Trichloroisocyanuric acid-mediated intermediate α-chlorination of fatty acids

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Abstract

A substantial amount of food waste, comprising both edible and inedible components, is made up of fat biomasses, which are frequently used inefficiently or disposed of incorrectly, leading to environmental problems. Converting their primary ingredients, fatty acids (FAs), into α-hydroxy FAs (α-HFAs), which are wonderful compounds with enormous promise but are currently mostly unrealized, maybe because of their limited availability, could open up interesting avenues for their management and valuation. A straightforward and effective method is described here for converting α-chloro FAs into α-HFAs without the need for prior purification by reacting them with trichloroisocyanuric acid (TCCA), a green halogenating agent, in a solvent-free environment. The process was used to replicate an FAs combination that may be obtained from a fat biomass. It was also successfully used to stearic, palmitic and myristic acid, as well as their mixture.

Keyword: Trichloroisocyanuric acid, stearic, palmitic and myristic acid

Introduction

Food waste, which includes both edible and inedible parts that is, components linked to a food that are not meant for human consumption amounted to 1300 million tonnes per year in 2011 across the food supply chain, from initial agricultural production to final household consumption [1]. One According to the Food Waste Index study from 2019, 931 million tons of food waste were produced year by homes, businesses, and the food service sector [2].

Fatty acids (FAs) can make up a sizable or high weight percentage of the compounds included in food waste and inedible portions related to food production [3,4]. That is the case, for instance, of peels and seeds of some fruits, of waste cooking oils, and of animal fats that include the grease of shared fleeces. In particular, this last waste biomass, annually amounting, just in EU, to more than 200 thousand tons of low quality shorn wool, equivalent to 30 thousand tons of wool grease, is an example of inevitable byproduct, in this instance of the farming of sheep reared only for food [5]. It is a biomass limited in quantity but very problematic to be managed. In fact, disposing such a waste by burning or sending it to landfill is an unsustainable practice and, on the other hand, its scouring to obtain clean wool and wool wax is costly and pollutant. Therefore, in the perspective of a circular and environmentally friendly economy, new approaches to exploit waste biomasses that, like this, have a high content of fats are highly desirable.

It is precisely the unique and subtle feature of wool fat, namely, its high content of α-hydroxy-FAs (α-HFAs). FA [6,7] suggested the conversion of FAs to α-GFAs. Helps to maximize the value of abundant biomass Realizes more profitable and sustainable management of LCDs. Indeed, α-HFAs are very valuable fine chemicals, unlike short-chain α-hydroxy acids such as lactic acid, which have much less potential completely used, perhaps due to limited commercial availability. Indeed, the α-carbon of FAs has rarely been targeted for chemical/biological hydroxylation. Thanks to their physical, chemical, and biological features, α-HFAs are used in the field of cosmetics for their surfactant and antimicrobial properties, but they could be applied also in the (bio)-remediation field for their surfactant and chelating ability and in the production of biodegradable polymers [8-12]. Recently, they have been reported as the useful precursors of non canonical long-chain α-amino acids, which are of increasing interest and demand in many fields [13].

Apart from the biocatalytic hydroxylations [14], the simplest way to convert a carboxylic acid into the corresponding α-hydroxy acid by chemical synthesis is to α-halogenate it and then to substitute halogen with hydroxyl [15]. However, the traditional Hell−Volhard−Zelinsky α-halogenation of carboxylic acids with molecular halogens is not environmentally friendly, and its scaling up raises many problems because halogens are hazardous, corrosive, and toxic, by produced hydrogen halide requires special attention for waste disposal and banned or not recommended solvents are necessarily used as reaction media [16].

Here, conversely, we describe an efficient and green two-step conversion of FAs into α-HFAs by α-chlorination, followed by the substitution of chlorine by hydroxyl, which uses, in the α-chlorination step, an inexpensive, safe, environmentally benign and atom-economic organohalogen like trichloroisocyanuric acid (TCCA, 1) (Fig. 1) [17-20]. The procedure was applied to single FAs first and then to their mixture, ad hoc created to simulate a FAs mixture obtainable from wool grease and, typically, also from other waste fat biomasses.

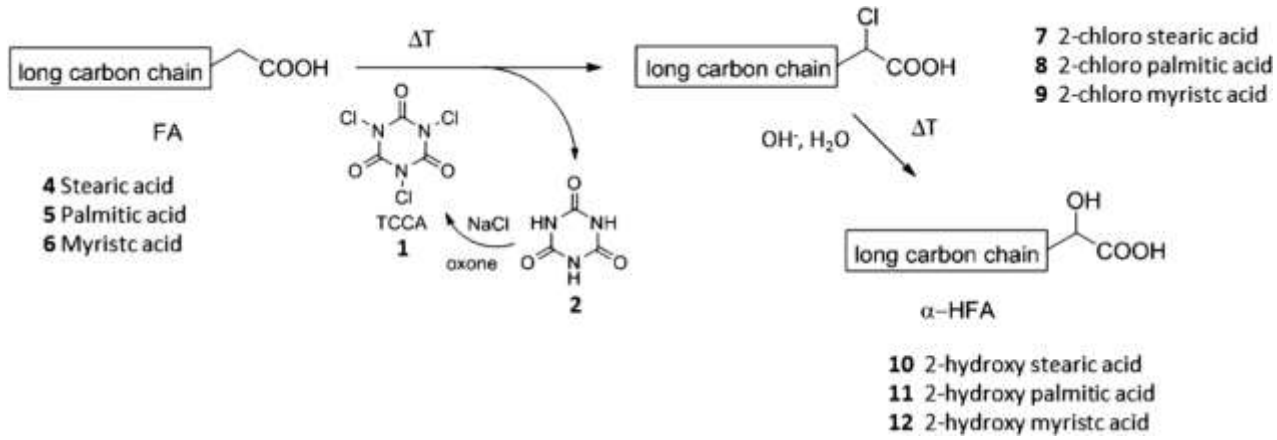


Fig. 1 Convert the FAS with a long chain to α-HFA by intermediate α-clarity using TCCA.

Experimental

Materials and Methods

Stearic acid, palmitic acid, myristic acid, 1 and phosphorus trichloride were purchased from Sigma and used without further purification. ^{1}H-NMR and ^{13}C-NMR spectrums were recorded in $CDCl_3$, DMSO-d_6 and CD_3OD at 300 and 75 MHz, respectively, with a Varian Mercury 300 spectrometer and elaborated with Mnova software. Chemical shifts are reported in ppm relative to a residual solvent as internal standard.

GC/FID analyses were performed using a gas chromatograph Trace GC with a FID and autosampler AS2000 (Thermo Fisher). Before the analysis, the sample (5 mg) was derivatized, as methyl ester, using a 500 µL of HCl 3 M solution in MeOH and left in the oven at 55 °C overnight. Hexane (1.2 mL) was then used as an extraction solvent, and 1 mL was transferred into a 2 mL vial and analyzed. Chromatographic separation was carried out on a DB-5 MS UI fused silica capillary column (30 m, 0,25 mm I.D., 0,25 µm film thickness, Agilent). The GC-FID system was operated under the following conditions: injection temperature 280 °C (split mode 30:1); the initial column temperature was 180 °C and was subsequently increased to 280 °C at a rate of 5 °C/ min. Helium was used as the carrier gas at a flow rate of 1.0 mL/min. The FID was operated at 300 °C.

GC/MS analyses were performed on a Varian-Agilent 3900 gas chromatograph with an ion trap mass selective detector Saturn 2100T (Varian-Agilent) and autosampler CP8400. Chromatographic separation was carried out on a HP-1 MS UI fused silica capillary column (12 m × 0.18 mm i.d., film thickness 0.18 µm, Agilent). The GC/MS system was operated under the following conditions: injection temperature 250 °C (split mode 50:1); interface transfer line 300 °C; and the initial column temperature 150 °C, which was subsequently increased to 250 °C at a rate of 5 °C/min. Helium was used as the carrier gas at a flow rate of 0.9 mL/min. MS analysis was performed in a SCAN MODE (35/650 m/z) operated in a chemical ionization mode with methanol as a reactant gas and an emission current of 10 µA. The injection volume was 1 µL with a solvent delay of 2 min.

High resolution electrospray mass spectra were acquired with Q-TOF Synapt G2 Si (WATERS). The percent of conversion, selectivity, and the identity of the compounds were determined using GC/FID, GC/MS, and high-resolution mass spectrometry (HRMS) analysis.

General Procedure for α-Chlorination of FAs

In a round-bottom flask wrapped in aluminum foil, the FA (35 mmol) was heated under magnetic stirring at 80 °C until melting. The liquid mass was added of PCl3 (1.2 mmol, 104 µL) and left reacting for 1 h. TCCA (16.3 mmol, 3.78 g) was slowly added over 30 min. The mixture was then stirred for 24 h at 80 °C. After this time, the reaction mixture was cooled down at room temperature, and ethyl acetate

was added: a white precipitate was formed. The solid was then removed by filtration, and the filtrate was washed with a solution of sodium metabisulfite (10% w/v) and with brine. The organic layer was collected, dried over sodium sulfate, and concentrated under vacuum to give the desired alpha-chloro acid.

Synthesis of 2-chloro stearic acid (7)

Obtained as a white solid crude (10.83 g, 97.0% of theoretical amount): mp 62.2 °C, Rf (dichloromethane/methanol 9:1) = 0.55, ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.42 (dd, J = 7.7, 5.9 Hz, 1H), 1.98 − 1.68 (m, 2 H), 1.22 (s, 28 H), 0.83 (t, J = 6.7 Hz, 3H) (Fig. 2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.02, 57.08, 34.71, 31.91, 29.67, 29.65, 29.62, 29.57, 29.46, 29.34, 29.28, 29.17, 28.80, 25.87, 22.67, 14.09 (Fig. 3). GC−MS: [M + H] = 333.5 (Fig. 4), GC-FID: Rt = 12.65 min, conversion = 100%, purity = 91.7% (Fig. 5).

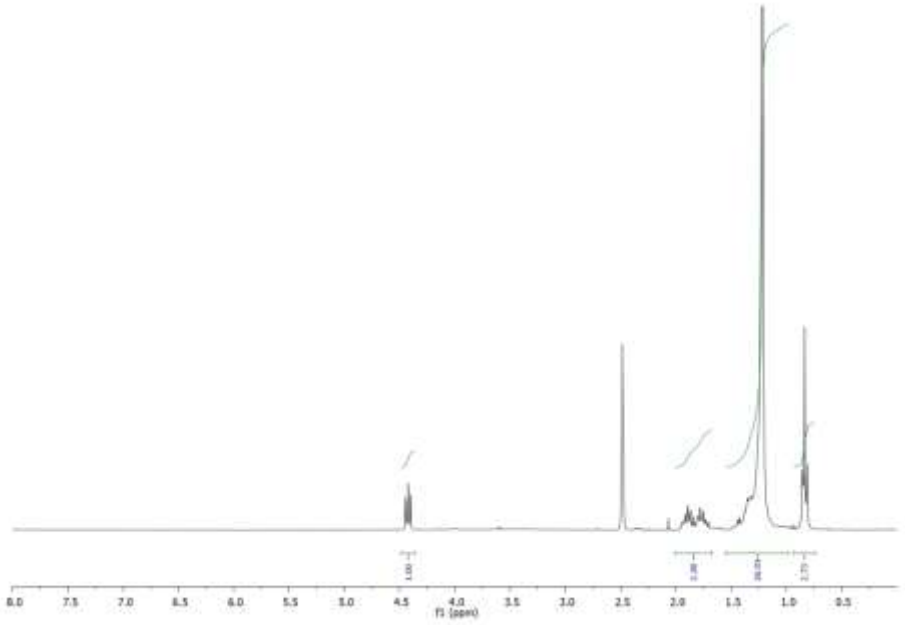


Fig. 2 ^{1}H NMR spectrums of 2-chloro stearic acid

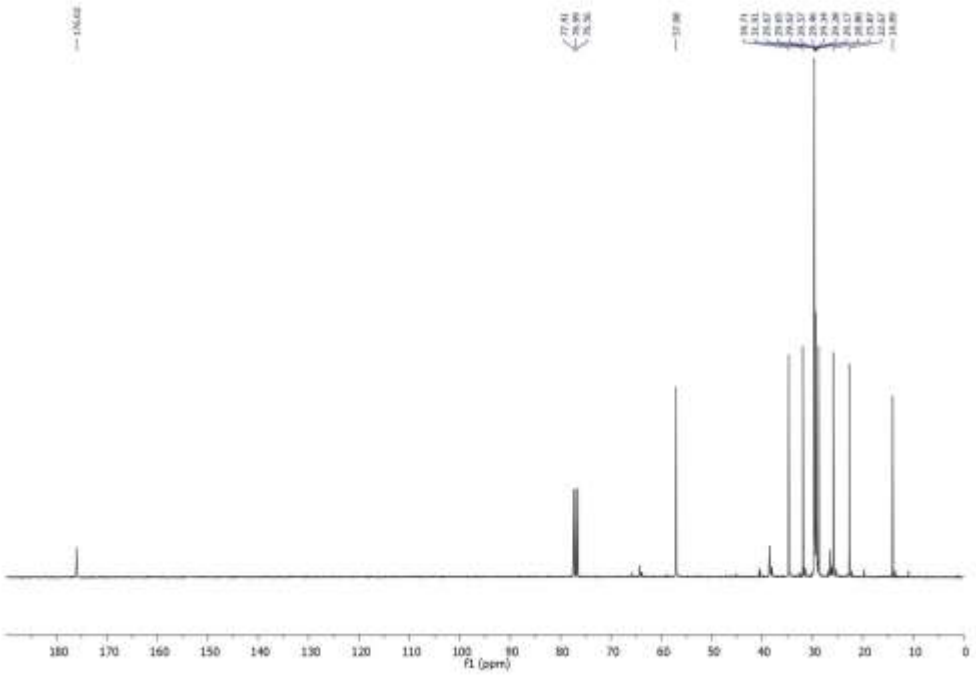


Fig. 3 ^{13}C NMR spectrums of 2-chloro stearic acid

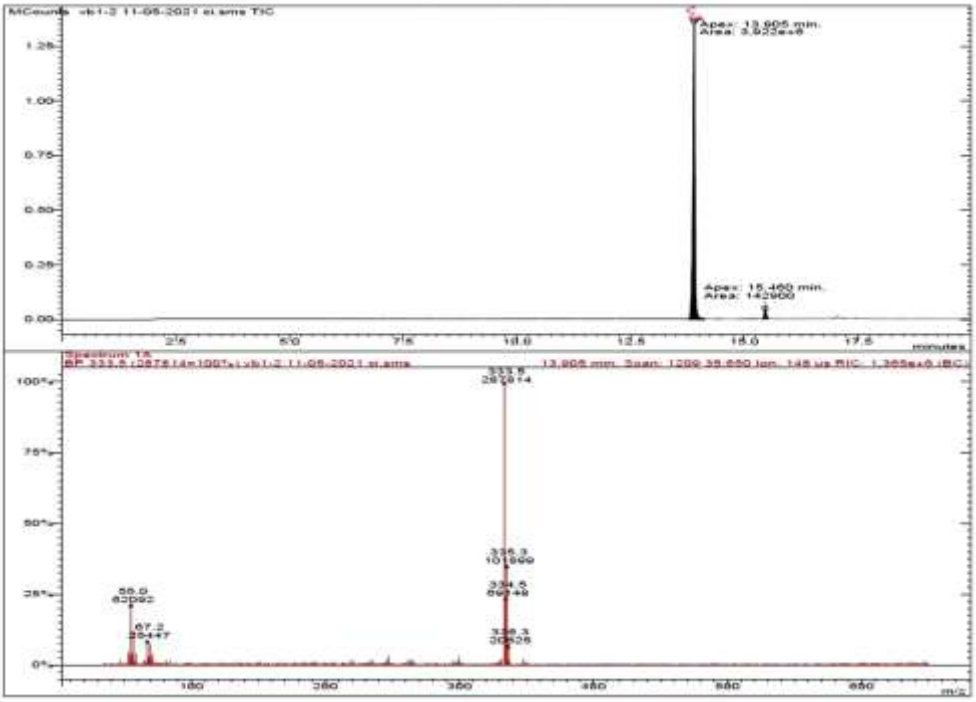
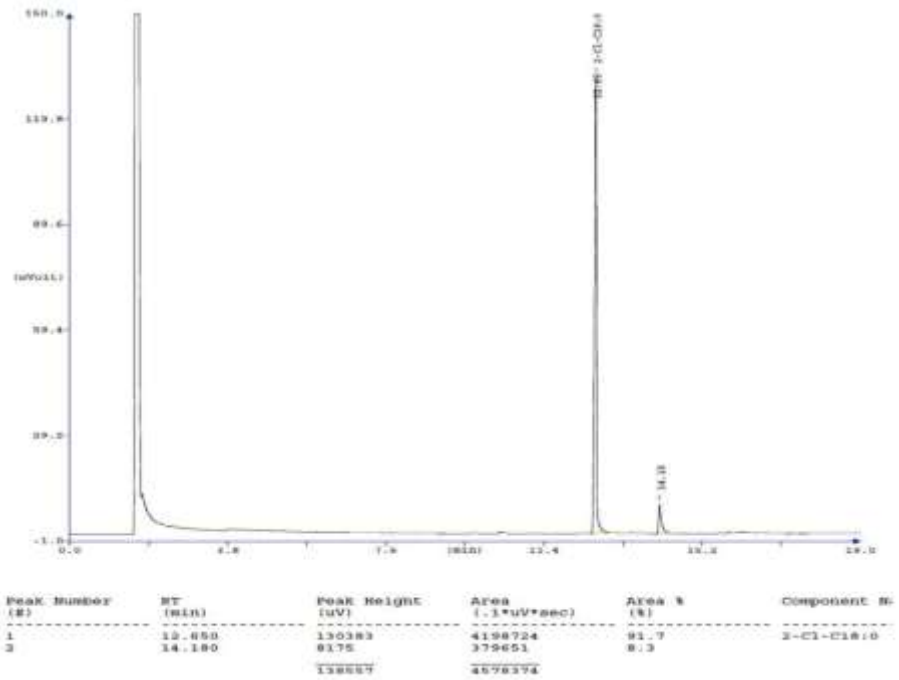


Fig. 4 GC-MS analysis of 2-chloro stearic acid



Peak Number (#)	RT (min)	Peak Height (uV)	Area (.1*uV*sec)	Area % (%)	Component Name
1	12.850	130383	4198724	91.7	2-Cl-C18:0
2	14.180	8175	379651	8.3	
		138557	4578374		

Fig. 5 GC-FID analysis of 2-chloro stearic acid

Synthesis of 2-chloro palmitic acid (8)

Obtained as a white solid crude (9.81 g, 96.4% of the theoretical amount): mp 55.7 °C, Rf (dichloromethane/methanol 98:2) = 0.6, ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.42 (dd, J = 7.7, 5.9 Hz, 1H), 2.01−1.68 (m, 2 H), 1.27 (s, 24 H), 0.83 (t, J = 6.6 Hz, 3H) (Fig. 6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.53, 57.07, 34.73, 31.90, 29.66, 29.65, 29.63, 29.61, 29.56, 29.46, 29.34, 29.27, 28.79, 25.86, 22.67, 14.09 (Fig. 7). GC−MS: [M + H] = 305.5 (Fig. 8), GC-FID: Rt = 9.58 min, conversion = 100%, purity = 89.0% (Fig. 9).

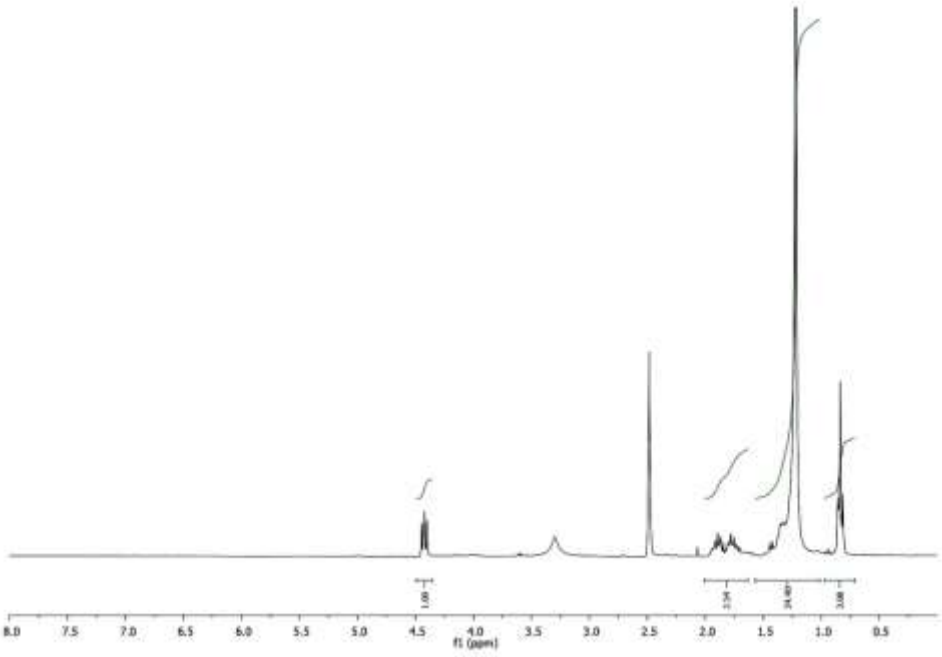


Fig. 6 ^{1}H NMR spectrums of 2-chloro palmitic acid

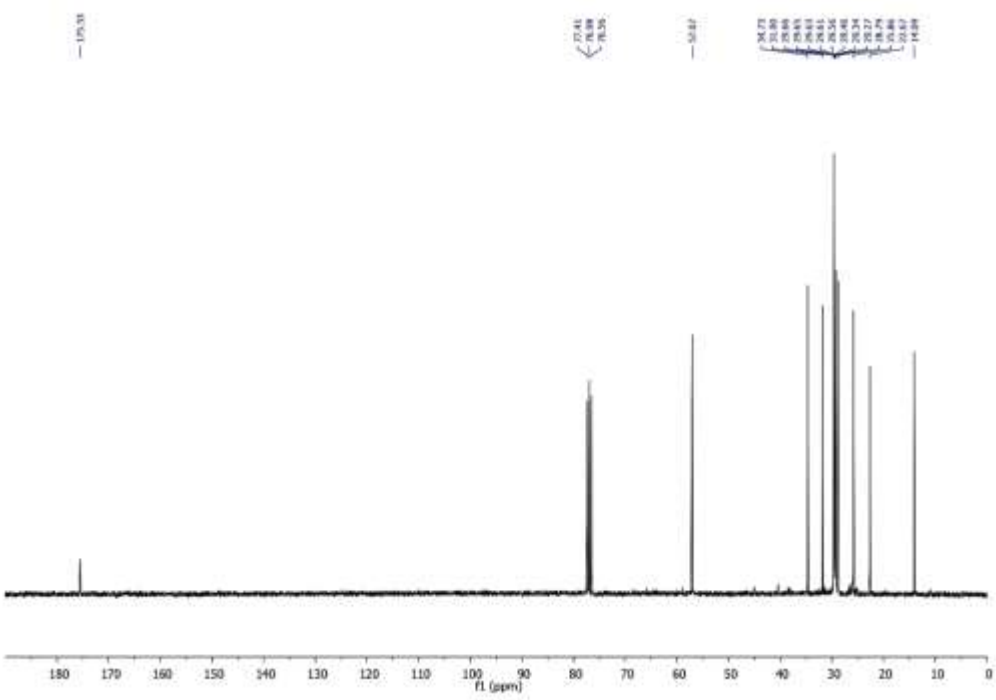


Fig. 7 ^{13}C NMR spectrums of 2-chloro palmitic acid

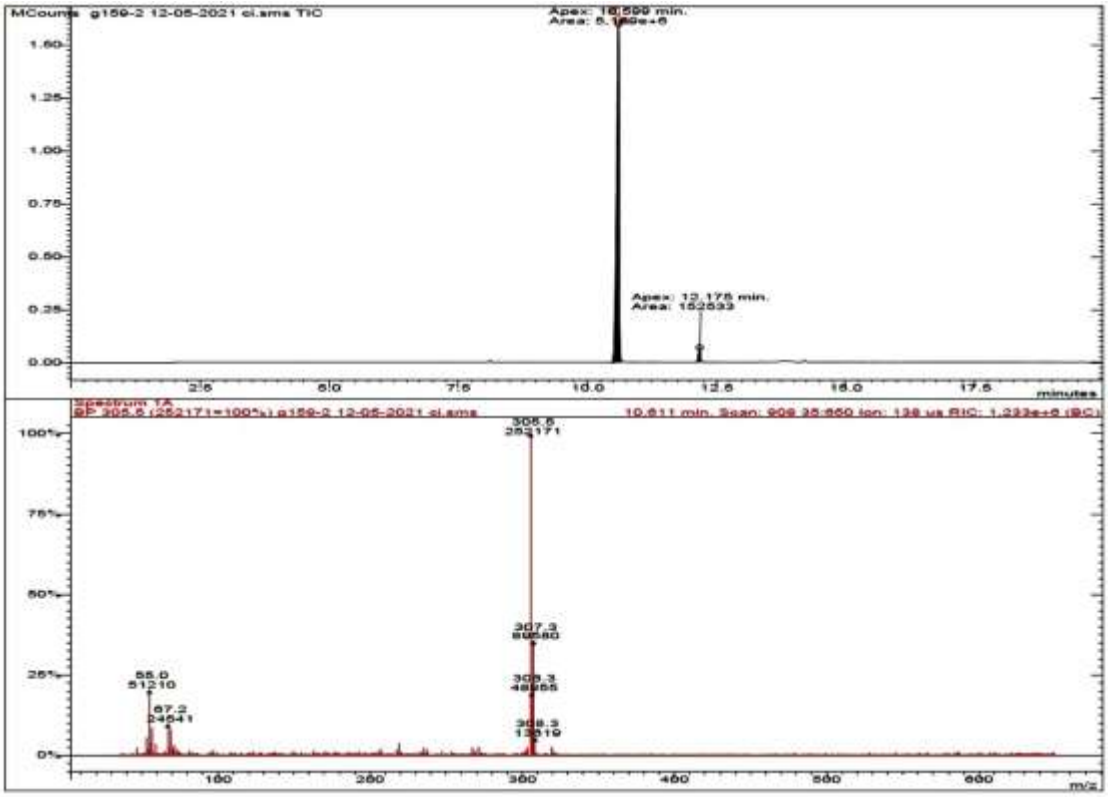


Fig. 8 GC-MS analysis of 2-chloro palmitic acid

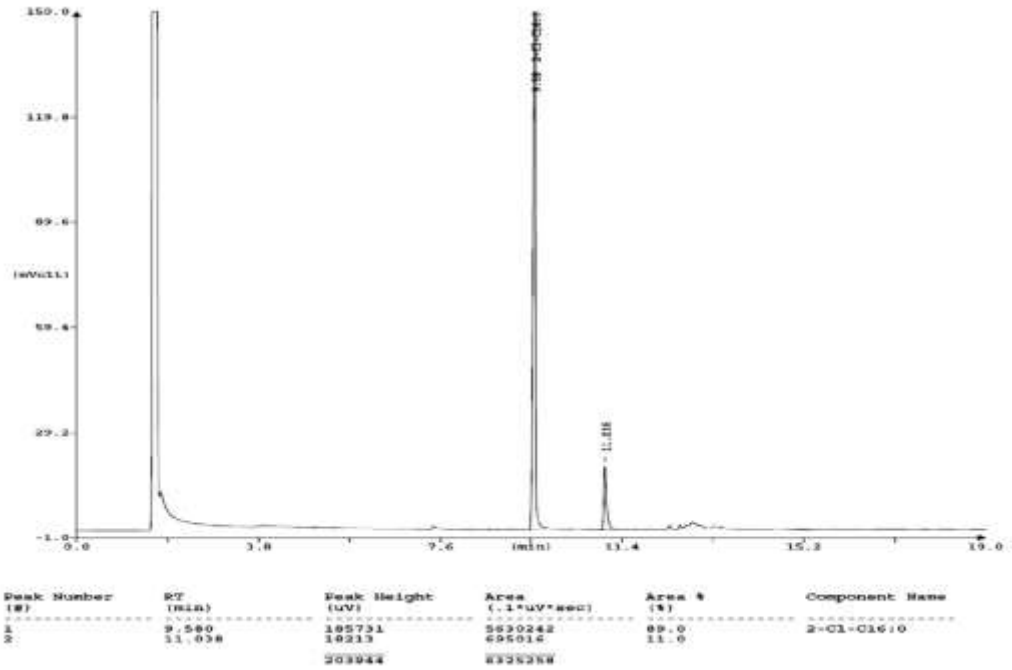


Fig. 9 GC-FID analysis of 2-chloro palmitic acid

Synthesis of 2-chloro myristic acid (9)

Obtained as a white solid crude (8.84 g, 96.1% of the theoretical amount): mp 43.7 °C, Rf (dichloromethane/methanol 98:2) = 0.4, ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.42 (dd, J = 7.7, 5.9 Hz, 1H), 1.99−1.67 (m, 2H), 1.49−1.13 (m, 20H), 0.84 (t, J = 6.7 Hz, 2H) (Fig. 10). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.54, 57.07, 34.73, 31.89, 29.61, 29.56, 29.52, 29.50, 29.49, 29.45, 29.32, 29.27, 29.24, 28.79, 25.86, 22.67, 14.09 (Fig. 11). GC−MS: [M + H] = 277.3 (Fig. 12), GC-FID: Rt = 6.728 min, conversion = 100%, purity = 84.6% (Fig. 13).

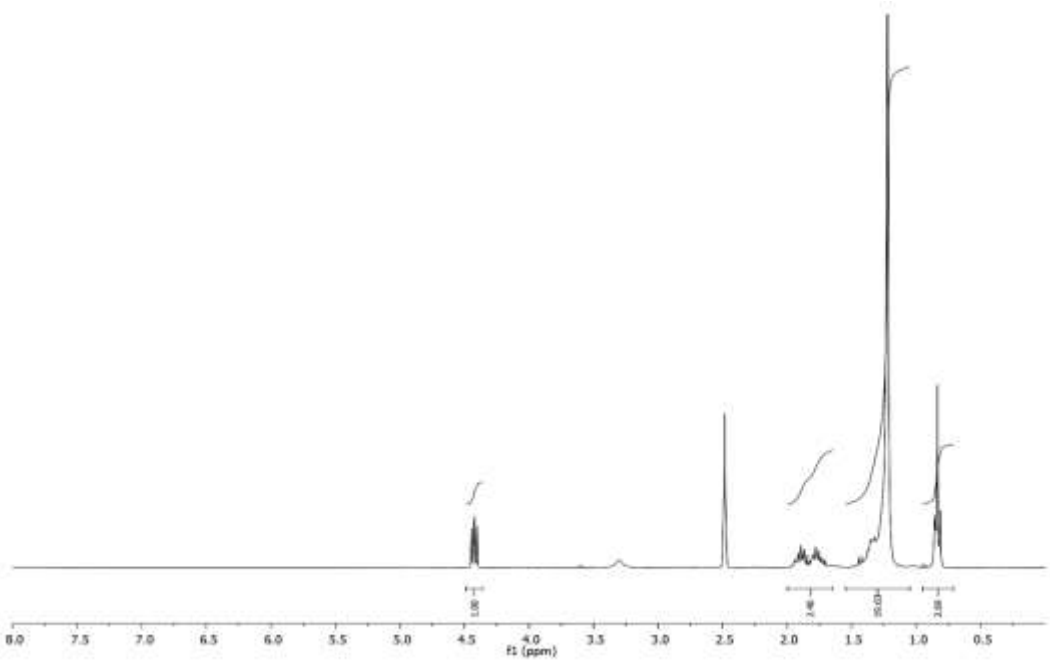


Fig. 10 ^{1}H NMR spectrums of 2-chloro myristic acid

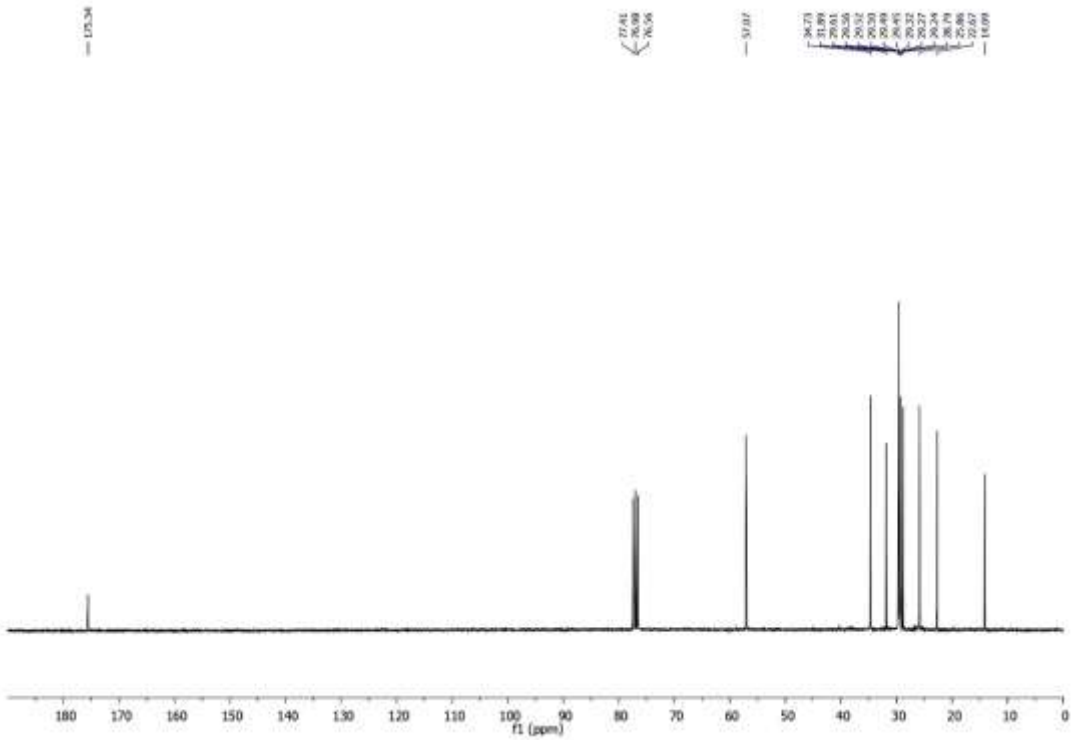


Fig. 11 ^{13}C NMR spectrums of 2-chloro myristic acid

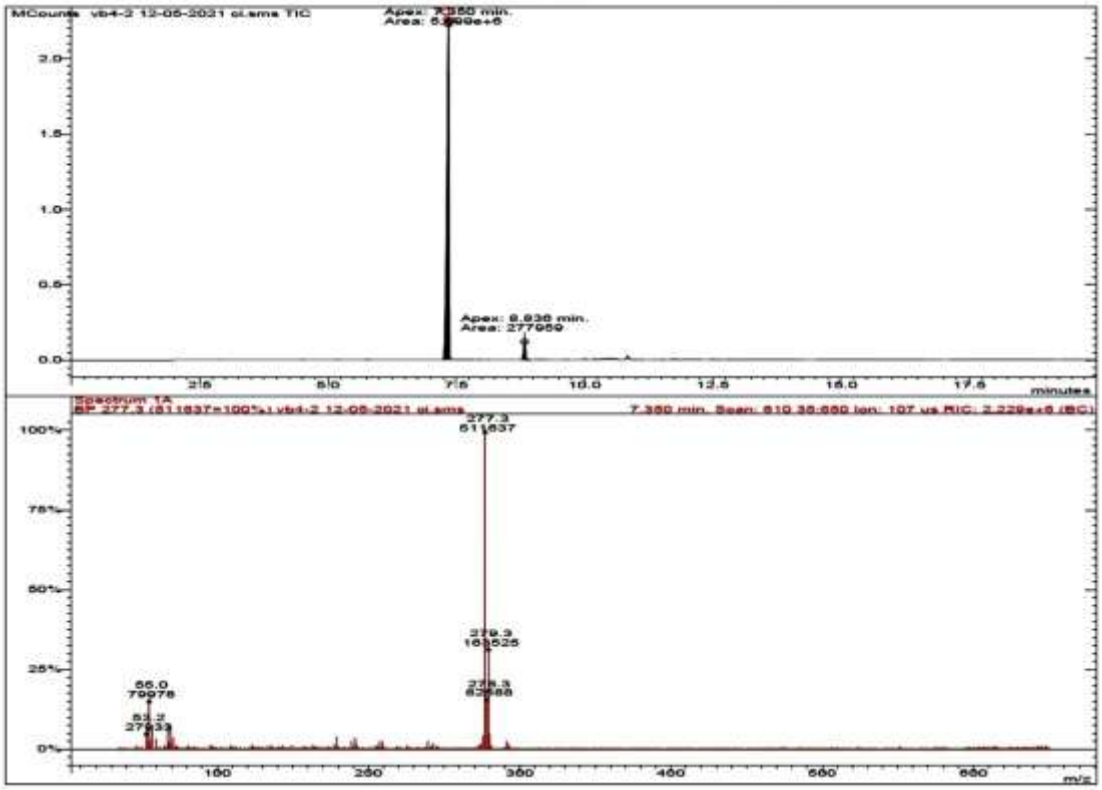
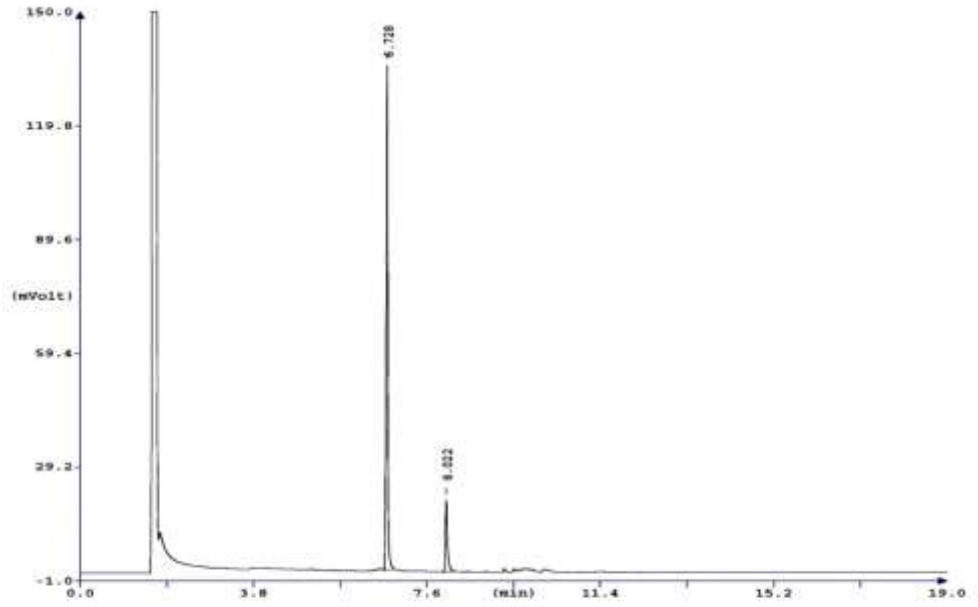


Fig. 12 GC-MS analysis of 2-chloro myristic acid

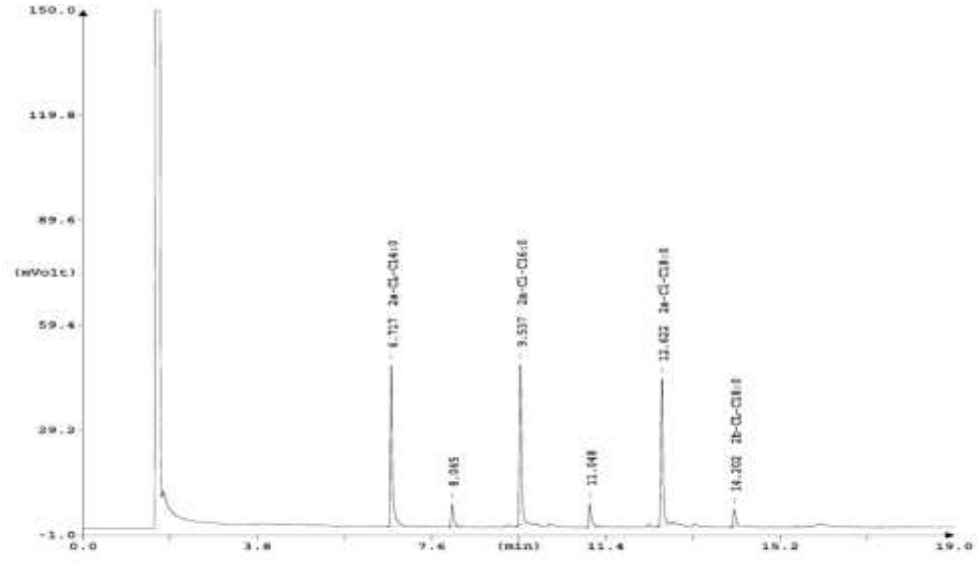


Peak Number (#)	RT (min)	Peak Height (uV)	Area (.1*uV*sec)	Area % (%)	Component Nam
1	6.728	134006	3192149	84.6	
2	8.022	18869	581040	15.4	
		152874	3773189		

Fig. 13 GC-FID analysis of 2-chloro myristic acid

Synthesis of 2-chloro stearic acid, 2-chloro palmitic acid, and 2-chloro myristic acid mixture

Obtained as a white solid crude (9.33 g, 91.7% of the theoretical amount) from 35 mmol of an equimolar mixture of 4, 5, and 6 according to the general procedure adopted for the single FAs: mp 40.9 °C, GC-FID: Rt = 6.717 min, 9.537 min, 12.622 min, conversion = 100%, purity = 85.5%. (Fig. 14)



Peak Number (#)	RT (min)	Peak Height (uV)	Area (.1*uV*sec)	Area % (%)
1	6.717	46199	1428583	28.5
2	8.045	6459	251344	5.0
3	9.537	46016	1424593	28.4
4	11.648	6770	275261	5.5
5	12.622	41992	1435147	28.6
6	14.202	5038	202869	4.0

Fig. 14 GC-FID analysis 2-chloro stearic acid, 2-chloro palmitic acid, 2-chloro myristic acid and mixture

General Procedure for the Conversion of α-chloro FAs into α-HFAs

In a round-bottom flask, KOH (140 mmol, 7.85 g) and water (200 mL) were stirred at 80 °C for 30 min. The crude 2-chloro FA resultant from the chlorination step was added to the KOH water solution, and the mixture was refluxed for 24 h. Then, the mixture was cooled down at room temperature and the pH was adjusted to 1 using HCl 1 M. A white solid precipitated. The mixture was filtered, and the solid was recovered. After purification by trituration with acetonitrile, in a 1:3 ratio, the desired α-HFA was obtained as a white solid.

Synthesis of 2-hydroxy stearic acid (10)

Obtained as a white solid in 68% yield: mp 90.8 °C, Rf (dichloromethane/methanol 9:1) = 0.62, ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.88 (dd, J = 7.6, 4.5 Hz, 1H), 3.38 (bs, 1H, exchange with D_2O), 1.64−1.37 (m, 2H), 1.25 (s, 28H), 0.83 (t, J = 6.7 Hz, 3H) (Fig. 15). ^{13}C NMR (75 MHz, CD3OD): δ 176.62, 70.03, 34.00, 31.64, 29.35, 29.33, 29.26, 29.21, 29.05, 24.70, 22.31, 13.01 (Fig. 16). ESI negative HRMS: calcd for $C_{18}H_{35}O_3$[M−H]−, m/z, 299.2586; found, 299.2585 (Fig. 17), GC-FID: Rt = 12.142 min, purity = 98.9% (Fig. 18).

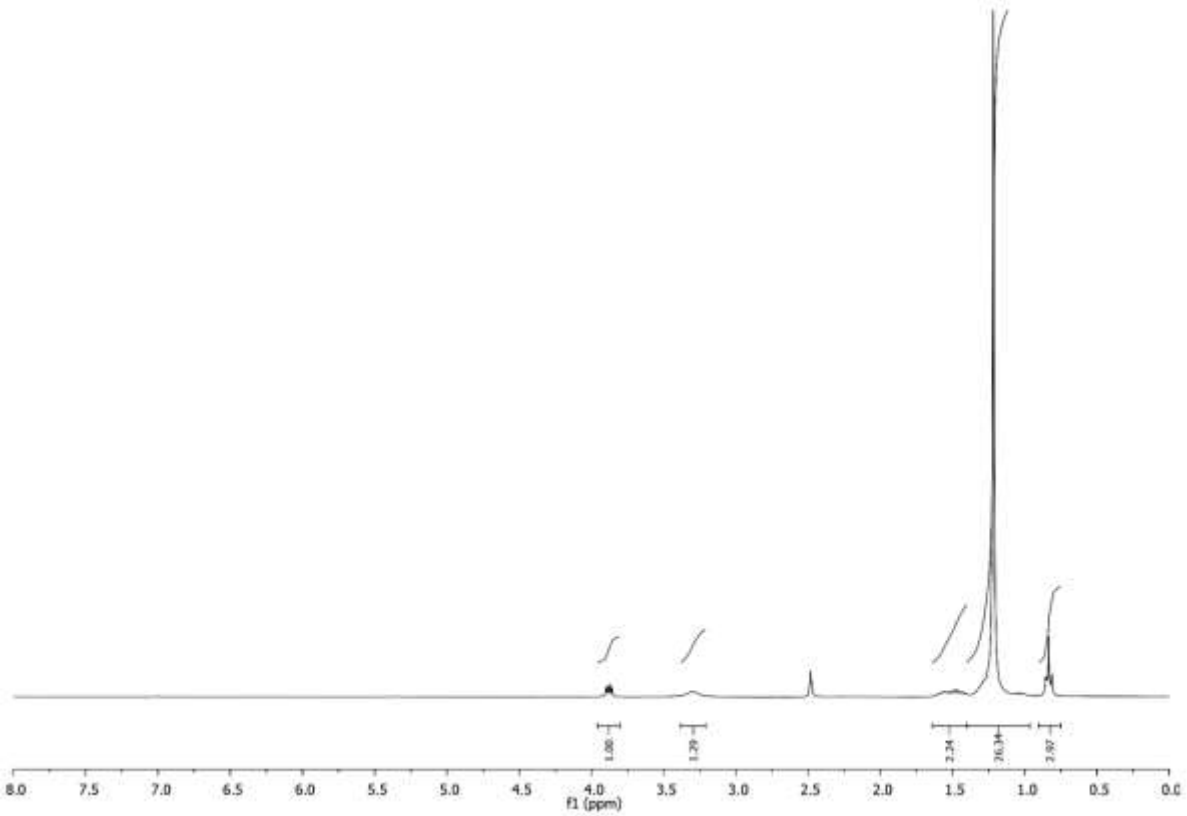


Fig. 15 ^{1}H NMR spectrums of 2-hydroxy stearic acid

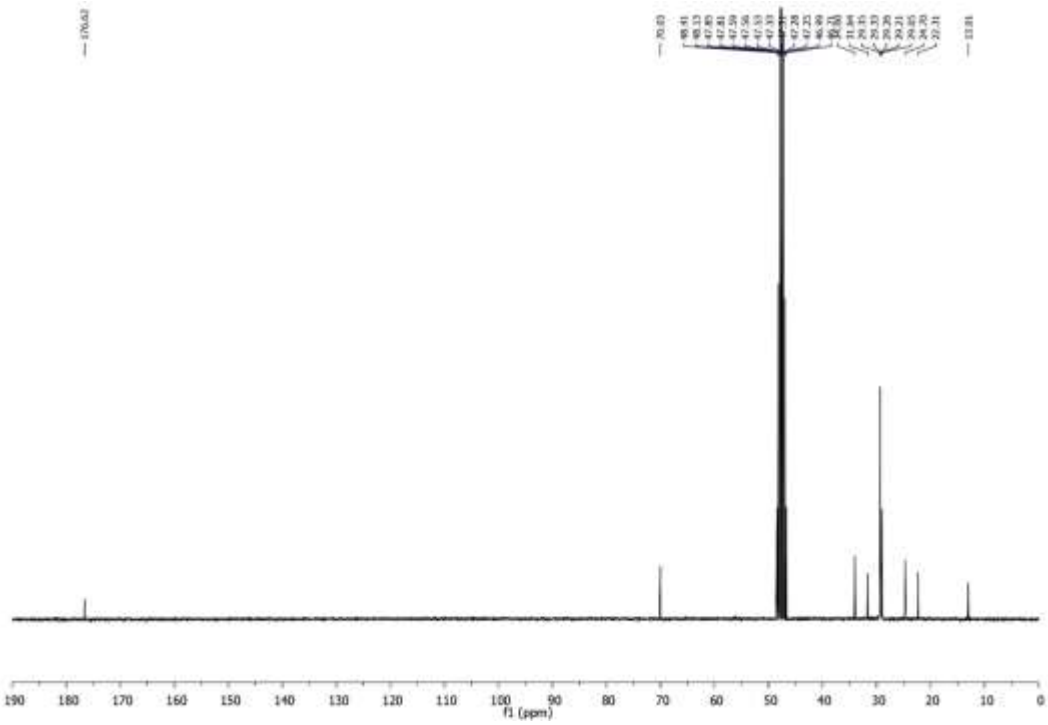
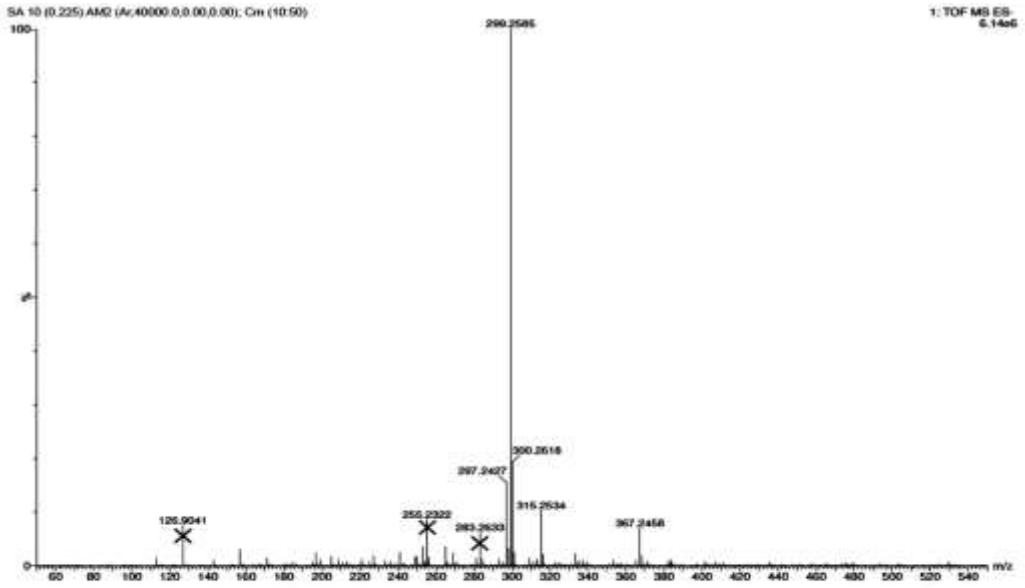
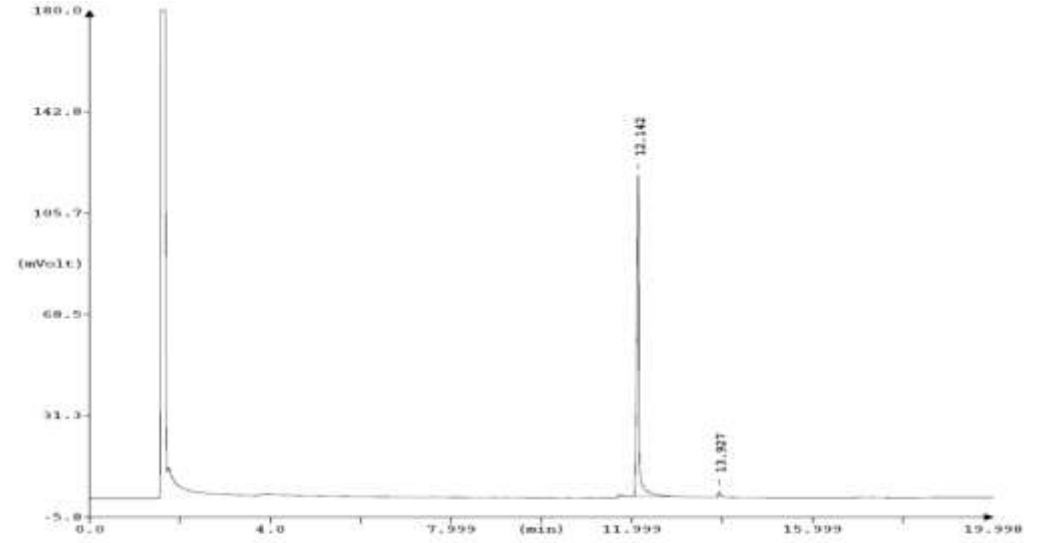


Fig. 16 ^{13}C NMR spectrums of 2-hydroxy stearic acid



Minimum:				-2.5				
Maximum:		5.0	5.0	200.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
299.2585	299.2586	-0.1	-0.3	1.5	1479.3	n/a	n/a	C18 H35 O3

Fig. 17 HRMS of 2-hydroxy stearic acid



Peak Number (#)	RT (min)	Peak Height (uV)	Area (.1*uV*sec)	Area % (%)	Component Nam
1	12.142	117738	4147402	98.9	
2	13.927	1621	47618	1.1	
		119358	4194979		

Fig. 18 GC-FID of 2-hydroxy stearic acid

Synthesis of 2-Hydroxy Palmitic Acid (11)

Obtained as a white solid in 64% yield: mp 85.7 °C, Rf (dichloromethane/methanol 9:1) = 0.53, ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.88 (dd, J = 7.6, 4.6 Hz, 1H), 3.30 (bs, 1H, exchange with D_2O), 1.85−1.45 (m, 2H), 1.22 (s, 24H), 0.85 (t, J = 6.7 Hz, 3H) (Fig. 19). ^{13}C NMR (75 MHz, CD_3OD): δ 176.59, 70.02, 34.00, 31.65, 29.36, 29.34, 29.26, 29.20, 29.05, 24.70, 22.30, 13.01 (Fig. 20). ESI negative HRMS: calcd for $C_{16}H_{31}O_3$[M−H]−, m/z, 271.2273; found, 271.2272 (Fig. 21). GC-FID: Rt = 9.062 min, purity = 99.4% (Fig. 22).

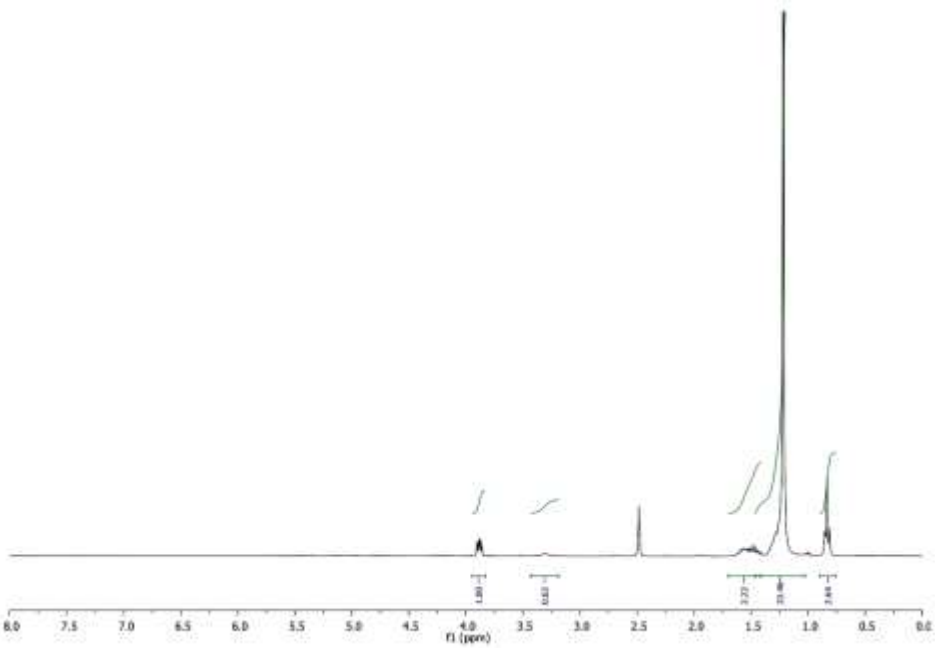


Fig. 19 ^{1}H NMR spectrums of 2-hydroxy palmitic acid

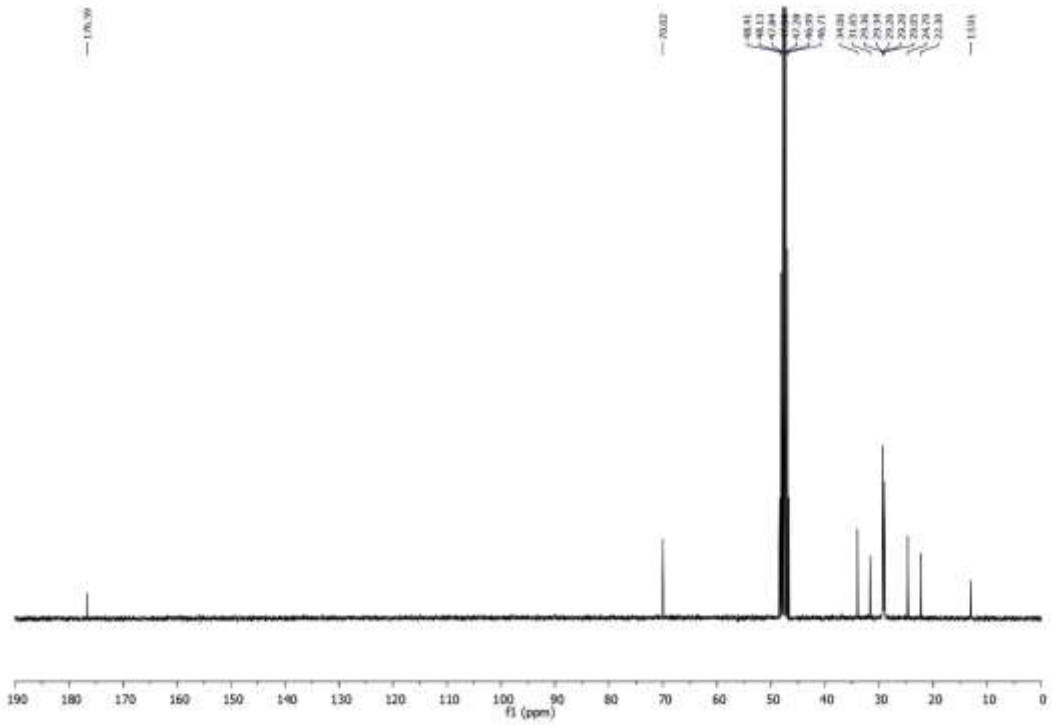


Fig. 20 ^{13}C NMR spectrums of 2-hydroxy palmitic acid

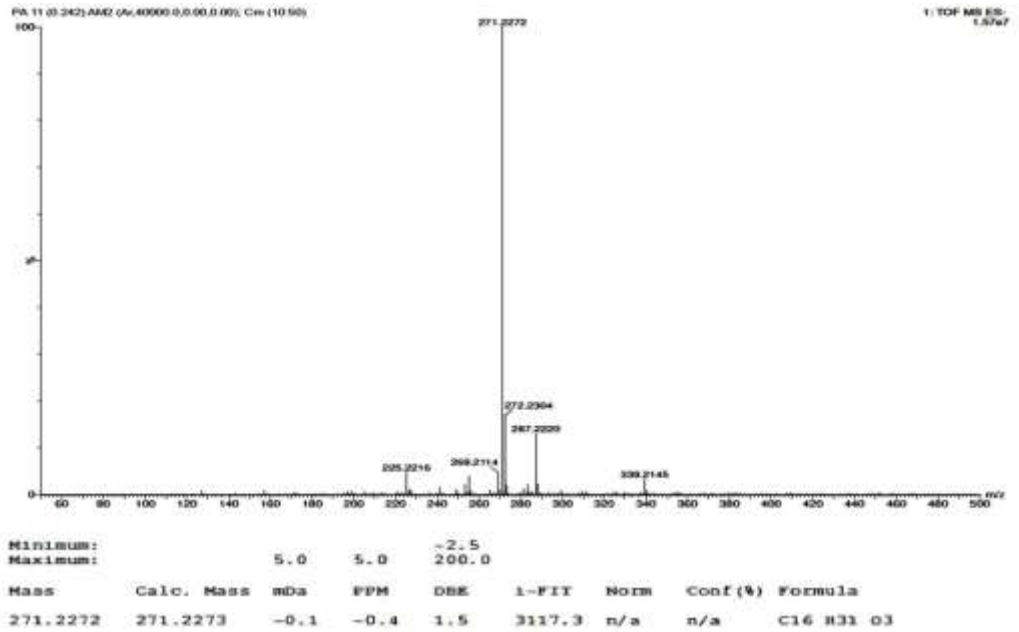
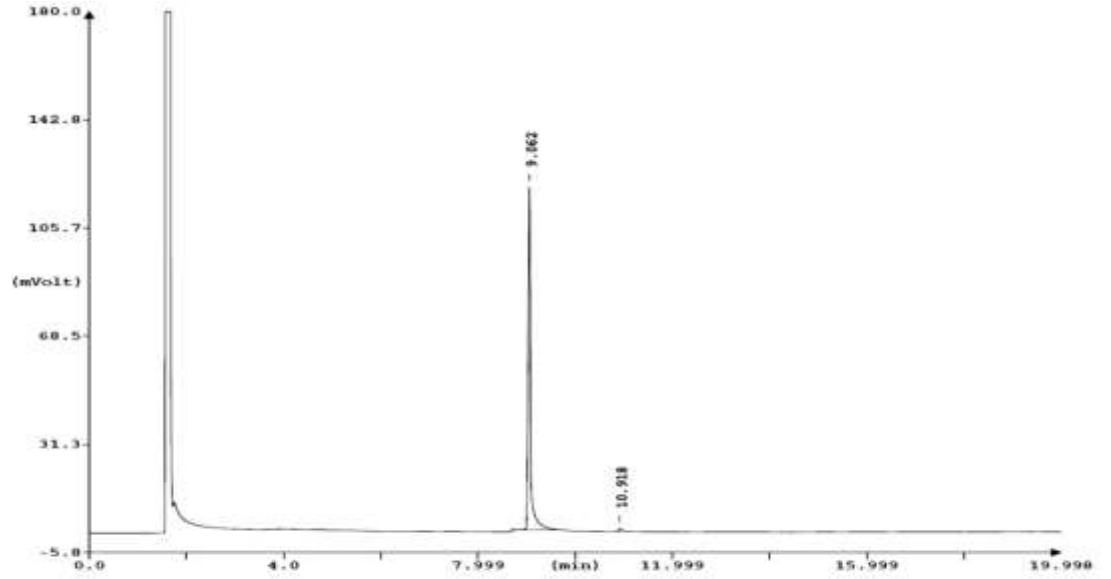


Fig. 21 HRMS of 2-hydroxy palmitic acid



Peak Number (#)	RT (min)	Peak Height (uV)	Area (.1*uV*sec)	Area % (%)	Component Nam
1	9.062	117727	3976403	99.4	
2	10.918	687	25347	0.6	
		118413	4001749		

Fig. 22 GC-FID of 2-hydroxy palmitic acid

Synthesis of 2-hydroxy myristic acid (12)

Obtained as a white solid in 66% yield: mp 83.5 °C, Rf (dichloromethane/methanol 9:1) = 0.46, ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.88 (dd, J = 7.6, 4.6 Hz, 1H), 1.66−1.42 (m, 2 H), 1.25 (s, 20H), 0.83 (m, 3H) (Fig. 23). ^{13}C NMR (75 MHz, CD_3OD): δ 177.11, 70.23, 34.15, 31.71, 29.45, 29.42, 29.37, 29.31, 29.17, 29.13, 24.81, 22.37, 13.15 (Fig. 24). ESI negative HRMS: calcd for $C_{14}H_{27}O_3$[M−H]−, m/z, 243.1960; found, 243.1958 (Fig. 25), GC-FID: Rt = 6.297 min, purity = 99.0% (Fig. 26).

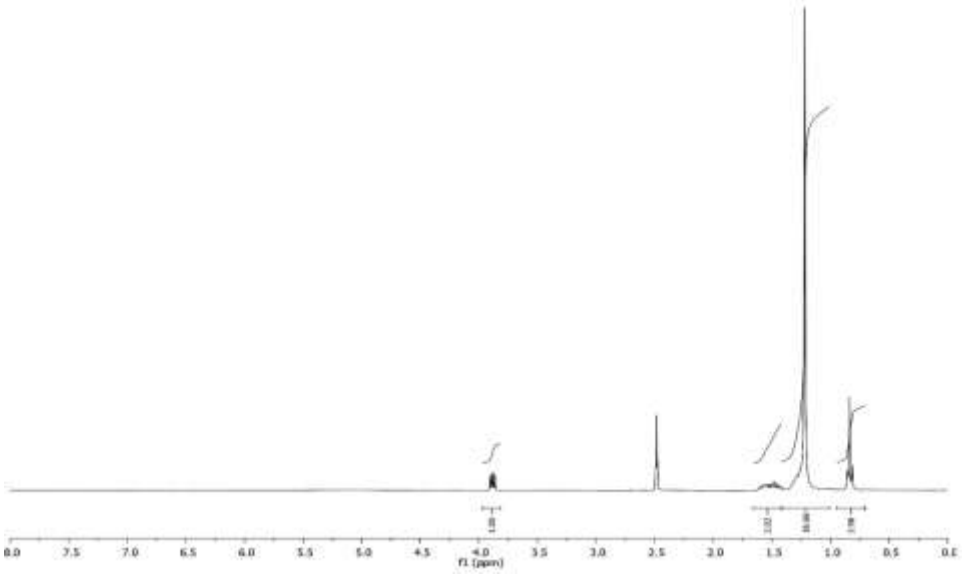


Fig. 23 ^{1}H NMR spectrums of 2-hydroxy myristic acid

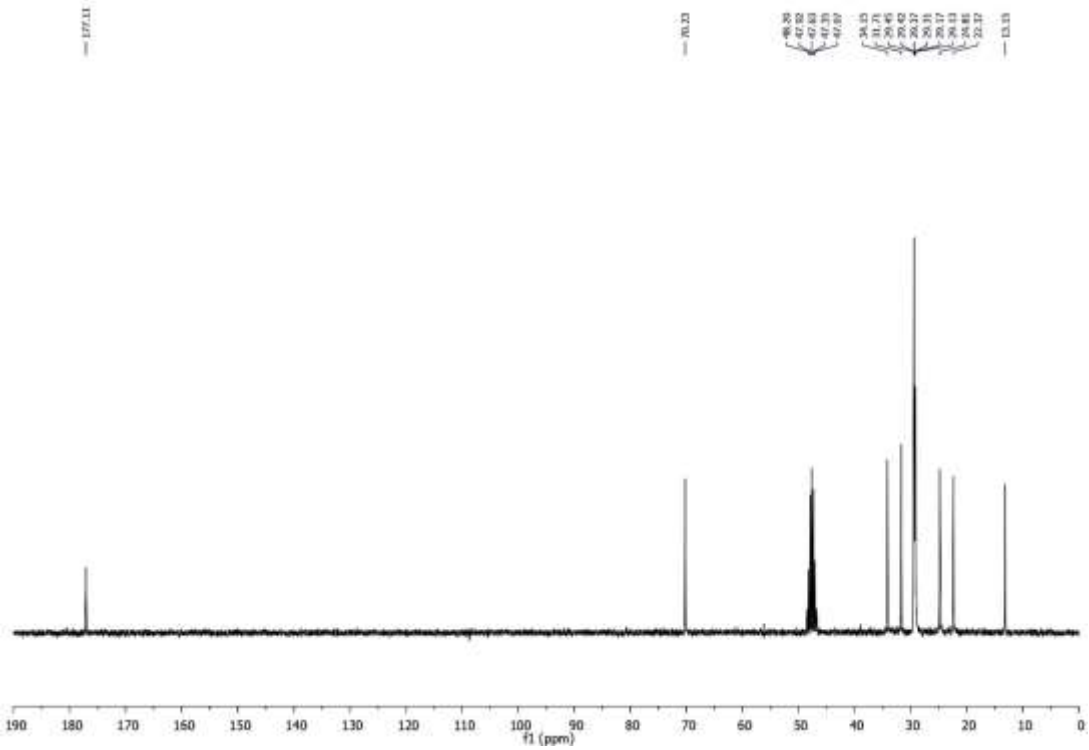
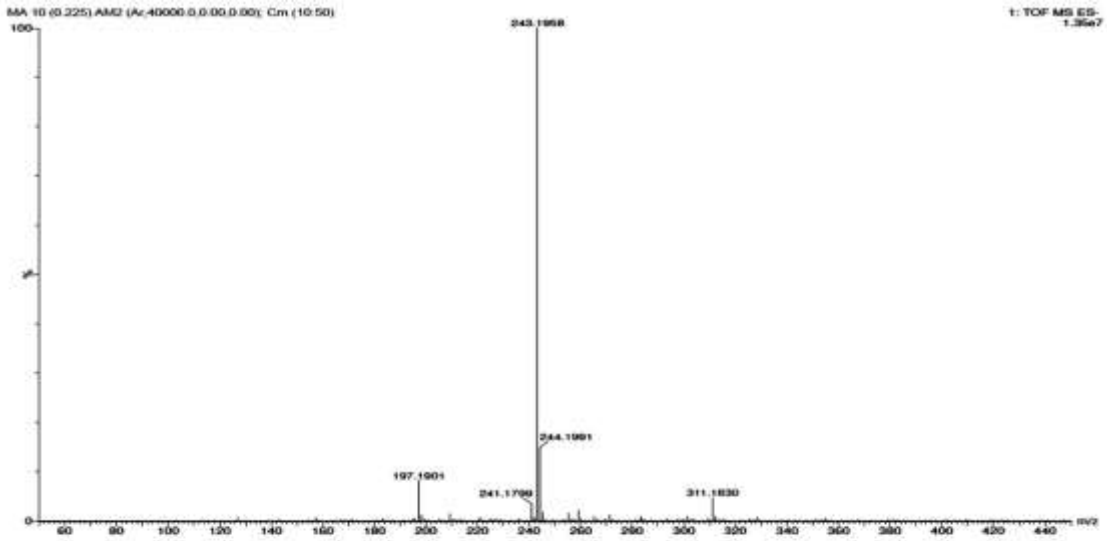
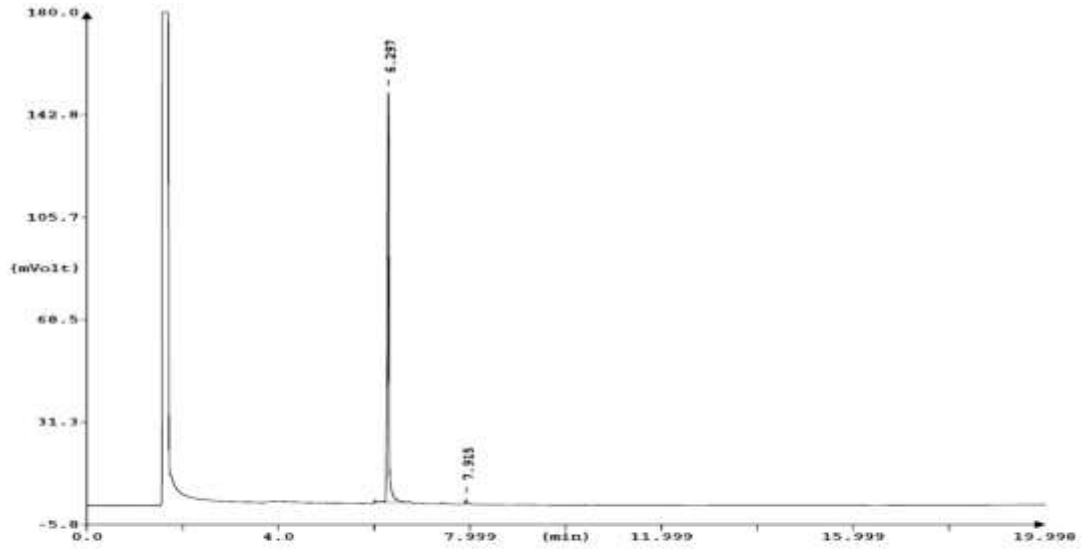


Fig. 24 ^{13}C NMR spectrums of 2-hydroxy myristic acid



Minimum:				-2.5				
Maximum:		5.0	5.0	200.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
243.1958	243.1960	-0.2	-0.8	1.5	3121.4	n/a	n/a	C14 H27 O3

Fig. 25 HRMS of 2-hydroxy myristic acid

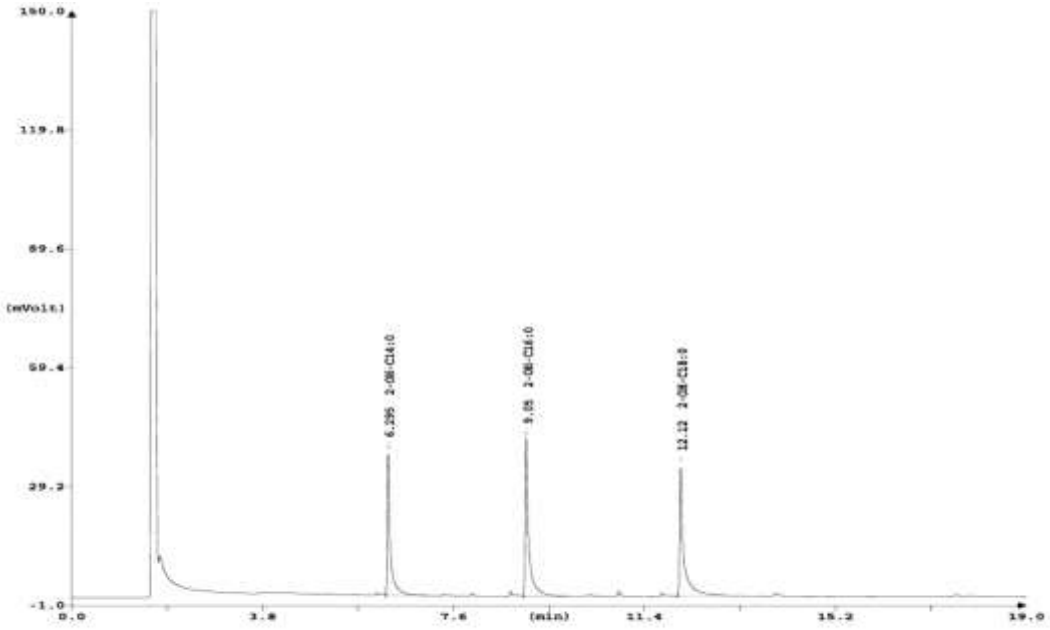


Peak Number (#)	RT (min)	Peak Height (uV)	Area (.1*uV*sec)	Area % (%)	Component Nam
1	6.297	148904	3701404	99.0	
2	7.915	1474	38645	1.0	
		150378	3740049		

Fig. 26 GC-FID of 2-hydroxy myristic acid

Synthesis of 2-hydroxy stearic acid, 2-hydroxy palmitic acid, and 2-hydroxy myristic acid mixture

It was obtained as a white solid in 74.2% yield from the mixture of crude α-chloro FAs, which was in turn obtained from 35 mmol of equimolar mixture of 4, 5, and 6, according to the procedure adopted for the hydroxylation of single crude α- chloro FAs: mp 69.3 °C, GC-FID: Rt = 6.295 min, 9.050 min, 12.120 min, purity = 100% (Fig. 27).



Peak Number (#)	RT (min)	Peak Height (uV)	Area (.1*uV*sec)	Area % (%)
1	6.295	35732	1550025	28.6
2	9.050	39409	1989050	36.7
3	12.120	32397	1874294	34.6

Fig. 27 GC-FID analysis of 2-hydroxy stearic acid, 2-hydroxy palmitic acid, 2-hydroxy myristic acid mixture

Results and discussion

TCCA as a Chlorinating Agent

A large variety of reagents for the chlorination of organic substrates can be found in the literature. Among these, 1 stands out for many fine qualities. It is inexpensive, innocuous, environmentally benign, and stable. With respect to atom economy, TCCA is better than other chlorinating agents, such as N-chlorosuccinimide, N-chlorosaccharin, chloramine-T, or 1-chlorobenzotriazole, as it is capable of transferring three chlorine atoms, corresponding to 45.5% of its mass [16]. Furthermore, the byproduct of chlorination is cyanuric acid (2), which can be reused by conversion into more TCCA through a green process using NaCl and oxone [21]. Importantly, 1 is soluble in many organic solvents, whereas 2, the chlorination byproduct, is highly insoluble. Alternatively, the water-soluble sodium dichloroisocyanurate (NaDCC, 3) can be used in biphasic water/organic solvent systems. Such a difference in the solubility profile between 1 and 2 allows chlorination to be driven to completion in suitably selected solvents and it facilitates the quantitative removal of 2 in the reaction work-up by simple filtration. 1 or 3 efficiently chlorinates the nitrogen of primary and secondary amines and amides, yielding intermediates whose dehydrohalogenation gives access to synthetically useful unsaturated derivatives, such as nitriles [22,23], imines [24], enamines [25], azo-compounds [26], isocyanates [27] and α,β-unsaturated α-amino esters [28]. C-Halogenation of alkenes [16,29], aromatics [17,19,30,31], alkyl aromatic hydrocarbons [19] and carbonyl compounds [16,17,19] is the other important chapter of the applications of 1 as a halogenating reagent in organic synthesis. In the development of new green technologies, the potential of 1 as a halogenating agent relies not only on its intrinsic environmental benignity but also on its suitability for newly conceived more efficient and sustainable procedures. Recent examples are the amplification of the electrophilicity of TCCA chlorine by visible-light catalysis to chlorinate electrondeficient arenes and heteroarenes under mild conditions [20], solvent-free chlorination of aromatics and carbonyl compounds in the solid state by ball milling [17] and conversion of methane into chloromethane by mechanochemical activation [32]. Based on these literature premises and on our experience with 1 use, we planned the α-chlorination of FAs with 1 under solvent-free conditions, at temperatures slightly higher than their melting points.

α-Chlorination of FAs

Three saturated long-chain FAs were chosen as substrates because the main exponents, besides α-HFAs, of carboxylic acids in wool wax are as follows: octadecanoic (stearic) acid (4), hexadecanoic (palmitic) acid (5), and tetradecanoic (myristic) acid (6). To our knowledge, the only example of FAs α-

chlorination is that of 4 by treatment with Cl_2 at 150 °C for about 1 h in the presence of chlorosulfonic acid (3 mol %) as a catalyst and 7,7,8,8-tetracyanoquinodimethane (TCNQ, 0.5 mol %) as a free radical inhibitor [33]. According to this procedure, α-chlorostearic acid (4a) was isolated with 88% yield by crystallization from acetonitrile. Although not exemplified, the same reaction was run with all of the even-chain saturated acids between C_6 and C_{16} by the same researchers claiming essentially identical results. As explained above, our approach was to avoid the use of chlorine by replacing it with much more acceptable 1 under solvent-free conditions. Slightly exceeding 1 (1.4 equiv) and catalytic PCl_3 (0.1 equiv), to generate, according to the generally accepted mechanism of the Hell−Volhard−Zelinsky α-halogenation of carboxylic acids, the necessary initial small amount of the acid chloride in enolic form, were used in all the experiments while varying time and temperature. Typically, the FA (35 mmol) was heated to melt (80 °C) under stirring and nitrogen in a flask wrapped with foil to exclude light. 1 h after adding catalytic PCl_3 (1.2 mmol), 1 (16.3 mmol) was added portion-wise over 30 min while heating was continued. The screening of temperatures ranging between 80 and 100 °C and of times ranging between 3 and 24 h indicated 80 °C and 24 has the best reaction conditions to be applied.

At the end, ethyl acetate was added to the reaction mixture at room temperature to precipitate cyanuric acid, which was removed by filtration. The filtrate was washed with aqueous sodium metabisulfite, to destroy the excess of 1, and then with brine. The concentration of the filtrate gave the crude α-chlorinated FAs 2-chlorostearic acid (7), 2-chloropalmitic acid (8), and 2-chloromyristic acid (9) as white solids with 96−97% yields. Gas chromatography (GC)−flame ionization detector (FID) analyses indicated purities ranging between 85 and 92% consistently with proton and carbon NMR spectra, all showing a largely predominant constituent with a prominent signal of chlorinated methine in the 2-position of the chain having, in the H NMR spectrum, the expected doublet of doublet multiplicity and near one proton integration. GC-FID analyses evidenced a main impurity, which was reasonably identified, on the basis of the GC−mass spectrometry (MS) spectra and of the minor signals in the H NMR spectra, as a minimal amount of the dichlorinated product. The catalytic amount of PCl_3 can be reduced but slowing the reaction. Under the same abovementioned reaction conditions, 50% conversion of 4 into 7 was observed using 0.03 instead of 0.1 equiv of PCl_3.

α-Hydroxylation of FAs

The conversion into α-hydroxy acids was performed on the three abovementioned crude α-chlorinated FAs by treatment with KOH (4 equiv) in water under reflux for 24 h. Crude α-hydroxylated FAs were precipitated from the reaction mixture as white solids by the acidification to pH 1 at room temperature in quantities higher than 90% of the theoretical amounts, calculated on initial 35 mmol FA, and with purities, determined using GC, ranging between 78 and 88%. Trituration of the crude solids in

different solvents, such as methanol, ethanol, 2-propanol, CPME, hexane, or acetonitrile, at room temperature was enough to achieve >95% purities. The best results in terms of the final yield (64−68%) and purity (99−100%) were obtained by trituration in acetonitrile, but the procedure is susceptible of further improvement both for yield and solvent choice.

α-Chlorination and Hydroxylation of FAs Mixtures

The successive step of the investigation was to apply the abovementioned chlorination and hydroxylation procedures starting from an equimolar mixture of the three FAs 4, 5, and 6 with the intent to mimic a mixture of long chain FAs obtainable by the hydrolysis of wool wax esters and subsequent separation, through selective extraction,6 from the very long chain and α-hydroxy long chain FAs. As expected on the basis of the similar reactivity shown by 4, 5, and 6, the equimolar mixture of 4, 5, and 6, when submitted to chlorination with TCAA and to successive hydroxylation, behaved as the three single FAs. In fact, it provided, with 92% yield, an 85% pure near equimolar mixture of 7, 8, and 9 in which the remaining 15% was a near equimolar mixture of the supposed corresponding dichlorinated acids. Then, the crude mixture of the three α-chlorinated acids yielded, with 100% purity and 74.2% yield, a mixture of 10, 11, and 12, which was, reasonably as a consequence of the final trituration in acetonitrile, slightly richer in 10 (34.6%) and 11 (36.7%) and poorer in 12 (28.6%). In the two steps, the recovered amounts and the purities are in line with the data obtained for the single FAs and 74.2% is the overall yield of the conversion of the mixed FAs into α-HFAs.

Conclusions

An efficient and environmentally benign procedure was developed to convert long-chain saturated FAs (stearic, palmitic, and myristic acid) into α-HFAs without purifying the intermediate α-chlorinated FAs. This was possible because of a green halogenating agent, such as TCCA, which proved to be able, used in slight excess, to quantitatively α-chlorinate melted FAs under solvent-free conditions with the concomitant minimal formation of a dichlorinated product. Therefore, the successive treatment of crude halogenated FAs with aqueous KOH under reflux could provide the corresponding α- HFAs, isolable pure by simple precipitation from the acidified reaction medium and successive trituration in a suitable solvent. The robustness of the whole two-step procedure was demonstrated by its successful application to the equimolar mixture of the three FAs, which were converted into the corresponding α-HFAs with a near unaltered molar ratio. The process, designed to valorize the saturated FAs of wool wax and to indirectly make the waste wool management more sustainable, provides appealing opportunities for converting other FAs and FA mixtures, recoverable from lipid-based waste biomasses, into valuable fine chemicals of great potential, such as α-HFAs.

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