from the downstream solvent, and stearic acid (3%) and oleic acid (81%) were isolated from the upstream solvent and membrane. Thus, the isolated ratio of stearic acid to oleic acid in the upstream solvent was 1:27. These results were very promising and demonstrated that the membranes could be used to separate oleic acid from stearic acid.

This experiment was repeated with a 1:1:1:1:4 molar ratio of stearic acid:oleic acid:linoleic acid:linolenic acid:triisobutylamine using CH_2Cl_2 as the solvent. This experiment was to simulate the separation of a small amount of a saturated fatty acid (stearic acid) from a mixture of three different *cis*-fatty acids. Four extractions were completed and the samples were analyzed as described in the Supporting Information. The downstream solvent possessed 92% of the stearic acid and only 5% of the *cis*-fatty acids that were originally added to the apparatus, but the upstream solvent and membrane had 4% of the stearic acid and 86% of the *cis*-fatty acids. Thus, most of the stearic acid was removed from the *cis*-fatty acids and the isolated ratio from the upstream solvent of stearic acid to *cis*-fatty acids was 1:22.

Use of Pressure to Increase Flux. The *cis*-fatty acid salts were selectively retained while the saturated and *trans*-fatty acids salts readily permeated the membranes, but the values for flux were very low. No pressure was applied in these experiments, so the driving force for flux was based on differences in concentration of the molecules in solvent upstream and downstream of the membranes. Typical values for the flux of solvent through size selective membranes used in industry are around 10 L m^{-2} h^{-1}, and these filtrations require less than an hour to complete.[39−45] There are two important points to consider about how the industrial separations are completed and interpreted. First, they required the use of pressure on one side of the membrane; otherwise, the separations were very slow. The use of pressure is not only acceptable, it is almost mandatory such that the filtrations are quick. Second, the values for flux are typically reported for the solvent rather than the substrate of interest (i.e., the product of a reaction). If the concentration of a product is approximately 100× lower than that of the solvent, then values for the flux of the products in a solvent are approximately 0.1 L m^{-2} h^{-1}. Separations using PDCPD membranes required days to reach completion because no pressure was applied. An approximate value for the flux of a fatty acid through PDCPD membranes was 10^{-10} L m^{-2} h^{-1} which was far too slow for industrial applications.

Because the flux was very slow for the fatty acids, the use of pressure was studied. A metal vessel was used to apply pressure to solvent upstream of the membrane. A membrane was placed horizontally within a metal vessel, and 100 mL of solvent with stearic acid, oleic acid, and triisobutylamine (1:1:2 molar ratio) were added to the vessel. The reaction vessel was pressurized to

90 psi, and all of the solvent permeated within 20 min. It is important to note that that solvent was found on only one side of the membrane unlike in the experiments that did not use pressure. Initial experiments with mixtures of CH_2Cl_2 and methanol were unsuccessful due to the poor selectivity of the membrane (entries 1−3 in Table 6). Nearly all of the stearic acid salt (93−97%) permeated the membrane and was found in the solvent downstream of the membrane, but 77−80% of the oleic acid salt was found in the downstream solvent.

Table 6. Use of Pressure to Increase the Flux through PDCPD Membranes

		amount permeated (%)[a]	
entry	solvent	stearic acid	oleic acid
1	90/10 CH_2Cl_2/MeOH	97	78
2	75/25 CH_2Cl_2/MeOH	93	80
3	60/40 CH_2Cl_2/MeOH	95	77
4	40/60 toluene/hexanes	94	36
5	35/65 toluene/hexanes	99	22
6	30/70 toluene/hexanes	[b]0	[b]0

[a]These values refer to the fraction of each acid found in the downstream solvent relative to the amount of acid originally added to the upstream solvent. [b]The fatty acid salts did not permeate the membranes.

When a mixture of toluene and hexanes were studied, the difference in flux was much higher. At an optimal concentration of 35/65 (v/v) of toluene/hexanes, 99% of the stearic acid was found in the solvent downstream of the membrane but only 22% of the oleic acid was found in the downstream solvent. Some selectivity was lost compared to the experiments without pressure, but the time required for permeation was only 20 min which yielded a flux of for the solvent of 39 L m^{-2} h^{-1}. This value for the flux was similar to values reported for membranes used in industry and represented a large improvement for the use of PDCPD membranes.

The use of multiple membranes to increase the selectivity for permeation of one molecule is commonly used in industrial laboratories, and this method was successful here too. To increase the separation of oleic acid from the stearic acid, the solvent downstream of the membrane was passed through a second PDCPD membrane using pressure. When the downstream solvent from entry 5 of Table 6 was passed through a second membrane, the amount of stearic acid that permeated was 96% of the original amount. In contrast, the amount of oleic acid that permeated decreased to only 7.5% of the original amount. Thus, the 1:1 molar ratio of stearic acid to oleic acid that was originally added was concentrated to a 13/1 ratio of stearic acid to oleic acid after passing through two PDCPD membranes.

This experiment was repeated to investigate the ratio of stearic acid to oleic acid upstream and downstream of the membranes. Briefly, a 1:1:2 molar ratio of stearic acid:oleic acid:triisobutylamine was passed through a PDCPD membrane using a 35/65 (v/v) toluene/hexanes mixture. The downstream solvent was then passed through a second PDCPD membrane under pressure. The downstream solvent after filtration through two PDCPD membranes had 95% of the original amount of stearic acid and only 7% of the original amount of oleic acid. The remainder of the oleic and stearic acid had permeated into the membranes and was retained within them. The membranes were removed from the apparatus and swollen in CH_2Cl_2 with Et_3N to extract the fatty acids. The CH_2Cl_2 extracts were then combined, the solvent was evaporated, and the distributions of products were analyzed by ^1H NMR spectroscopy. The recovery of oleic acid from the membrane was high (89% of the original amount added) and only 3% of the stearic acid was recovered from the membranes.

These results indicated a high level of success both in the overall recovery of the fatty acids and in the separation of saturated and *cis*-fatty acids. Nearly all of the stearic acid (98%) and oleic acid (96%) that was used at the beginning of the experiment was accounted for at the end. Most of the stearic acid (95%) was found downstream of the membrane and the ratio of stearic acid to oleic acid was 13.6/1 in the downstream solvent. In contrast, most of the oleic acid (89%) was retained by the membranes and the ratio of retained oleic acid to stearic acid was 30/1. These membranes were successful at separating a mixture of oleic acid/stearic acid.

Use of Pressure to Purify Fatty Acids Derived from Soybean Oil. The separation of fatty acids derived from soybean oil was completed with PDCPD membranes under pressure. Soybean oil was chosen because it is produced in large quantities (over 35 million tons per year) that make it an important biorenewable feedstock. A mixture of 14% stearic acid, 18% oleic acid, 55% linoleic acid, and 13% linolenic acid was formulated from commercially available fatty acids. This mixture of fatty acids was added to 100 mL of hexanes:toluene (35/65, v/v) with 1 mol equiv of triisobutylamine for every mole of fatty acid. This mixture was pressurized and allowed to permeate through two PDCPD membranes in series. The downstream solvent was removed, and the residual was analyzed by ^1H NMR spectroscopy. The PDCPD membranes were soaked in CH_2Cl_2 with Et_3N to remove any fatty acids that had permeated into the matrix.

Nearly all of the stearic acid (94%) was found in the downstream solvent as expected based on its fast flux through PDCPD membranes (Table 7). Only 3% of oleic acid and 4% of the linolenic acid/linoleic acid permeated the membranes. The original mixture of fatty acids was only 14% by weight stearic acid, but after filtration through two PDCPD membranes, the downstream solvent was 79% by weight stearic acid. Importantly, nearly all of the saturated fatty acid was removed from the unsaturated fatty acids. The fatty acids isolated from the PDCPD membranes contained less than 1% stearic acid. These membranes were very efficient at separating the saturated from unsaturated fatty acids.

Table 7. Separation of Soybean Oil through Two PDCPD Membranes under Pressure

molecule	initial amount (mmol)	downstream solvent (mmol)	upstream solvent (mmol)
stearic acid	0.426	0.401	0.022
oleic acid	0.547	0.018	0.505
linolenic acid/ linoleic acid	2.065	0.086	1.949

It was hypothesized that the linolenic and linoleic acids could be selectively retained while oleic acid permeated the membranes. This hypothesis was based on the differences in shapes of the *cis*-fatty acid salts. Specifically, linoleic and linolenic acid had higher curvatures than oleic acid, and it was hypothesized that an oleic acid salt would possess a higher flux through PDCPD than the polyunsaturated acid salts (see

dx.doi.org/10.1021/am3025867 | ACS Appl. Mater. Interfaces 2013, 5, 924−933

Figure 7 for the energy minimized structures of these fatty acids)

To test this hypothesis, the composition of fatty acids that were retained by the two PDCPD membranes as shown in Table 7 were made into salts by the addition of 1 mol equiv of Et_3N. The *cis*-fatty acid salts had very low flux when triisobutylamine was used, so smaller amines were investigated to find an amine salt where oleic acid permeated but linoleic and linolenic acid salts were retained. All of the fatty acid salts permeated the membrane after the application of pressure, and no separation between oleic acid and the polyunsaturated fatty acid salts was found when Et_3N was used. This experiment was repeated with the same ratio of fatty acids salts that were retained by the membranes as shown in Table 7 but with Pr_3N to form the salts. Here, pressure was applied across the membrane to reach fast values for the flux.

The oleic acid salt permeated the membrane and 0.33 mmol were found in the downstream solvent, but only 0.43 mmol of the polyunsaturated fatty acid salts permeated. The original mixture of fatty acids had a 1:3.8 ratio of oleic acid:-polyunsaturated fatty acids, but after permeation, the ratio was 1:1.3. In the upstream solvent and the membrane, the ratio of oleic acid:polyunsaturated fatty acids was 1:7.3. Although this experiment did not lead to complete separation of oleic acid from linoleic and linolenic acid, it demonstrated that their salts possessed different flux. It may be possible, with some optimization, to find an amine that allows the oleic acid salt to permeate as linoleic and linolenic acid salts are retained.

CONCLUSIONS

The addition of amines led to the selective retention of *cis*-fatty acid salts due to two effects. First, the amines increased the critical areas of the fatty acids to the size range where PDCPD membranes could separate them. The free fatty acids were too small to be retained by the membranes, but the fatty acid salts were larger and in the size range where PDCPD membranes retain molecules. Second, the addition of the amines led to a larger difference in critical areas of the salts compared to the free fatty acids. The critical areas for the free fatty acids fell within a narrow range (0.067−0.36 nm^2), but the critical areas for the fatty acid salts fell within a large range (0.38−1.27 nm^2).

It was surprising and unexpected that the formation of a noncovalent, reversible interaction between a fatty acid and an amine led to a large difference in permeation. The hooks on the *cis*-fatty acids were distant from the amines which were the largest, bulkiest part of the salts. Furthermore, fatty acids have large numbers of C−C single bonds that rotate at room temperature and lead to a wide variety of different conformations—and critical areas—for each fatty acid. It would have been reasonable to assume that the flexibility of the fatty acids coupled with the distance between the hooks and the amine would have led to little or no effective difference in critical areas or flux between the fatty acid salts. Yet, the addition of amines led to a difference in critical areas and a significant difference in permeation.

The separation of fatty acids using membranes is an important advancement in this field. Vegetable oils are the most important biorenewable feedstrock, but over 96% of the 140 million tons of these oils is used for food, feed for animals, or biodiesel. There are surprisingly few other industrial applications of fatty acids despite their low cost and abundance. The reason for the limited industrial applications to turn fatty acids into more valuable materials is that they are isolated as mixtures, and it is not possible to separate these mixtures into individual components on a large, industrial scale. Currently, any industrial application of fatty acids requires using a mixture of fatty acids. Our method to separate fatty acids using membranes is an important advance because membranes are widely used in industry and can be used to purify large quantities of a molecule. The purification of fatty acids by organic nanofiltration membranes may lead to methods to purify fatty acids on the millions of tons per year size scale which will make fatty acids an attractive starting material for industrial applications.

ASSOCIATED CONTENT

Supporting Information

Separation of stearic and oleic acid using multiple extractions, use of pressure to separate fatty acids derived from soybean oil, and the retention of molecules through PDCPD membranes are discussed in the Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors thank the NSF (CHE-0848162 and CHE-1213325) for financial support of this research.

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