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ORIGINAL PAPER

Conversion of Methyl Oleate to Branched-Chain Hydroxy Fatty Acid Derivatives

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Abstract As part of a project to develop new and expanded uses of oilseed products and by-products (such as biodiesel, fuel additives, and lubricants), studies were conducted on the synthetic conversion of oleic acid (in the ester form) to branched-chain fatty acid ester derivatives. In these studies, methyl oleate was epoxidized and subsequently treated with four different organocuprate reagents in the presence of boron trifluoride diethyl etherate to produce novel branched-chain hydroxy acid derivatives. For each reaction, the two distinct isomeric products (methyl 9-alkyl-10-hydroxyoctadecanoate and methyl 9-hydroxy-10-alkyloctadecanoate) were isolated in the pure forms. Details of the synthesis and characterization (GC–MS, NMR, and differential scanning calorimetry) of these compounds will be discussed.

Keywords Branched-chain fatty acids · DSC · Hydroxy fatty acids · Low-temperature properties · NMR · Organocuprate reagents

Introduction

Oleic acid and linoleic acid are the most abundant fatty acids in many vegetable oils, including cottonseed oil. As part of a project to develop new value-added industrial applications for cottonseed oil (for example biodiesel, fuel additives, and lubricants), we are conducting studies on the synthetic conversion of oleic acid (in the ester form) to branched-chain fatty acid esters. This research was prompted in part by reports that the conversion of vegetable oils and animal fats into esters of branched-chain alcohols, for example isopropyl or 2-butyl, resulted in improved low-temperature properties, as demonstrated by their reduced crystallization onset temperatures [1–3]. The relatively poor low-temperature properties (freezing in cold climates) of currently available biodiesel products (for example methyl soyate) are an obstacle to their continued development and commercialization [1, 4].

Because methyl oleate (**1**) is readily available and is a major constituent of biodiesel products such as methyl soyate, it was selected as a model compound. In our previously reported studies, **1** was brominated in the allylic position and subsequently treated with cuprate reagents to produce branched-chain derivatives [5–7]. Several of these derivatives had significantly lower re-crystallization temperatures than methyl oleate itself [7].

Developments in the "synthesis of alkyl-branched fatty acids" were recently reviewed [8]. For example, branched-chain fatty acids may be obtained as the final products via radical additions to unsaturated fatty acids or by Lewis acid-catalyzed cationic additions such as the ene addition of formaldehyde [9]. The conversion of oleic acid and methyl oleate to saturated branched-chain derivatives has been reported [10].

Epoxidized methyl oleate and biodiesel have been studied extensively as precursors to products with desirable properties. For example, Moser and Erhan [11] reported the synthesis of α-hydroxy ethers by treatment of a number of alkyl 9,10-epoxystearates with a variety of aliphatic alcohols. It was determined that the product containing the

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most bulky ester and ether groups, 2-ethylhexyl 9(10)-(2-ethylhexoxy)-10(9)-hydroxystearate, had the best low-temperature properties. In a related study, epoxidized methyl, ethyl, and butyl biodiesel were alkoxylated, but there was no improvement in low-temperature properties [12]. Finally, the products obtained upon reaction of epoxidized methyl oleate with a number of aliphatic carboxylic acids were evaluated (pour point, cloud point, viscosity index) for potential use as lubricants, surfactants, and fuel additives. The octanoic ester had the most desirable properties, especially as a lubricant [13].

In these studies, novel alkyl and aryl branched-chain hydroxy acid derivatives were produced by reaction of epoxidized methyl oleate with a number of organocuprate reagents in the presence of boron trifluoride diethyl etherate. The two isomeric products were chromatographically separated. Details of the syntheses and characterization (GC–MS, NMR, DSC) of the two distinct isomeric products will be discussed.

Experimental Procedures

Materials

Methyl oleate (99%), methyllithium (2.6 M in diethyl ether), *n*-butyllithium (2.5 M in hexanes), hexyllithium (2.3 M in hexane), phenyllithium (1.8 M in di-*n*-butyl ether), boron trifluoride diethyl etherate (purified, redistilled), silica gel (Merck, grade 9385, 230–400 mesh), Merck analytical TLC plates (silica gel 60, 5 × 10 cm), and diethyl ether (anhydrous, 99%+, ACS reagent) were purchased from Aldrich (Milwaukee, WI, USA). Cuprous iodide (98%) was purchased from Alfa-Aesar (Ward Hill, MA, USA). Calcium hydride (97%+) was purchased from Fluka (Milwaukee, WI, USA). Formic acid (98.2%) and hydrogen peroxide (31.3% solution) were obtained from J.T. Baker (Philipsburg, NJ, USA). Diethyl ether was distilled from calcium hydride and stored over Type 4A molecular sieves under a nitrogen atmosphere.

Gas Chromatography–Mass Spectroscopy (GC–MS)

A 1-μl aliquot of the sample was injected into a split/splitless injector (300 °C) on an Agilent (Palo Alto, CA, USA) 6890 gas chromatograph. The initial column pressure was held at 25 psi and a constant flow rate of 1.2 ml/min was maintained through the column using electronic pressure control (EPC). The oven temperature was held at 50 °C for 1 min, and then raised at 3 °/min to 80 °C; the rate was changed to 10 °/min and the oven temperature raised to 340 °C and held for 18 min for a total run time of 55 min. The GC was equipped with a 0.25 mm ID × 30 m capillary column coated with a 0.25-μm film of 5% diphenyl 95% dimethylsiloxane (DB-5MS, J&W Scientific). The effluent from the column was analyzed by a Pegasus III TOFMS (Leco, St Joseph, MI, USA) employing electron-impact ionization. Masses from 35 to 1,000 amu were collected at 20 spectra per second. The NIST 2000 mass spectral library and the Palisade (Ithaca, NY, USA) Complete MS Library 600K were used for preliminary identification of compounds.

Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) was performed using a TA Instruments DSC Q100 thermal analytical device. The standard experiment consisted of heating the samples (4–9 mg) from −120 to +50 °C at 10 °/min followed by a cooling from +50 to −120 °C at the same rate. The cycle was then repeated, and the thermal transitions recorded. For epoxidized methyl oleate (**2**), the temperature range was −100 to +50 °C. The second cooling scan was used to find the re-crystallization temperature, T_c. The second heating scan was used to find the melting temperature, T_m, and the onset and midpoint of the glass-transition temperature, T_g. The second run is considered more reliable since the first run produces a more uniform sample. For compounds **3b**, **4b**, and **4c**, a heating scan was run at 5 °/min and for **3b** and **4b**, a heating scan was run at 2 °/min.

Nuclear Magnetic Resonance Spectroscopy (NMR)

Solution-state NMR spectra were recorded at 9.4 Tesla on a Varian Inova NMR Spectrometer, using a 5 mm indirect-detect probe and operating at 25 °C. The ^1H (proton) spectra, at 400 MHz, had a sweep-width of 6,000 Hz, were acquired with a 90° pulse angle and a 2.5 s relaxation delay, and were referenced to internal tetramethylsilane (TMS). The ^{13}C spectra, at 100 MHz, had a sweep-width of 30,000 Hz for ^{13}C, were acquired with a 45° pulse angle and a 2 s relaxation delay, and were referenced to the $CDCl_3$ peak, 77.23 ppm from TMS. For chemical shift assignment, the standard numbering system for carbons of compounds **3** and **4** (Fig. 2) was followed. For compounds **3a**, **4a**, **3b**, **4b**, **3c**, **and 4c** and diols **5a** and **6a**, a DEPT (distortionless enhancement polarization transfer) experiment was run using the standard flip angle of 135° to distinguish among the CH, CH_2 and CH_3 resonances. While most resonances could be determined by comparison with standard chemical shift values, some required 2D NMR for assignment or confirmation. 2D NMR experiments were run on samples **3a**, **4a**, and **3b** and diols **5a** and **6a**. All homonuclear gCOSY and TOCSY experiments used ^1H spectral widths of 8,000 Hz and were acquired with 16 transients and either 400 or 512 indirectly detected transients. Gradient-enhanced versions of HMQC (phase-insensitive) and HMBC (8 Hz) were performed to assign the ^{13}C signals. These heteronuclear 2D experiments had ^{1}H spectral widths of 8,000 Hz and ^{13}C spectral widths of 25,000 Hz, and were acquired with 64–96 directly detected transients and 400–512 indirectly detected transients. The F1 dimension of all heteronuclear spectra were forward linear predicted up to two times the number of data points, using the half data set as the basis. Spectra were apodized with a sine-squared function and a shift of 70°.

Epoxidation of Methyl Oleate

Using a smaller-scale version of the procedure of Doll and Erhan [14], methyl oleate (6.29 g, 21.2 mmol) was added to a three-necked 100-ml round-bottomed flask equipped with stirring bar, thermometer, and nitrogen inlet. Formic acid (3.13 g, 66.8 mmol) was added and the vigorously stirred mixture was cooled to 0 °C. Hydrogen peroxide (31.3%, 4.93 g, 45.3 mmol) was added dropwise over 5 min. The temperature did not exceed 10 °C. The mixture was stirred at 5 °C for 2 h, then allowed to gradually warm to 23 °C overnight. After a total reaction time of 24 h, 50 ml of hexanes was added to the stirred reaction mixture. The mixture was shaken in a separatory funnel. After separation of layers, the aqueous layer was extracted with hexanes (30 ml). Combined organic layers were washed with saturated sodium bicarbonate solution (2 × 50 ml) and brine (2 × 100 ml), then dried (Na_2SO_4). Removal of solvent afforded 6.55 g (98.8%) *cis*-3-octyloxiraneoctanoic acid methyl ester (**2**).

Reaction of Epoxide 2 with Lithium Dialkylcuprate Reagents

General Procedure

A 34 to 54% excess of lithium dimethylcuprate, lithium di-*n*-butylcuprate, lithium di-*n*-hexyllithium, or lithium diphenylcuprate was prepared in 50 ml dry diethyl ether at −60 °C (acetone–Dry Ice bath) in a three-necked 200-ml flask equipped with thermometer, nitrogen inlet, and septum. The stirred mixture was warmed to −40 or −30 °C as necessary in order to obtain a homogeneous solution. After 5–30 min at −40 °C, the solution was cooled to −70 to −75 °C and a solution of **2** in 20 ml diethyl ether was added by syringe. After 5–15 min, a solution of boron trifluoride diethyl etherate (1.03–1.54 equiv.) in 5 ml diethyl ether was added [15]. The reaction mixture was stirred for 75 min at −70 to −75 °C, and then quenched by dropwise addition of methanol (10 ml), with the temperature maintained at −50 °C or below during the addition. The reaction mixture was stirred at −65 to −70 °C for 30 min. Thereupon, the Dry Ice bath was replaced with an ice bath, and the reaction mixture was allowed to warm to 0 °C. Saturated ammonium chloride solution (50 ml, adjusted to pH 8 with aqueous ammonia) was added and the mixture was allowed to warm to room temperature overnight. The precipitate was removed by filtration and washed with 50 ml ether. The aqueous and organic components of the filtrate were separated. The ether solution (containing the organic product) was washed with saturated ammonium chloride solution (pH 8) (2 × 50 ml). The combined aqueous layers were extracted with ether (50 ml); the combined ether layers were washed with deionized water (100 ml) and brine (100 ml), then dried over $MgSO_4$. Solvent was removed in vacuo and the product was dried to a constant weight at ca. 1 torr.

Synthesis of Methyl 9-Methyl-10-Hydroxyoctadecanoate 3a and Methyl 9-Hydroxy-10-methyloctadecanoate 4a (Scheme 1)

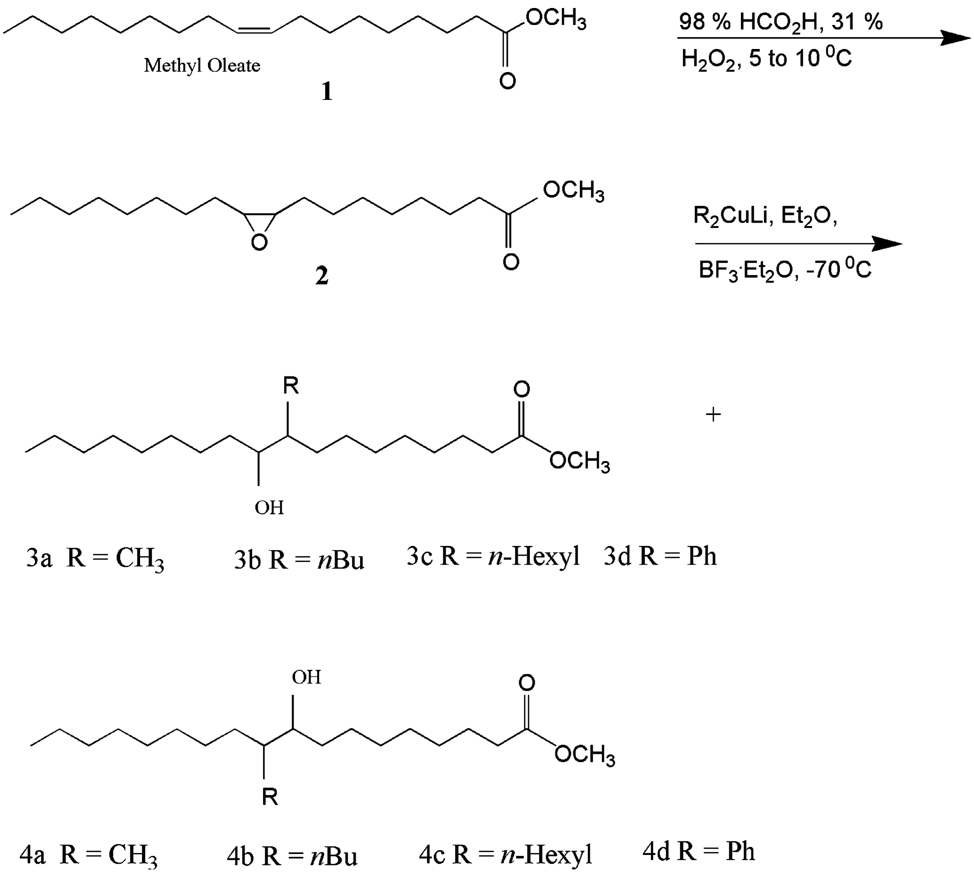
Lithium dimethylcuprate was prepared in situ by the addition of 10.4 ml (16.6 mmol) methyllithium (1.6 M in diethyl ether) to 1.59 g (8.35 mmol) cuprous iodide stirred in 50 ml dry ether under nitrogen at −60 °C. The stirred mixture was warmed to −40 °C, resulting in a colorless solution. After 30 min. at −40 °C, the solution was cooled to −75 °C and 1.945 g (6.22 mmol) **2** in 20 ml ether was added. Within 5 min, the solution turned light yellow, and 1.05 ml (8.36 mmol) boron trifluoride diethyl etherate (dissolved in 5 ml ether) was added, resulting in a dark yellow mixture. The mixture was stirred at −70 °C for 75 min., and then the reaction was quenched with 10 ml methanol. Following work-up as described above, 2.07 g crude product was isolated as a colorless liquid (theoretical yield: 2.04 g). A 1.05 g sample was placed upon a column containing 100 g silica gel and was eluted (flash chromatography [16]) with 250 ml petroleum ether, followed by 15% ether in petroleum ether (20-ml fractions). A total of 756 mg (72.8% yield) of products **3a** and **4a** (either pure or as a mixture) were isolated. Fractions containing only the least polar isomer (R_f 0.21, SiO_2, 20% diethyl ether in petroleum ether) yielded 78.5 mg **3a**: mass spectrum *m*/*z* (rel intensity) 215 (3), 188 (2), 187(17), 186 (34), 183 (8), 171 (0.2), 157 (9), 143 (54), 129 (17), 115 (8), 101 (20), 95 (9), 87 (100), 83 (15), 81(15), 74 (68), 71 (10), 69 (62), 67 (13), 59 (13), 57 (35), 55 (73), 43 (48), 41 (47); ^{1}H NMR ($CDCl_3$) δ 0.86 (d, 3, branched-chain CH_3), 0.88 (t, 3, main-chain $C\boldsymbol{H}_3$), 1.10–1.50 (m, 25, 12 $C\boldsymbol{H}_2$ and $CH_2CHOHC\boldsymbol{H}{-}CH_3$), 1.62 (pentet, 2, $C\boldsymbol{H}_2{-}CH_2CO_2CH_3$), 2.30 (t, 2, $C\boldsymbol{H}_2CO_2CH_3$), 3.48 (m, 1, $C\boldsymbol{H}{-}OH$), and 3.67 (s, 3, $OC\boldsymbol{H}_3$); ^{13}C NMR ($CDCl_3$) δ, 13.76 (branched-chain $\boldsymbol{C}H_3$), 14.30 (C-18), 22.86, 25.12 (C-3), 26.48, 27.52, 29.31, 29.42, 29.49, 29.80, 29.91, 29.95, 32.07, 33.47, 34.27 (C-2), 34.66 (C-11), 38.34 (C-9), 51.63 (O*C*H_3), 75.34 (C-10), 174.54 (***C***=O).

Fractions containing only the most polar isomer (R_f 0.18, SiO_2, 20% diethyl ether in petroleum ether) yielded 113 mg of **4a:** mass spectrum *m*/*z* (rel intensity) 188 (2), 187 (36), 171 (0.6), 156 (11), 155 (100), 115 (8), 109 (26), 87 (24), 83 (12), 74 (27), 71 (11), 69 (18), 67 (31), 59 (13), 57 (32), 55 (49), 43 (48), 41 (36); ^{1}H NMR ($CDCl_3$) δ 0.86 (d, 3, branched-chain C***H***$_3$), 0.88 (t, 3, main-chain C***H***$_3$), 1.10–1.50 (m, 25, 12 C***H***$_2$ and CH_2CHOHC***H***–CH_3), 1.62 (pentet, 2, C***H***$_2$–$CH_2CO_2CH_3$), 2.30 (t, 2, C***H***$_2$$CO_2CH_3$), 3.48 (m, 1, C**H**–OH), and 3.67 (s, 3, OC***H***$_3$); ^{13}C NMR ($CDCl_3$) δ, 13.77 (branched-chain *C*H_3), 14.30 (C-18), 22.86, 25.09 (C-3), 26.48, 27.60, 29.26, 29.41, 29.52, 29.70, 29.81, 30.14, 32.09, 33.51, 34.25 (C-2), 34.59 (C-8), 38.38 (C-10), 51.63 (O*C*H_3), 75.30 (C-9), 174.50 (***C***=O).

Synthesis of Methyl 9-*n*-Butyl-10-Hydroxyoctadecanoate 3b and Methyl 9-Hydroxy-10-*n*-Butyloctadecanoate 4b. Isolation of the Diols 5a and 6a (Fig. 1)

Lithium di-*n*-butylcuprate was prepared in situ by addition of 7.70 ml (19.25 mmol) *n*-butyllithium (2.5 M in hexanes) to 1.83 g (9.63 mmol) cuprous iodide stirred in 50 ml dry ether under nitrogen at −60 °C. The stirred mixture was warmed to −40 °C, resulting in a black solution. After 30 min at −40 °C, the solution was cooled to −75 °C and 1.97 g (6.30 mmol) **2** in 20 ml ether was added. After 15 min, 1.21 ml (9.63 mmol) boron trifluoride diethyl etherate (dissolved in 5 ml ether) was added. Following completion of the experiment as described in the general procedure, 2.37 g crude product was isolated as a colorless liquid (theoretical yield: 2.34 g). A 817 mg sample was placed upon a column containing 100 g of silica gel and was eluted (flash chromatography) with 250 ml petroleum ether, followed by 10% ethyl acetate in petroleum ether (20-ml fractions). A total of 417 mg (51.8% yield) of products **3b** and **4b** (either pure or as a mixture) was isolated. Fractions containing only the least polar isomer (R_f 0.37, SiO_2, 10% ethyl acetate in petroleum ether) yielded 111.5 mg **3b**: mass spectrum *m*/*z* (rel intensity) 257 (2), 229 (22), 228 (34), 213 (0.2), 199 (8), 187 (2), 185 (19), 171 (7), 157 (8), 143 (39), 129 (21), 97 (23), 87 (82), 83 (41), 74 (79), 69 (84), 57 (52), 55 (100), 43 (60), 41 (57); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3, main-chain C***H***$_3$), δ 0.90 (t, 3, branched-chain C***H***$_3$), 1.17–1.53 (m, 33, 16 CH_2 and CH_2CHOHC***H***–*n*Bu), 1.62 (pentet, 2, C***H***$_2$–$CH_2CO_2CH_3$), 2.31 (t, 2, C***H***$_2$$CO_2CH_3$), 3.58 (m, 1,

Scheme 1 Synthetic route to branched-chain hydroxy fatty acid methyl esters **3** and **4**



C*H*–OH), and 3.67 (s, 3, OCH_3); ^{13}C NMR ($CDCl_3$) δ, 14.30 (C-18 and branched-chain CH_3), 22.87, 23.38, 25.14 (C-3), 26.61, 27.67, 29.00, 29.34, 29.43, 29.49, 29.82, 29.95, 30.11 (2C), 30.39, 32.09, 34.20 (C-11), 34.29 (C-2), 43.74 (C-9), 51.63 (OCH_3), 73.83 (C-10), 174.55 (*C*=O).

Continued elution with 10% ethyl acetate in petroleum ether did not provide any fractions containing only **4b** (R_f 0.33, SiO_2, 10% ethyl acetate in petroleum ether). The column was flushed with 500 ml 20% ethyl acetate in petroleum ether, then 500 ml petroleum ether. Material isolated from the fractions richest in **4b** (400 mg) was placed upon the column and eluted with 8% ethyl acetate in petroleum ether, affording an additional 37.8 mg **3b** and 93.1 mg pure **4b**: mass spectrum *m/z* (rel intensity) 213 (0.7), 188 (6), 187 (48), 155 (100), 109 (27), 97 (8), 87 (12), 83 (15), 74 (12), 69 (22), 57 (38), 55 (42), 43 (40), 41 (30); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3, main-chain CH_3), δ 0.90 (t, 3, branched-chain CH_3), 1.17–1.50 (m, 33, 16 CH_2 and CH_2CHOHC*H*–*n*Bu, 1.62 (pentet, 2, CH_2–$CH_2CO_2CH_3$), 2.30 (t, 2, C$H_2$$CO_2CH_3$), 3.58 (m, 1,

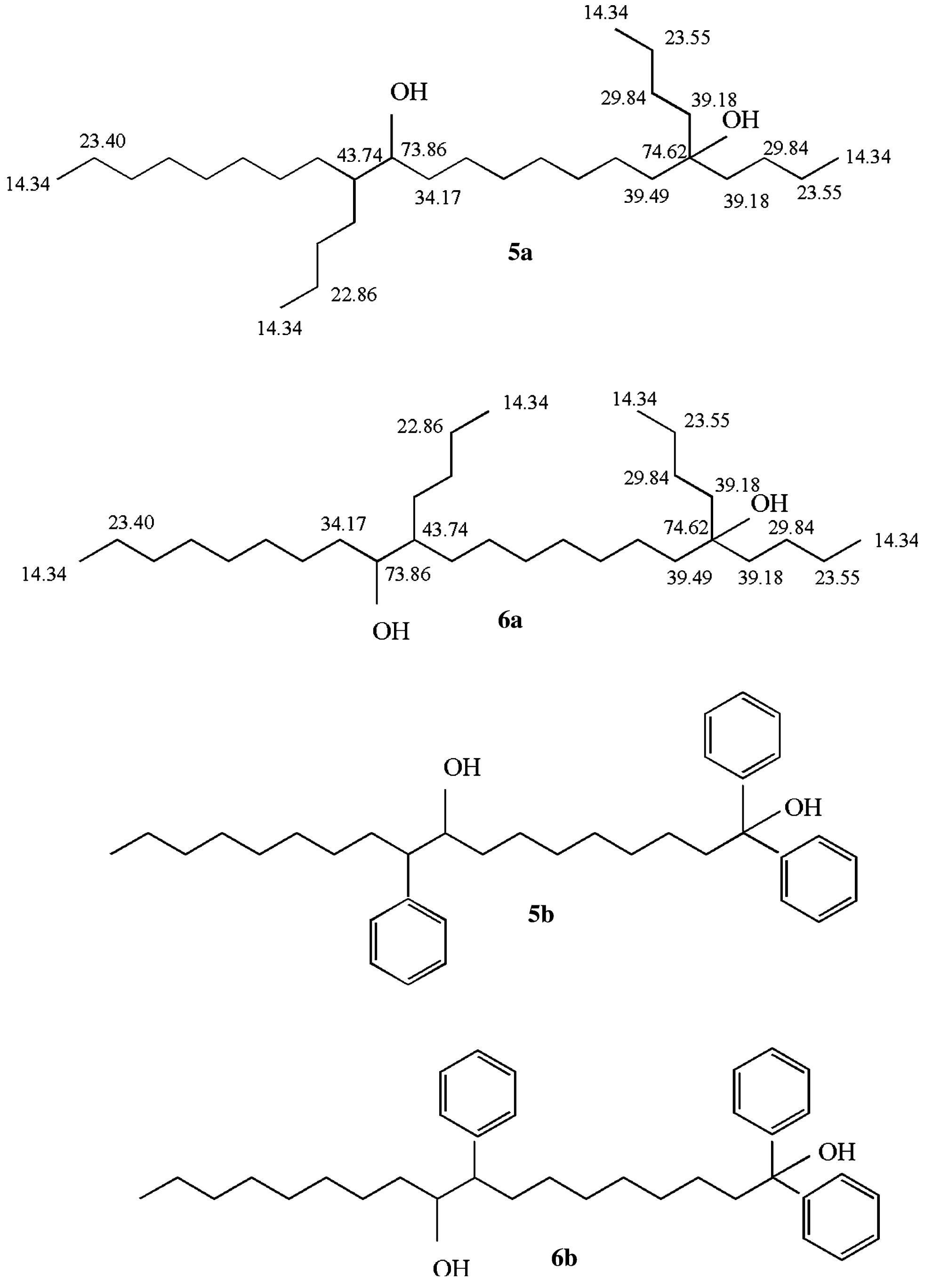


Fig. 1 Structures of the diols **5** and **6**. Observed ^{13}C chemical shift assignments are given for *n*-butyl derivatives **5a** and **6a**

C*H*–OH), and 3.66 (s, 3, OC***H***$_3$); ^{13}C NMR (CDCl$_3$) *δ*, 14.30 (C-18 and branched-chain ***C***H$_3$), 22.87, 23.38, 25.11 (C-3), 26.52, 27.73, 29.00, 29.28, 29.43, 29.53, 29.71, 29.81, 30.10, 30.32, 32.09, 34.17 (C-8), 34.27 (C-2), 43.78 (C-10), 51.62 (O***C***H$_3$), 73.83 (C-9), 174.50 (***C***=O).

A total of 417 mg (51.8% yield) of products **3b** and **4b** (either pure or as a mixture) was isolated.

Continued elution of the column with 8% ethyl acetate in petroleum ether provided 77.4 mg diols **5a** and **6a** (R_f 0.28, SiO$_2$, 10% ethyl acetate in petroleum ether): mass spectrum *m*/*z* (rel intensity) 418 (1.2), 379 (4), 361 (1.2), 213 (0.1), 195 (6), 143 (33), 140 (111), 125 (13), 123 (10), 113 (12), 111 (17), 109 (13), 98 (15), 97 (31), 96 (13), 95 (20), 85 (41), 83 (53), 71 (30), 70 (28), 69 (100), 67 (22), 57 (90), 55 (87), 43 (50), 41 (48) ^{1}H NMR (CDCl3) *δ*, 0.88 (t, 3, C***H***$_3$), 0.90 (t, 3, C***H***$_3$), 0.91 (t, 6, 2 C***H***$_3$), 1.27–1.32 [m, 38, –C***H***$_2$–C***H***$_2$–CH$_3$ and –(CH$_2$)$_n$–] (1.38 and 1.43) [m, 6, (–C***H***$_2$–)$_3$C–OH], 1.65 [m, 1, C***H***CH(OH)], 3.58 [m, 1,–C***H***(OH)-]; ^{13}C NMR (CDCl$_3$) *δ*, 14.34 (4C), 23.66, 25.90 (2C), 26.62, 27.75, 29.00, 29.51, 29.84 (2C), 29.97, 30.11, 30.33, 30.41, 30.51, 32.10, 34.17, 39.18 (2C), 39.49, 43.74, 73.86, 74.62. The ^{13}C NMR assignments are provided pictorially in Fig. 1.

Synthesis of Methyl 9-*n*-Hexyl-10-Hydroxyoctadecanoate **3c** and Methyl 9-Hydroxy-10-*n*-Hexyloctadecanoate **4c**

The reaction of **2** (2.05 g, 6.56 mmol) with 9.08 mmol lithium di-*n*-hexylcuprate, afforded 2.80 g crude product as a colorless liquid (theoretical yield: 2.61 g). A 1.03 g sample was placed upon a column containing 100 g silica gel and was eluted (flash chromatography) with 10% ethyl acetate in petroleum ether (20-ml fractions). Fractions containing only the least polar isomer (R_f 0.40, SiO$_2$, 10% ethyl acetate in petroleum ether) yielded 64.5 mg **3c**: mass spectrum *m*/*z* (rel intensity) 285 (2), 257 (25), 256 (33), 241 (0.2), 213 (14), 199 (10), 185 (7), 171 (8), 157 (16), 143 (37), 129 (12), 111 (14), 101 (17), 98 (13), 97 (24), 87 (91), 83 (49), 81 (20), 75 (19), 74 (93), 69 (91), 67 (23), 57 (67), 55 (100), 43 (82), 41 (65); ^{1}H NMR (CDCl$_3$) *δ* 0.88 (t, 6, main-chain and branched-chain C***H***$_3$), 1.10–1.50 (m, 37, 18 C***H***$_2$ and CH$_2$CHOHC***H***-*n*-Hexyl), 1.62 (pentet, 2, C***H***$_2$–CH$_2$CO$_2$CH$_3$), 2.30 (t, 2, C***H***$_2$CO$_2$CH$_3$), 3.59 (m, 1, C***H***–OH), and 3.67 (s, 3, OC***H***$_3$); ^{13}C NMR (CDCl$_3$) *δ*, 14.31 (C-18 and branched-chain ***C***H$_3$), 22.88, 25.12 (C-3), 26.60, 27.65, 27.81, 29.28, 29.32, 29.42, 29.50, 29.81, 29.95, 30.01, 30.09, 30.33 (2C), 32.06 (2C), 34.13 (C-11), 34.28 (C-2), 43.73 (C-9), 51.65 (O***C***H$_3$), 73.79 (C-10), 174.55 (***C***=O).

Continued elution with 8% ethyl acetate in petroleum ether did not provide any fractions containing only **4c** (R_f 0.35, SiO$_2$, 10% ethyl acetate in petroleum ether). Material isolated from the fractions richest in **4c** (324 mg) was rechromatographed on the column (6% ethyl acetate in petroleum ether), affording 47.4 mg of pure **4c**: mass spectrum *m*/*z* (rel intensity) 241 (0.4), 188 (7), 187 (57), 156 (10), 155 (100), 115 (6), 111 (5), 109 (20), 97 (8), 95 (6), 87 (16), 85 (7), 83 (15), 81 (8), 74 (18), 71 (15), 69 (23), 67 (22), 57 (41), 55 (47), 43 (47), 41 (32); ^{1}H NMR (CDCl$_3$) *δ* 0.88 (t, 6, main-chain and branched-chain C***H***$_3$), 1.17–1.50 (m, 37, 18 C***H***$_2$ and CH$_2$CHOHC***H***-*n*-Hexyl), 1.62 (pentet, 2, C***H***$_2$–CH$_2$CO$_2$CH$_3$), 2.31 (t, 2, C***H***$_2$CO$_2$ CH$_3$), 3.59 (m, 1, C**H**–OH), and 3.67 (s, 3, OC***H***$_3$); ^{13}C NMR (CDCl$_3$) *δ*, 14.33 (C-18 and branched-chain ***C***H$_3$), 22.90, 25.12 (C-3), 26.54, 27.74, 27.82, 29.23, 29.30, 29.46, 29.56, 29.73, 29.83, 29.96, 30.03, 30.34, 30.38, 32.07, 32.11, 34.14 (C-8), 34.29 (C-2), 43.79 (C-10), 51.67 (O***C***H$_3$), 73.82 (C-9), 174.54 (***C***=O).

A total of 385 mg (41.3% yield) of products **3c** and **4c** (either pure or as a mixture) was isolated.

Synthesis of Methyl 9-Phenyl-10-Hydroxyoctadecanoate **3d** and Methyl 9-Hydroxy-10-Phenyloctadecanoate **4d.** Isolation of the Diols **5b** and **6b** (Fig. 1)

Reaction of **2** (2.36 g, 7.55 mmol) with 10.35 mmol lithium diphenylcuprate, afforded 3.68 g crude product as a colorless liquid (theoretical yield: 2.95 g). A 2.01 g sample was placed upon a column containing 100 g silica gel and was eluted (flash chromatography) with 10% ethyl acetate in petroleum ether (20-ml fractions). Fractions containing only the least polar isomer (R_f 0.24, SiO$_2$, 10% ethyl acetate in petroleum ether) gave 169 mg **3d**: mass spectrum *m*/*z* (rel intensity) 249 (3), 248 (17), 217 (9), 216 (46), 143 (2), 125 (11), 117 (23), 112 (20), 105 (27), 104 (36), 98 (24), 92 (55), 91 (100), 87 (25), 74 (56), 69 (26), 57 (20), 55 (51), 43 (31), 41 (37); ^{1}H NMR (CDCl$_3$) *δ* 0.87 (t, 3, C***H***$_3$), 1.10–1.75 (m, 26, 13 C***H***$_2$), 2.30 (t, 2, C***H***$_2$CO$_2$CH$_3$), 2.55 (m, 1, (CH$_2$CHOHC***H***Ph), 3.66 (s, 3, OC***H***$_3$), 3.70 (m, 1, C***H***–OH), 7.18–7.28 (m, 3, *p* aromatic H and *o* aromatic H) and 7.31 (m, 2, *m* aromatic H); ^{13}C NMR (CDCl$_3$) *δ*, 14.29 (C-18), 22.84, 25.03 (C-3), 26.02, 27.69, 29.22, 29.45, 29.61, 29.68, 29.77, 29.87, 32.03, 32.21, 34.21 (C-2), 35.31 (C-11), 51.60 (O***C***H$_3$), 52.19 (C-9), 75.13 (C-10), 126.72 (*p* aromatic C) 128.55 (*o* aromatic C), 129.12 (*m* aromatic C), 141.70 (quaternary phenyl C), 174.47 (***C***=O).

Continued elution with 10% ethyl acetate in petroleum ether did not provide any fractions containing only **4d** (R_f 0.19, SiO$_2$, 10% ethyl acetate in petroleum ether) but provided 77.4 mg diols **5b** and **6b** (R_f 0.11): mass spectrum *m*/*z* (rel intensity) 478 (3), 293 (2), 292 (2), 264 (2), 233 (0.7), 220 (3), 219 (2), 206 (9), 205 (26), 204 (12), 193 (15), 180 (12), 178 (8), 167 (16), 165 (7), 143 (2), 129 (7), 117 (13), 115 (34), 105 (20), 104 (8), 92 (58), 91 (100), 78

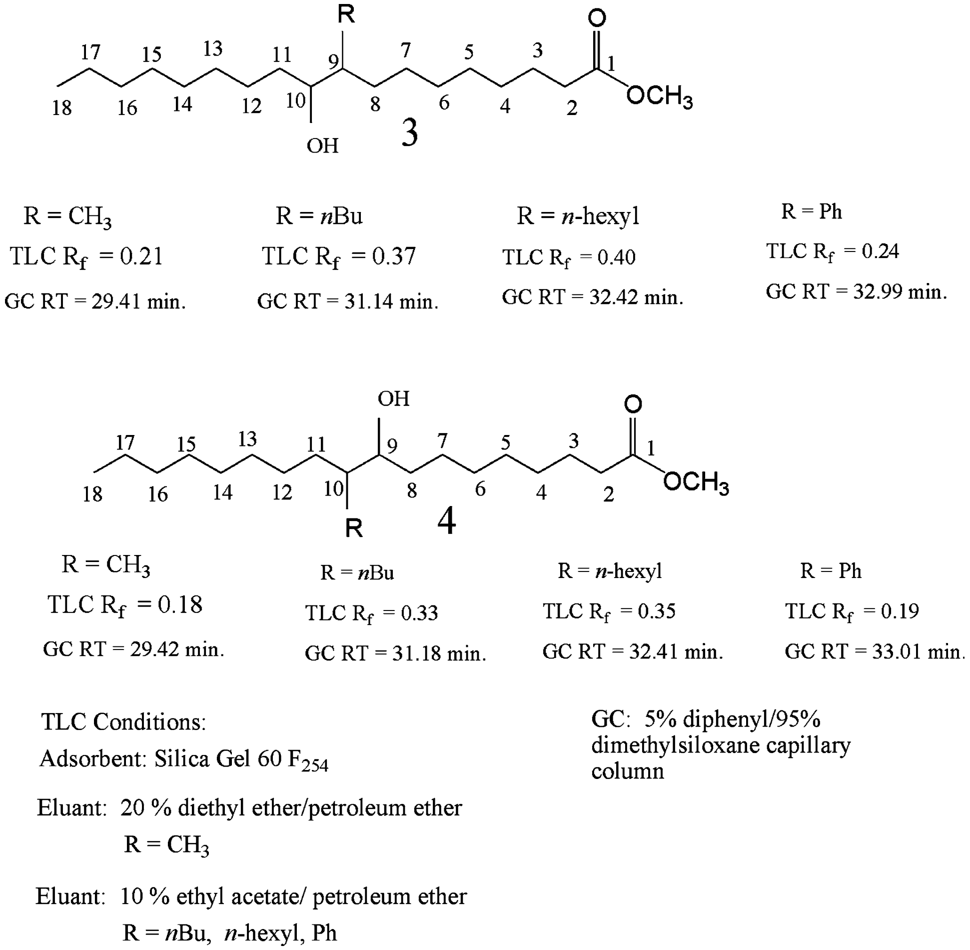
(7), 57 (9), 55 (8), 43 (11), 41 (13); ^{1}H NMR (CDCl$_3$) δ ^{13}C NMR (CDCl$_3$) δ, 14.32 (***C***H$_3$), 22.86, 23.90, 25.96, 27.81, 29.48, 29.65 (2C), 29.80, 29.89, 30.14, 32.04, 32.2, 35.28 (***C***H$_2$–CH–OH), 42.16 [***C***H$_2$C(Ph)$_2$OH)], 52.26 (CH$_2$CHOH***C***HPh), 75.17 [***C***–OH (secondary)], 78.24 [***C***–OH (tertiary)], 126.21 (4C), 126.77 (*p* aromatic C, side chain), 126.93 (2C, *p* aromatic), 128.31 (4C), 128.62 (*o* aromatic C, side chain), 129.15 (*m* aromatic C, side chain), 141.74 (quaternary phenyl C, side chain), 147.36 (2C, quaternary phenyl).

Material isolated from the fractions richest in **4d** (364 mg) was rechromatographed on the column (8% ethyl acetate in petroleum ether), providing 34.1 mg pure **4d**: mass spectrum *m*/*z* (rel intensity) 341 (1), 233 (0.2), 205 (3), 204 (19), 188 (6), 187 (49), 156 (8), 155 (80), 133 (12), 117 (13), 109 (18), 105 (25), 104 (18), 92 (100), 91 (89), 79 (8), 74 (10), 69 (9), 67 (22), 59 (10), 57 (21), 55 (33), 43 (27), 41 (28); ^{1}H NMR (CDCl$_3$) δ 0.86 (t, 3, C***H***$_3$), 1.10–1.75 (m, 26, 13 C***H***$_2$), 2.30 (t, 2, C***H***$_2$CO$_2$CH$_3$), 2.55 (m, 1, CH$_2$CHOHC***H***Ph), 3.67 (s, 3, OC***H***$_3$), 3.71 (m, 1, C***H***–OH), 7.18–7.28 (m, *p* aromatic H, and m, 2, *o* aromatic H) and 7.32 (m, 2, *m* aromatic H); ^{13}C NMR (CDCl$_3$) δ, 14.32 (C-18), 22.86, 25.11 (C-3), 27.80, 29.28, 29.47 (2C), 29.67 (2C), 29.89, 32.04, 32.29, 34.29 (C-2), 35.29 (C-8), 51.68 (O***C***H$_3$), 52.29 (C-10), 74.96 (C-9), 126.78 (*p* aromatic C) 128.62 (*o* aromatic C), 129.15 (*m* aromatic C), 141.75 (quaternary phenyl C), 174.55 (***C***=O).

Results and Discussion

The synthesis of the branched-chain hydroxy fatty acid derivatives **3** and **4** is outlined in Scheme 1. The successful ring opening of a number of oxiranes with lithium dimethylcuprate at 0 °C and of cyclopentene oxide with lithium di-*n*-butylcuprate at −40 °C has been reported [17]. However, reaction of **2** with lithium di-*n*-butylcuprate at −70 °C or with lithium dimethylcuprate at −30 °C afforded primarily unreacted starting material. The lower temperatures were considered necessary in order to minimize side reactions. Alexaxis et al. [15] reported that the presence of boron trifluoride greatly enhanced the reaction rate of lithium organocuprates with epoxides. Indeed, reaction of **2** with the selected organocuprate reagents under the

Fig. 2 Chromatographic properties of the isomers **3** and **4**



R = CH$_3$	R = *n*Bu	R = *n*-hexyl	R = Ph
TLC R$_f$ = 0.21	TLC R$_f$ = 0.37	TLC R$_f$ = 0.40	TLC R$_f$ = 0.24
GC RT = 29.41 min.	GC RT = 31.14 min.	GC RT = 32.42 min.	GC RT = 32.99 min.

R = CH$_3$	R = *n*Bu	R = *n*-hexyl	R = Ph
TLC R$_f$ = 0.18	TLC R$_f$ = 0.33	TLC R$_f$ = 0.35	TLC R$_f$ = 0.19
GC RT = 29.42 min.	GC RT = 31.18 min.	GC RT = 32.41 min.	GC RT = 33.01 min.

TLC Conditions:
Adsorbent: Silica Gel 60 F$_{254}$

Eluant: 20 % diethyl ether/petroleum ether
R = CH$_3$

Eluant: 10 % ethyl acetate/ petroleum ether
R = *n*Bu, *n*-hexyl, Ph

GC: 5% diphenyl/95% dimethylsiloxane capillary column conditions described (small excess of organocuprate reagent, equimolar amount of boron trifluoride diethyl etherate, −70 °C, ca. 1 h reaction time) gave primarily the desired products (**3** and **4**).

The chromatographic properties of the isomers **3** and **4** are shown in Fig. 2. The two isomers were inseparable on the GC capillary column. As shown, the GC retention times were virtually identical for each isomeric pair. However, TLC conditions were found that enabled separation. Flash chromatography did not result in complete separation of the isomers, but did provide sufficient quantities of pure isomers **3** and **4** for characterization (MS, NMR, DSC).

The structural assignments of the isomers **3** and **4** were made on the basis of their mass spectra (Fig. 3). The two isomers can be distinguished by the fragment ions formed by cleavage on either side of the carbon bearing the hydroxy group. The least polar isomer **3** can be identified by fragment Ion 1 (*m/z* 143). This ion is prominent in the mass spectra of **3a**, **3b**, and **3c**, but is less abundant in the spectrum of the phenyl derivative **3d**. Fragment ion 2 is observable (relative intensity $\leq$3) in the mass spectra of **3a**, **3b**, and **3c**, but not **3d**. The most polar isomer **4** can be identified by fragment ion 1 (*m/z* 187) [12]. This ion is prominent in the mass spectra of **4a**, **4b**, **4c**, and **4d**. In addition the fragment at $m/z = 155$ is the most abundant for **4a**, **4b**, and **4c** and is very prominent in the mass spectrum of **4d**. This fragment ion can be explained by the loss of methanol from fragment ion 1 [12]. Fragment ion 2

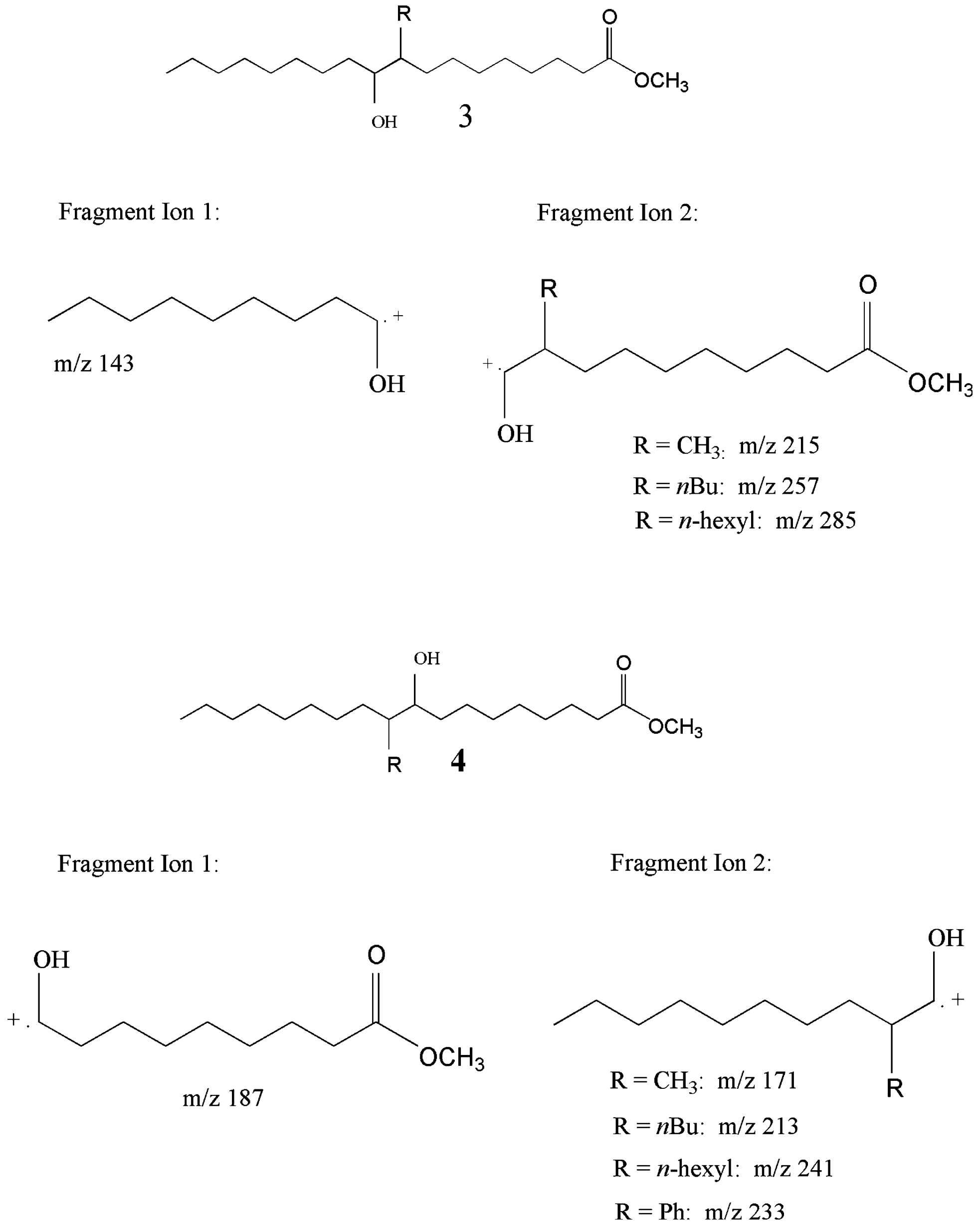


Fig. 3 Structural assignments of isomers **3** and **4** as based on mass spectra

is barely observable for all four side chains. Finally, for all four side chains, the fragment ions at *m*/*z* = 87, 74, 69, and 55 are considerably more abundant in the mass spectra of isomer **3** than those of isomer **4**.

The NMR spectra of isomers **3** and **4** were consistent with their structures. The proton NMR spectra of the methyl isomers **3a** and **4a** are shown in Fig. 4. The two spectra are virtually identical with one exception: one broad peak appears in the methylene region (1.2–1.4 ppm) in the spectrum of **3a** whereas two distinct peaks appear in the same region in the spectrum of **4a**. The same differences were observed in the spectra of the other three isomeric pairs. Owing to their structural similarity, the ^{13}C NMR spectra of the four isomeric pairs were very similar, but there were observable differences in the methylene carbons. The assignments of primary, tertiary, and quaternary carbon atoms were confirmed by DEPT studies. Table 1 summarizes the ^{13}C chemical shift assignments for the isomeric pairs that can be made unambiguously. Please note that C-9 chemical shifts for the compounds **3** are comparable with C-10 chemical shifts for the compounds **4**, C-10 chemical shifts (**3**) are comparable with C-9 chemical shifts (**4**), and C-11 chemical shifts (**3**) are comparable with C8 chemical shifts (**4**).

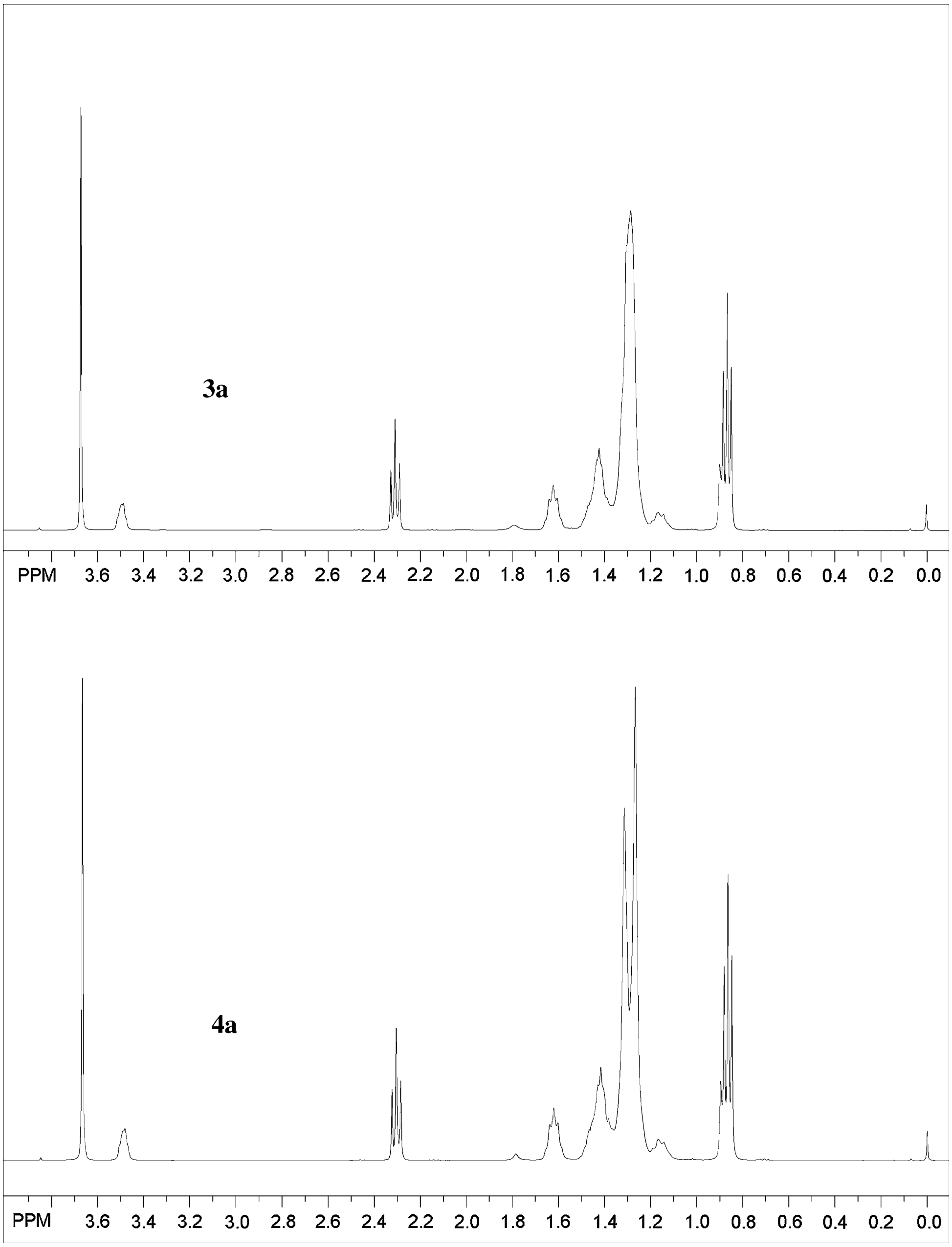


Fig. 4 Proton NMR spectra of the methyl isomers **3a** and **4a**

Table 1 Comparison of ^{13}C NMR spectra of isomers **3** and **4**

Compound	C-1	C-2	C-3	C-8	C-9	C-10	C-11	C-18	OCH_3
3a	174.54	34.27	25.12		38.34	75.34	34.66	14.30	51.63
4a	174.50	34.25	25.09	34.59	75.30	38.38		14.30	51.63
3b	174.55	34.29	25.14		43.74	73.83	34.20	14.30	51.63
4b	174.50	34.27	25.11	34.17	73.83	43.78		14.30	51.63
3c	174.55	34.28	25.12		43.73	73.83	34.13	14.31	51.65
4c	174.54	34.29	25.12	34.14	73.79	43.79		14.33	51.67
3d	174.55	34.21	25.03		52.19	75.13	35.31	14.29	51.60
4d	174.55	34.29	25.11	35.29	74.96	52.29		14.32	51.68

Chemical shifts are given in ppm

As observed previously [5, 7], the side products **5** and **6** were formed as a consequence of attack on the ester functionality in the fashion of a Grignard reagent. The ^{13}C NMR spectra of these diols were consistent with their structures. The spectra were void of olefinic and carbonyl carbons and showed distinct chemical shifts for the carbons bearing the hydroxy groups. A DEPT experiment enabled unambiguous assignment of the carbons bearing the secondary and tertiary hydroxy groups in the diols **5a** and **6a**; analogous assignments could be made with confidence for diols **5b** and **6b**. The assignment of chemical shifts was aided by the fact there are two identical *n*-butyl groups in the diols **5a** and **6a** and two identical phenyl groups in the diols **5b** and **6b.** Although the heteronuclear 2D NMR experiments could identify three different ^{13}C methyl resonances in **5a** and **6a**, their assignments remained ambiguous because of extensive overlap in the ^{1}H dimension. For clarity, chemical shift assignments for the diols **5a** and **6a** are given in Fig. 1.

The most abundant fragment ions above *m/z* 400 in the mass spectra of **5** and **6** were consistent with the loss of two molecules of water from the parent compounds (*m/z* 418 for **5** and *m/z* 478 for **6**).

Table 2 DSC properties of branched-chain hydroxy fatty acid derivatives

Compound(s)	T_c, °C	T_m, °C	T_g, °C
Methyl oleate			
1	−45.8, −47.2	−19.5	
2	−3.77, −5.47	+10.66	
3a	−64.04	−9.25	
4a	−64.49	+7.47	
3b		+10.70	−80.15
4b		+15.59	−79.39
3c	−42.24	+17.15	
4c		+8.97	−78.49
3d			−67.91
4d			−64.91

Data are given for methyl oleate **1** and epoxide **2** for comparison purposes

The results of DSC studies on the isomeric pairs **3** and **4** are summarized in Table 2. A variety of branched chains were introduced to evaluate the relationship between chain length and re-crystallization temperature, T_c. The DSC thermogram of methyl oleate has been reported previously [6] but is included for comparison purposes. Data for the epoxide **2** are also included for comparison purposes. The DSC thermogram of methyl isomer **3a** (Fig. 5) showed T_c at −64.0 °C and T_m at −9.25 °C. The DSC thermogram for **4a** (Fig. 5) showed a comparable T_c at −64.5 °C, but two prominent T_m were observed at +7.5 °C and −53.6 °C. In addition, there was a pronounced exotherm at −8 °C. The DSC thermograms of the *n*-butyl isomers (Fig. 6) were very similar but atypical. The thermograms displayed glasslike characteristics with no observable T_c. The DSC thermogram of **3b** showed $T_m = +10.7$ °C, $T_g = -80.2$ °C, and an exotherm at −52.4 °C. For **4b**, the values were 15.6 °C (T_m), −79.4 °C (T_g), and −41.7 °C (exotherm). Owing to the atypical appearance of the thermograms recorded for **3b** and **4b** at the usual heating and cooling rate of 10 °/min., the heating scans were repeated at rates of 5 and 2 °/min. The results for **3b** are shown in Fig. 6. There was no fundamental change in the thermogram; T_m and T_g were unchanged, but the exotherm moved to slightly lower temperatures at the slower rates. The results obtained for **4b** were comparable with those obtained for **3b**. The DSC thermograms of the *n*-hexyl derivatives were quite dissimilar. The thermogram for **3c** (Fig. 7) was normal in appearance with T_c at −44.2 °C and T_m at +17.2 °C. The DSC thermogram of **4c** (Fig. 7) showed $T_m = +8.97$ °C, $T_g = -78.5$ °C, and a pronounced exotherm at −45.0 °C. The DSC thermograms of the branched-chain phenyl derivatives showed only a glass-transition temperature (−67.9 °C for **3d** and −64.9 °C for **4d**). The exotherms observed in the heating curves of **4a**, **3b**, **4b**, and **4c** may be due to a change in crystalline structure.

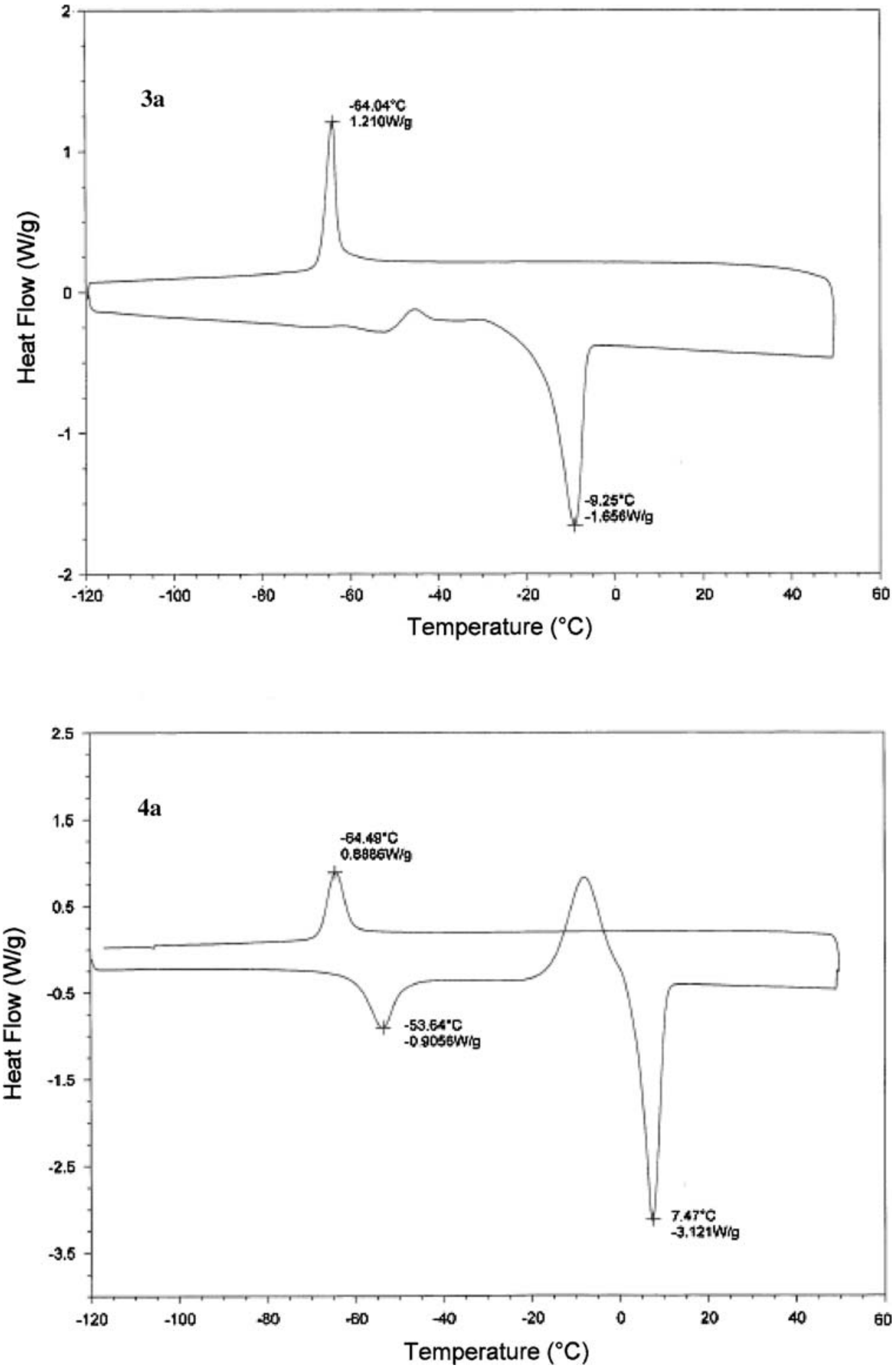
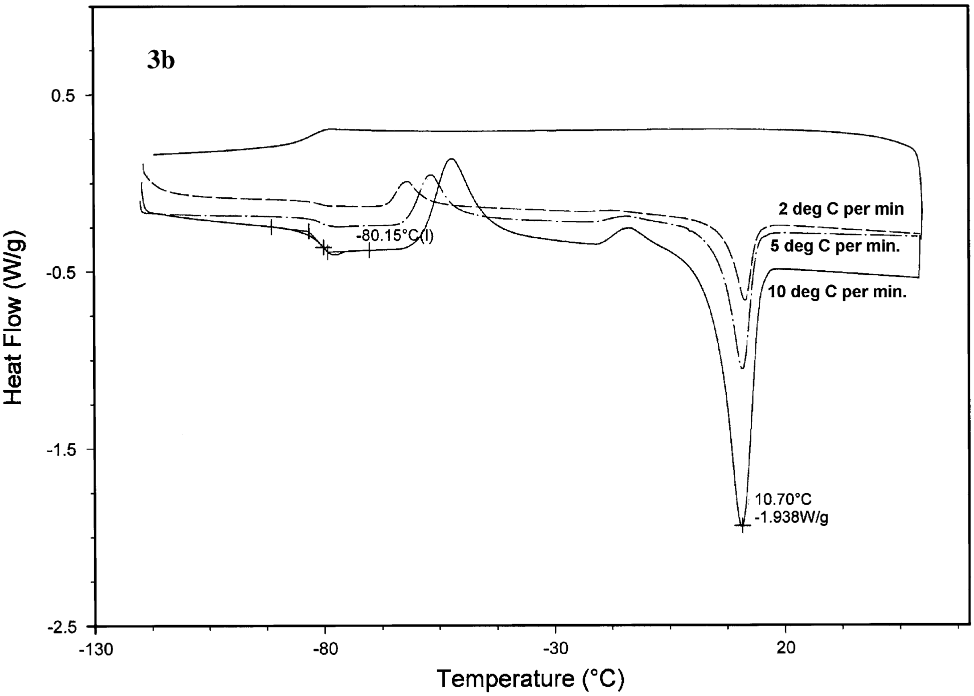


Fig. 5 DSC thermograms of methyl isomers **3a** and **4a.** In each thermogram, the lower scan is the heating curve and the upper scan is the cooling curve. Exothermal processes are shown as an amplitude upwards (+)

Conclusion

In these studies, methyl oleate was epoxidized and subsequently treated with four different organocuprate reagents in the presence of boron trifluoride diethyl etherate to produce novel branched-chain hydroxy acid derivatives. For each reaction, the two distinct isomeric products (methyl 9-alkyl-10-hydroxyoctadecanoate and



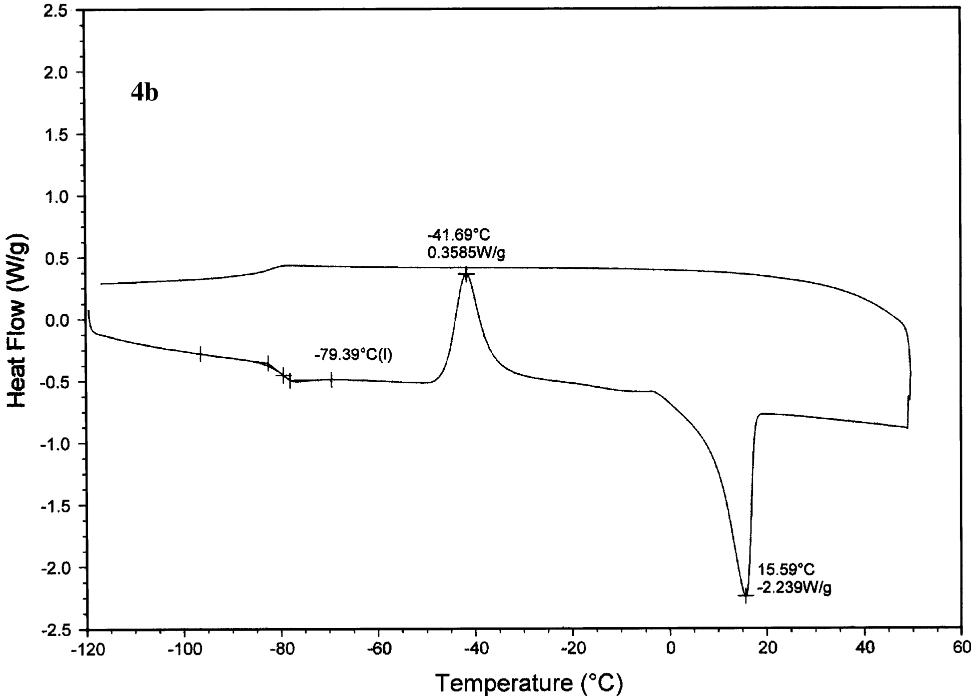


Fig. 6 DSC thermograms of *n*-butyl isomers **3b** and **4b**. In each thermogram, the lower scan is the heating curve and the upper scan is the cooling curve (recorded at a rate of 10 °/min). For **3b**, the heating scan was performed at rates of 10, 5, and 2 °/min. Exothermal processes are shown as an amplitude upwards (+)

methyl 9-hydroxy-10-alkyloctadecanoate) were isolated in the pure form and characterized by GC–MS, NMR, and DSC.

There was no correlation between length of the branched chain and DSC properties. In fact, the best low-temperature properties were observed for the methyl isomers **3a** and **4a**. The re-crystallization temperature (T_c) was significantly lower than that of methyl oleate for these compounds. This observation provides evidence that simple monoalkyl esters of some alkyl-branched chain hydroxy fatty acids

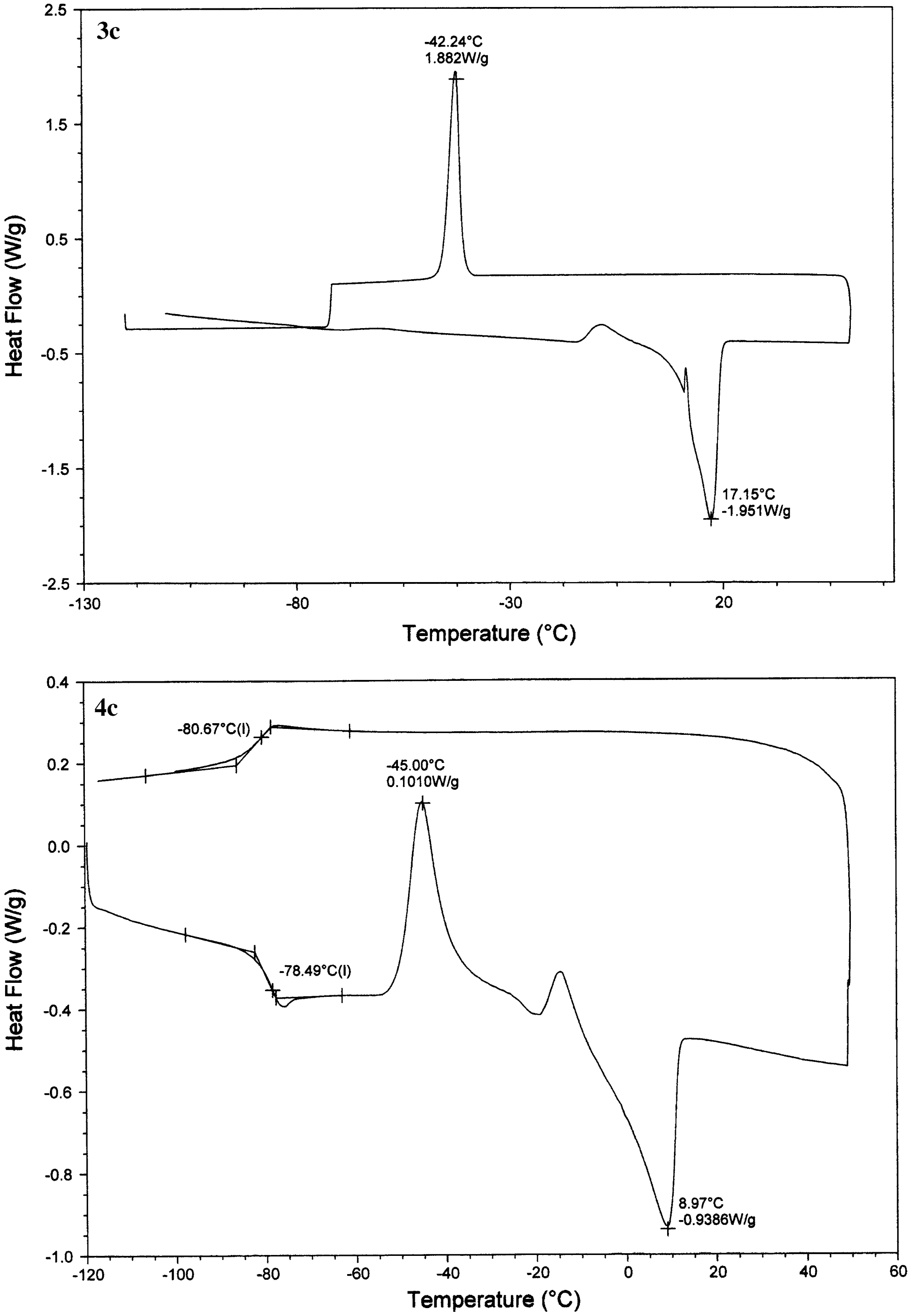


Fig. 7 DSC thermogram of *n*-hexyl isomers **3c** and **4c**. In each thermogram, the lower scan is the heating curve and the upper scan is the cooling curve. Exothermal processes are shown as an amplitude upwards (+)

could have improved or superior low-temperature properties comparable with those observed for analogous compounds [11, 13] and may prove useful as additives to biodiesel for use at low temperatures. In addition, the presence of the hydroxy functionality in compounds **3** and **4** makes them amenable to transformation to other compounds with potentially useful properties. For example, reaction with fatty acids will produce estolides [18]. Estolides which have favorable low-temperature properties have great potential for use as biodegradable lubricants [18–20]. Oleic-castor and lesquerella estolide esters were reported to have superior low-temperature properties [18].

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References

1. Lee I, Johnson LA, Hammond EG (1995) Use of branched-chain esters to reduce the crystallization temperature of biodiesel. J Am Oil Chem Soc 72:1155–1160
2. Foglia TA, Nelson LA, Dunn RO, Marmer WN (1997) Low-temperature properties of alkyl esters of tallow and grease. Ibid 74:951–955
3. Wu W-H, Foglia TA, Marmer WN, Dunn RO, Goering CE, Briggs TE (1998) Low-temperature property and engine performance evaluation of ethyl and isopropyl esters of tallow and grease. Ibid 75:1173–1178
4. Dunn RO (1999) Thermal analysis of alternative diesel fuels from vegetable oils. Ibid 76:109–115
5. Dailey OD Jr, Prevost N (2007) Conversion of methyl oleate to branched-chain derivatives. J Am Oil Chem Soc 84:565–571
6. Dailey OD Jr, Prevost NT, Strahan GD (2008) Synthesis and structural analysis of branched-chain derivatives of methyl oleate. Ibid 85:647–653
7. Dailey OD Jr, Prevost NT, Strahan GD (2008) Synthesis and characterization of branched-chain derivatives of methyl oleate. Clean 36:687–693
8. Biermann U, Metzger JO (2008) Synthesis of alkyl-branched fatty acids. Eur J Lipid Sci Technol 110:805–811
9. Biermann U, Friedt W, Lang S, Lühs W, Machmüller G, Metzger JO, Klaas MRg, Schäfer H, Schneider MP (2000) New syntheses with oils and fats as renewable raw materials for the chemical industry. Angew Chem Int Ed 39:2206–2224
10. Biermann U, Metzger JO (2004) Alkylation of alkenes: ethylaluminum-sesquichloride-mediated hydro-alkyl additions with alkylchoroformates and di-*tert*-butylpyrocarbonate. J Am Chem Soc 126:10319–10330
11. Moser BR, Erhan SC (2007) Preparation and evaluation of a series of α-hydroxy ethers from 9,10-epoxystearates. Eur J Lipid Sci Technol 109:206–213
12. Smith PC, Ngothai Y, Nguyen QD, O'Neill BK (2009) Alkoxylation of biodiesel and its impact on low-temperature properties. Fuel 88:605–612
13. Doll KM, Sharma BK, Erhan SZ (2007) Synthesis of branched methyl hydroxy stearates including an ester from bio-based levulinic acid. Ind Eng Chem Res 46:3513–3519
14. Doll KM, Erhan SZ (2005) Synthesis of carbonated fatty methyl esters using supercritical carbon dioxide. J Agric Food Chem 53:9608–9614
15. Alexaxis A, Jachiet D, Normant JF (1986) Boron fluoride promoted opening of epoxides by organocopper and cuprate reagents. Tetrahedron 42:5607–5619
16. Still WC, Kahn M, Mitra A (1978) Rapid chromatographic techniques for preparative separation with moderate resolution. J Org Chem 43:2923–2925
17. Johnson CR, Herr RW, Wieland DM (1973) Reactions of lithium diorganocuprates(I) with oxiranes. Ibid 38:4263–4268
18. Cermak SC, Brandon KB, Isbell TA (2006) Synthesis and physical properties of estolides from lesquerella and castor fatty acid esters. Ind Crops Prod 23:54–64
19. Isbell TA, Frykman HB, Abbott TP, Lohr JE, Drozd JC (1997) Optimization of the sulfuric acid-catalyzed estolide synthesis from oleic acid. J Am Oil Chem Soc 74:473–476
20. Cermak SC, Isbell TA (2003) Synthesis and physical properties of estolide-based functional fluids. Ind Crops Prod 18:183–196