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ORIGINAL PAPER

Use of Glycerol Carbonate in an Efficient, One-Pot and Solvent Free Synthesis of 1,3-*sn*-Diglycerides

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Abstract An efficient solvent-free synthesis of a variety of highly pure 1,3-*sn*-diglycerides (1,3-*sn*-diacylglycerols) in a two-step one pot process is described. Heating glycerol carbonate (4-hydroxymethyl-1,3-dioxolan-2-one) with fatty acid anhydrides **2a–d** affords 1:1 mixtures of glycerol carbonate fatty esters **3a–3d** and the corresponding fatty acids. Further heating the reaction mixtures in the presence of catalytic amounts of 1,4-diazabicyclo[2.2.2]octane (DABCO) at 195–200 °C yields highly pure 1,3-*sn*-diglycerides **4a–4d**.

Keywords Glycerol carbonate · Glycerol carbonates fatty esters · Fatty acid anhydrides · DABCO · 1,3-*sn*-Diglycerides · Low HLB surfactants

Introduction

1,3-*sn*-Diglyceride rich fatty compositions, are popular in the food industry as benign low HLB[1] [1] (co)emulsifiers [2], rheological modifiers [3] and dietary fat and oils [4]. They are used in bakery and confectionary dough [5], ice cream coating [6], chewing gum [7], fried food [8], potato chips and French fries [9], cocoa butter substitutes for the chocolate industry [10] and shortening [11]. Kao Corporation and associates have marketed high diglyceride (HiDi) edible oils in Japan and elsewhere, with several attributed nutritional benefits [12]. Favorable nutritional properties of 1,3-diglycerides in comparison with normal fats and oils is believed to be due to their different metabolic pathways. [13].

In addition to their use in the food industry, 1,3-*sn*-diglycerides can be functionalized in the second position directly with a drug bearing a carboxylic group such as the anti-inflammatory niflumic acid or through a dicarboxylic linker binding an alcohol such as bupranolol [14]. Similar processes are used to produce lipid soluble prodrugs [15]. Diglycerides are also used as drug carriers, delivering drugs with better absorption, improved bioavailability and reduced side effects of the original drugs [16, 17].

Diglycerides are traditionally produced by processes such as glycerolysis of natural fats and oils [18, 19] or direct esterification of glycerol with fatty acids [20, 21]. These processes can be catalyzed chemically or enzymatically [22, 23] especially by 1,3-selective lipase e.g. "Lilipase A-10" [24, 25]. Naturally these processes lack full positional selectivity and produce fatty mixtures enriched in 1,3-diglycerides, containing 1,2-diglycerides as well as mono and triglycerides. Due to commercial unavailability of pure 1,3-diglycerides, even major pharmacopeias describe diglycerides as mixtures containing mono and

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[1] The hydrophilic-lipophilic balance (HLB) of a surfactant is a measure of the degree to which it is hydrophilic or lipophilic, determined by calculating values for the different regions of the molecule, as described by Griffin in 1949.

triglycerides. For many applications, multistep and at times tedious processes [25] for the separation of pure symmetrical 1,3-*sn*-diglycerides from such mixtures is often unnecessary. Nonetheless commercial availability of a variety of pure symmetrical or unsymmetrical 1,3-*sn*-diglycerides, shall allow predesigned and precise formulations for more demanding applications in surfactant and drug delivery areas.

Earlier multistep and low yield synthesis of pure 1,3-*sn*-diglycerides using expensive dihydroxyacetone or allyl alcohol as starting materials [26] are clearly wasteful, hence uneconomical for industrial applications.

Pure 1,3-diglycerides were traditionally obtained by acylation of 1-monoacylglycerides with fatty acid chlorides [27]. Use of noxious reagents (Such as thionyl chloride), for the production of acid chlorides as well as handling problems of fatty acid chlorides themselves, do not favor industrialization of this process.

An improved synthesis of pure 1,3-*sn*-diglycerides has been reported by reacting pure fatty acids with glycidyl fatty esters [28], which are themselves prepared from fatty acid salts and epichlorohydrin [29] a highly toxic, corrosive and more importantly carcinogenic chemical [30].

A clean synthesis of pure symmetrical 1,3-*sn*-diglycerides by reacting fatty acid anhydrides with glycidol has been reported [31]. However, the high cost of intermediate glycidol and its transportation as well as possible spontaneous self-polymerization on storage [32] makes techno-economical feasibility of the process for industrial application very doubtful.

We have previously reported use of glycerol carbonate as a glycerol synthon for the selective production of pure α-monoglycerides [33]. We now report the synthesis of highly pure symmetrical 1,3-*sn*-diglycerides in good yields by condensation of fatty acid anhydrides with glycerol carbonate. This solvent free, two-step and one-pot process uses DABCO as catalyst (Scheme 1).

This type of reaction is not unprecedented. Reactions of ethylene carbonates with benzoic anhydride at 240–250 °C to produce ethylene dibenzoate has previously appeared in patent literature [34].

Food grade fatty acid anhydrides were synthesized using a simplified version of the reported processes [35]; by a one-pot reaction of appropriate pure fatty acids with acetic anhydride while distilling the co-produced acetic acid and excess acetic anhydride (Scheme 2).

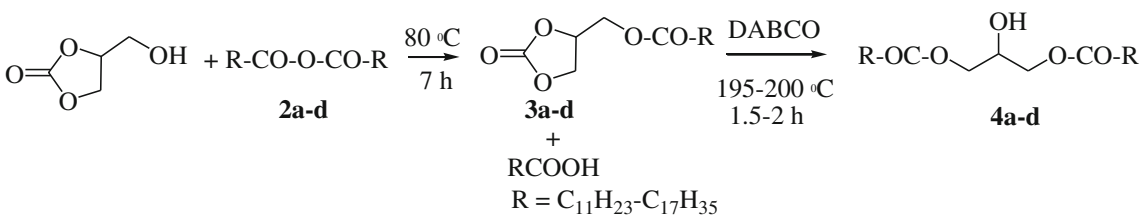
Experimental Procedures

Chemicals and Measurements

Glycerol carbonate (95 % purity) was prepared by a previously reported procedure [36]. All chemicals and reagents including fatty acids (lauric 99 %, myristic 98 %, palmitic 98 %, stearic 97 %) and acetic anhydride were purchased from Merck and used without further purification. Melting points were determined with an Electrothermal model 9100 apparatus. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker DRX-500 AVANCE Spectrometer. Mass spectra of the products were obtained on an Agilent Technology (HP) 5937 Mass Selective Detector, with Electron Impact (EI) 70 eV, and Quadrupole Analyzer.

*Synthesis of Fatty Acid Anhydrides **2a–d**: General Procedure*

Fatty acid **1a–d** (0.10 mol) was placed in a magnetically stirred 100-mL three-neck round-bottom flask equipped with a thermometer and a pressure-equalizing addition funnel. The middle neck of the flask was connected to a distillation set via a 20-cm vacuum-jacketed Vigreux column. Temperature was raised to 140 °C and excess acetic anhydride (12.24 g, 0.12 mol) was added drop-wise to the molten fatty acid within 30 min while distilling the co-produced acetic acid at a head temperature of 115–125 °C. When the distillation slowed down, the temperature of the boiling mixture was raised to 165–185 °C and the mixture was kept at this temperature until acetic acid (by product) and excess acetic anhydride were mostly distilled off under normal pressure. A vacuum (200 mm Hg) was then applied to remove all volatile materials. The reaction mixture was cooled to 45 °C and light petroleum ether (100 mL) was added. The mixture was refluxed for 15 min. Pure fatty acid anhydrides **2a–d** were obtained as colorless crystalline



Scheme 1

$$(CH_3CO)_2O + RCOOH \xrightarrow[30\ min]{165\text{-}185\ ^{o}C} R\text{-}CO\text{-}O\text{-}CO\text{-}R$$

$$R = C_{11}H_{23}\text{-}C_{17}H_{35} \qquad \textbf{2a-d}$$

Scheme 2

materials upon cooling the petroleum ether solution followed by filtration.

Lauric Acid Anhydride ***2a*** (18.7 g, 98 %), colorless crystalline solid, MP 42–44 °C, IR (KBr) ν_{max}: 2,910, 2,830, 1,810, 1,730, 1,460 cm^{-1}, ^1H NMR ($CDCl_3$) δ: 0.90 (t, *J* 7.1 Hz, 6H, $2CH_3$), 1.30 (m, 32H, $16CH_2$), 1.67 (m, 4H, $2CH_2$), 2.47 (t, *J* 7.5 Hz, 4H, $2CH_2CO$).

Myristic Anhydride ***2b*** (21.7 g, 98 %), colorless crystalline solid, MP 54–55 °C, IR (KBr) ν_{max}: 2,910, 2,830, 1,810, 1,735, 1,460 cm^{-1}, ^1H NMR ($CDCl_3$) δ: 0.90 (t, *J* 7.0, 6H, $2CH_3$), 1.30 (m, 40H, $20CH_2$), 1.67 (m, 4H, $2CH_2$), 2.47 (t, *J* 7.5, 4H, $2CH_2CO$).

Palmitic Anhydride ***2c*** (24.7 g, 98 %), colorless crystalline solid, MP 62–64 °C, IR (KBr) ν_{max}: 2,920, 2,825, 1,800, 1,740, 1,470 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.90 (t, *J* 7.0, 6H, $2CH_3$), 1.30 (m, 48H, $24CH_2$), 1.67 (m, 4H, $2CH_2$), 2.47 (t, *J* 7.5, 4H, $2CH_2CO$).

Stearic Anhydride ***2d*** (27.5 g, 98 %), shiny white crystalline solid, MP 71–72 °C, IR (KBr) ν_{max}: 2,920, 2,830, 1,810, 1,740, 1,470 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.90 (t, *J* 7.0, 6H, $2CH_3$), 1.32 (m, 54H, $28CH_2$), 1.67 (m, 4H, $2CH_2$), 2.47 (t, *J* 7.5, 4H, $2CH_2CO$).

Synthesis of Glycerol Ester Carbonates ***3a–d****: General Procedure*

Fatty acid anhydride **2a–d** (10 mmol) and glycerol carbonate (1.2 g, 10.5 mmol) were placed in a 100-ml three-necked round-bottom flask, equipped with a thermometer, magnetic stirrer and a condenser connected to a gas bubble counter. The temperature was then raised to 80 °C and kept at this temperature for 7 h. After completion of the reaction, the mass was cooled to 25–30 °C and dissolved in dichloromethane (200 mL). A dispersion of calcium hydroxide (0.6 g) per 100 mL water was added. The mixture was stirred at ambient temperature for 15 min and filtered. Organic layer was separated from the filtrate. The aqueous layer was re-extracted with dichloromethane (100 mL). The combined dichloromethane layers were washed with water (200 mL) and the solvent was distilled under reduced pressure. Recrystallization of the residue from light petroleum ether afforded the pure products **3a–3d** as white powder in 57–70 % yield.

(2-Oxo-1,3-dioxolan-4-yl) Methyl Laurate ***3a*** (1.7 g, 57 %), White solid, MP 57–59 °C, IR (KBr) ν_{max}: 2,950, 2,852, 1,784, 1,736, 1,475 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.9 (t, *J* 6.8 Hz, 3H, CH_3), 1.3 (m, 16H, $8CH_2$), 1.62 (m, 2H, CH_2), 2.38 (t, *J* 7.5 Hz, 2H, CH_2CO), 4.26 (dd, *J* 4.1, 12.6 Hz, 1H, CH_2OCO_2), 4.31 (dd, *J* 7.3 Hz, 1H, CH_2OCO), 4.38 (dd, *J* 3.3,12.6 Hz, 1H, CH_2OCO_2), 4.57 (t, *J* 8.6 Hz, 1H, CH_2OCO), 4.94 (m, 1H, CH), ^{13}C NMR ($CDCl_3$) δ 14.5, 23.8, 25.1, 29.4–29.9, 32.3, 34.3, 63.2, 66.4, 74.2, 154.8, 173.6, MS calculated for $C_{16}H_{28}O_5^+$ = 300; found: 300.

(2-Oxo-1,3-dioxolan-4-yl) Methyl Myristate ***3b*** (2 g, 62 %), White solid, MP 67–69 °C, IR (KBr) ν_{max}; 2,921 (CH), 2,910, 1,784, 1,736, 1,472 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.9 (t, *J* 6.6 Hz, 3H, CH_3), 1.3 (m, 20H, $10CH_2$), 1.63 (m, 2H, CH_2), 2.39 (t, *J* 7.5 Hz, 2H, CH_2CO), 4.28 (dd, *J* 4.1, 12.6 Hz, 1H, CH_2OCO_2), 4.31 (dd, *J* 7.3 Hz, 1H, CH_2OCO), 4.39 (dd, *J* 3.3, 12.6 Hz, 1H, CH_2OCO_2), 4.58 (t, *J* 8.6 Hz, 1H, CH_2OCO), 4.94 (m, 1H, CH), ^{13}C NMR ($CDCl_3$): δ 14.5, 23.1, 25.1, 29.4–30.0, 32.3, 34.3, 63.2, 66.4, 74.1, 154.7, 173.6, MS calculated for $C_{18}H_{32}O_5^+$ = 328; found: 328.

(2-Oxo-1,3-dioxolan-4-yl) Methyl Palmitate ***3c*** (2.3 g, 66 %), White solid, MP 70–72 °C, IR (KBr) ν_{max}; 2,921, 2,850, 1,784, 1,735, 1,475 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.9 (t, *J* 6.7 Hz, 3H, CH_3), 1.29 (m, 24H, $12CH_2$), 1.63 (m, 2H, CH_2), 2.39 (t, *J* 7.5 Hz, 2H, CH_2CO), 4.28 (dd, *J* 4.1, 12.6 Hz, 1H, CH_2OCO_2), 4.32 (dd, *J* 7.3 Hz, 1H, CH_2OCO), 4.39 (dd, *J* 3.3, 12.6 Hz, 1H, CH_2OCO_2), 4.58 (t, *J* 8.5 Hz, 1H, CH_2OCO), 4.92 (m, 1H, CH), ^{13}C NMR ($CDCl_3$): δ 14.5, 23.1, 25.1, 29.4–30.1, 32.3, 34.3, 63.2, 66.4, 74.2, 154.7, 173.6, MS calculated for $C_{20}H_{36}O_5^+$ = 356; found: 356.

(2-Oxo-1,3-dioxolan-4-yl) Methyl Stearate ***3d*** (2.7 g, 70 %), White solid, MP 79–81 °C, IR (KBr) ν_{max}: 2,958, 2,850, 1,784, 1,736, 1,472 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.9 (t, *J* 7.1 Hz, 3H, CH_3), 1.29 (m, 28H, $14CH_2$), 1.63 (m, 2H, CH_2), 2.39 (t, *J* 7.6 Hz, 2H, CH_2CO), 4.28 (dd, *J* 4.1, 12.6 Hz, 1H, CH_2OCO_2), 4.32 (dd, *J* 7.3 Hz, 1H, CH_2OCO), 4.39 (dd, *J* 3.3, 12.6 Hz, 1H, CH_2OCO_2), 4.58 (t, *J* 8.6 Hz, 1H, CH_2OCO), 4.94 (m, 1H, CH), ^{13}C NMR ($CDCl_3$): δ 14.5, 23.1, 25.1, 29.5–30.1, 32.3, 34.3, 63.2, 66.4, 74.1, 154.7, 173.7, MS calculated for $C_{22}H_{40}O_5^+$ = 384; found: 384.

One-Pot Synthesis of 1,3-sn-Diglycerides ***4a-d*** *from* ***2a-d****: General Procedure*

Fatty acid anhydrides **2a–d** (20 mmol) and glycerol carbonate (2.5 g, 95 %, 20 mmol) were placed in a

magnetically stirred 100 mL three necked round bottom flask equipped with a thermometer, and a condenser connected to a gas bubble counter. Temperature was raised to 80 °C and kept at this temperature for 7 h after which time DABCO (6 mol %, 0.13 g) was added. The temperature was raised to 195–200 °C to start the condensation reaction as CO_2 evolution observed in the bubble counter. The mixture was kept at this temperature for an appropriate time (see Table 2) until CO_2 evolution ceased. The reaction mixture was then cooled to 45 °C and light petroleum ether (60 mL) was added. The mixture was refluxed for 15–20 min and allowed to stand for 30 min at 40–45 °C without stirring. A thin viscous liquid film, which was difficult to analyze, was deposited at the bottom of the flask, but was assumed to consist of polyglycerol derivatives. The upper hot petroleum ether layer was then separated by decantation. Crude 1,3-*sn*-diglycerides were obtained upon cooling the petroleum ether solution and filtration under vacuum. Pure products **4a–d** were obtained as colorless crystals by recrystallization from light petroleum ether using decolorizing clay.

Glycerol 1,3-dilaurate ***4a*** (8 g, 88 %), White solid, MP 55–57 °C, IR (KBr) ν_{max}: 3,500, 3,438, 2,914, 2,850, 1,735, 1,710, 1,471 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.90 (t, *J* 7.1 Hz, 6H, $2CH_3$), 1.30 (m, 32H, $16CH_2$), 1.65 (m, 4H, $2CH_2$), 2.37 (t, *J* 8.0 Hz, 4H, $2CH_2$), 2.51 (s, 1H, OH), 4.12 (m, 1H, CH), 4.16 (dd, *J* 5.7, 11.5 Hz, 2H, CH_2CHOH), 4.21 (dd, *J* 4.3, 11.4 Hz, 2H, CH_2CHOH), ^{13}C NMR ($CDCl_3$): δ 14.5, 23.1, 29.5–30.0, 32.3, 34.5, 65.4, 68.8, 174.3, MS calculated for $C_{27}H_{52}O_5^+ = 456$; Found: 457.

Glycerol 1,3-dimyristate ***4b*** (8.9 g, 87 %), White solid, MP 64–66 °C, IR (KBr) ν_{max}: 3,498, 3,438, 2,954, 2,850, 1,731, 1,709, 1,471 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.90 (t, *J* 7.0 Hz, 6H, $2CH_3$), 1.29 (m, 40H, $20CH_2$), 1.64 (m, 4H, $2CH_2$), 2.37 (t, *J* 7.6 Hz, 4H, $2CH_2$), 2.52 (s, 1H, OH), 4.10 (m, 1H, CH), 4.15 (dd, *J* 5.7, 11.5 Hz, 2H, CH_2CHOH), 4.21 (dd, *J* 4.3, 11.4 Hz, 2H, CH_2CHOH), ^{13}C NMR ($CDCl_3$): δ 14.5, 23.1, 29.5–30.0, 32.3, 34.5, 65.4, 68.8, 174.3, MS calculated for $C_{31}H_{60}O_5^+ = 512$; Found: 512.

Glycerol 1,3-dipalmitate ***4c*** (9.6 g, 85 %), White solid, MP 72–74 °C, IR (KBr) ν_{max}: 3,490, 3,438, 2,954, 2,850, 1,731, 1,709, 1,473 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.90 (t, *J* 7.0 Hz, 6H, $2CH_3$), 1.30 (m, 48H, $24CH_2$), 1.64 (m, 4H, $2CH_2$), 2.37 (t, *J* 7.6 Hz, 4H, $2CH_2$), 2.51 (s, 1H, OH), 4.12 (m, 1H, CH), 4.16 (dd, *J* 5.7, 11.5 Hz, 2H, CH_2CHOH), 4.21 (dd, *J* 4.4, 11.4 Hz, 2H, CH_2CHOH), ^{13}C NMR ($CDCl_3$): δ 14.5, 23.11, 29.5–30.1, 32.3, 34.5, 65.4, 68.8, 174.3, MS calculated for $C_{35}H_{67}O_5^+ = 567$; Found: 568.

Glycerol 1,3-distearate ***4d*** (10.3 g, 83 %), White solid, MP 77–79 °C, IR (KBr) ν_{max}: 3,490, 3,438, 2,954, 2,850, 1,731, 1,710, 1,473 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.90 (t, *J* 7.0 Hz, 6H, $2CH_3$), 1.29 (m, 56H, $28CH_2$), 1.64 (m, 4H, $2CH_2$), 2.35 (t, *J* 7.5 Hz, 4H, $2CH_2$), 2.54 (s, 1H, OH), 4.12 (m, 1H, CH), 4.17 (dd, *J* 5.7, 11.5 Hz, 2H, CH_2CHOH), 4.21 (dd, *J* 4.3, 11.4 Hz, 2H, CH_2CHOH), ^{13}C NMR ($CDCl_3$): δ 14.53, 23.11, 29.5–30.1, 32.3, 34.5, 65.4, 68.8, 174.3, MS calculated for $C_{39}H_{76}O_5^+ = 624$; Found: 623.

Result and Discussion

The quantities of glycerol produced in the world oleochemical industries exceed the market demand for this compound. Production of biodiesel also generates a large amount of crude glycerol. Recently conversion of this by-product to glycerol carbonate has been suggested as an outlet for this oversupply [37]. However, utilization of glycerol carbonate itself is of great importance in this respect. This report demonstrates a simple process for the production of higher valued derivatives of glycerol, such as diglycerides, using glycerol carbonate. This process may indeed improve the economic viability of the biodiesel production.

On the other hand, due to inaccessibility of industrial commercial quantities of individual 1,3-*sn*-diglycerides in pure form, considerable industrial, pharmaceutical and synthetic potentials of 1,3-*sn*-diglycerides have not been exploited or even examined to any great extent.

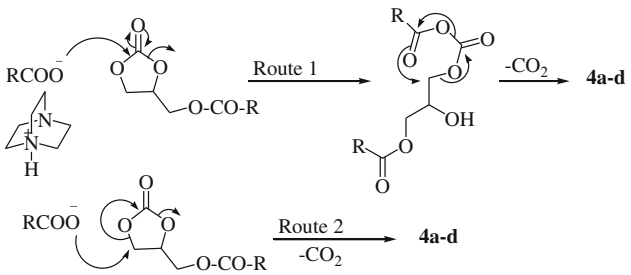
Presently no facile, efficient and benign process to produce individual 1,3-*sn*-diglycerides in pure form and industrially useful quantities is available. Therefore, presentation of a novel and practical method using easily available and eco-friendly starting materials in this field is desirable.

Controlled dehydration of fatty acids **1a–d** with excess acetic anhydride (Scheme 2) while removing acetic acid and excess acetic anhydride, afforded the corresponding fatty anhydrides as distillation residues. Distillation of volatile acetic acid and anhydride was performed at 165–185 °C reducing the pressure gradually from atmospheric pressure to 200 mm Hg.

Pure fatty acid anhydrides **2a–d** were obtained as colorless crystalline materials in almost quantitative yields by recrystallization from light petroleum ether (See "Experimental Procedure"). The results are presented in Table 1. Identification of **2a–d** was carried out using melting points, IR and ^1H-NMR spectral data. For example, IR spectrum of **2a** shows two absorption bands at 1,810 and 1,730 cm^{-1} characteristic of anhydrides. The presence of a triplet and a multiplet at δ 1.67 (4H) and 1.30 (4H) together with a triplet at δ 0.9 (6H) and a multiplets at δ 1.27–1.67 (32H) in ^1H NMR of **2a** is in agreement with lauric acid

Table 1 Reaction condition and results obtained for fatty acid anhydrides (**2a–2d**) prepared from fatty acids (**1a–1d**) with acetic anhydride

Fatty acid	Time (min)	Temperature (°C)	MP (°C)	Yield (%)
Lauric (**1a**)	30	165–185	45	98
Myristic (**1b**)	30	165–185	57	99
Palmitic (**1c**)	30	165–185	64	100
Stearic (**1d**)	30	165–185	72	100



Scheme 3

anhydride structure. The IR and ^{1}H NMR spectra of **2b–d** were similar to that of **2a**.

Lauric anhydride **2a** served for our early exploration of conversion into **4a.** Condensation of the lauric anhydride **2a** with glycerol carbonate was subsequently carried out initially at 80 °C to form a 1:1 mixture of ester carbonate and lauric acid. To this mixture was then added a catalytic amount of DABCO and was heated at 195–200 °C for 1.5 h (Scheme 1). Progress in the second step of the reaction was followed by observing the liberation of carbon dioxide as well as by withdrawing reaction samples periodically and taking their IR spectra. The formation of the product was monitored by the disappearance of the carbonyl peak of glycerol carbonate ester at 1,785 cm^{-1}. Recrystallization of the crude product from light petroleum ether afforded the crystalline 1,3-*sn*-diglyceride **4a** in 88 % yield. Based on the obtained results, fatty acid anhydrides **2b**, **2c** and **2d** were also transformed into **4b**, **4c** and **4d** (Scheme 1, Table 2). The results are shown in Table 2.

Identification of **4a** was carried out using IR and ^{1}H-NMR spectral data. The IR spectrum (KBr) of **4a** exhibited two double absorption bands at 3,500, 3,438 and 1,735, 1,710 cm^{-1} due to OH and CO stretchings respectively [38]. The characteristic peaks of **4a** in ^{1}H NMR appear as two AB systems at δ 4.21 (2H, *J* 4.4, 11.4 Hz, $\underline{CH_2}$CHOH) and 4.16 (2H, *J* 5.7, 11.5 Hz, $\underline{CH}$CHOH), a multiplets at 4.12 (1H, $\underline{CH}$OH) together with a broad singlet at δ 2.51 (1H, OH) and two triplets at δ 2.37 (4H *J* 8.0 Hz–$\underline{CH_2}$ CO_2), 0.90 (6H, *J* 7.1 Hz–CH_3). The MS of **4a** showed the M + 1 peak at 457 consistent with the molecular structure. In the mass spectrum, compound **4a** shows a base peak at *m/z* 183, assignable to the acylinium moiety $C_{12}H_{23}O^+$.

In the mass spectra of **4a–d**, base peaks were assigned to the acylinium moiety. The purity of these products was confirmed by high-field NMR spectroscopy. It has previously been shown that the glycerol backbone protons of acylglycerols can be highly useful in their identification and determination of their purity [39, 40].

In order to ascertain the intermediacy of carbonate esters, we tried to isolate these intermediates. But all attempts to isolate pure ester carbonate in good yield by fractional crystallization from various solvents were unsuccessful. We were able to isolate the carbonate esters in moderate yields by removing the free carboxylic acids from the solution of the mixture in dichloromethane using calcium hydroxide suspension. This method is inefficient due to extensive saponification of the carbonate ester.

The second stage of the reaction to produce diglycerides must be prevented till all the anhydride has been consumed. Otherwise a side reaction of diglyceride with the anhydride would result in the production of triglyceride. This is done by keeping the reaction temperature below 90 °C till completion of anhydride consumption.

To obtain the effect of temperature on the next stage, the reaction of fatty acid anhydrides **2a** and **2d** with glycerol carbonate were carried out at 145–150, 165, 195 or 230 °C. It was observed that increasing the reaction temperature not only speeds up the reaction rate, but also promotes the disproportionation reaction of the generated diglyceride to the relevant monoglyceride and triglyceride. Therefore, keeping the reaction temperature maximum at 195–200 °C was expected to safely afford the pure 1,3-*sn*-diglycerides.

A plausible mechanism for the transformation of **2a–d** into **4a–d** is shown in Scheme 3. The in-situ generated

Table 2 Reaction conditions and results obtained for diglycerides (**4a–4d**) prepared from condensation of fatty acid anhydrides (**2a–2d**) with glycerol carbonate in the presence of DABCO

Fatty acid anhydride	Time (h)	Temperature (°C)	MP (°C)	Yield (%)	Acid number
Lauric (**2a**)	1.5	195–200	58	88	1.2
Myristic (**2b**)	1.5	195–200	67	87	1.5
Palmitic (**2c**)	2	195–200	74	85	2
Stearic (**2d**)	2	195–200	82	83	1.8

3a–d from the initial condensation of glycerin carbonate with fatty acid anhydrides undergoes a reaction with the fatty acid salt obtained via the reaction of the liberated fatty acid with DABCO. As indicated in Scheme 3, the carboxylate anion might attack either the alkylene carbon (Paths 1) or the carbonyl group of the glycerol ester carbonates (Path 2), affording the desired **4a–4d**.

The striking advantage of the reported work in this manuscript is the utilization of the in-situ liberated fatty acid in the esterification step without introducing any fresh fatty acid.

In summary, we have described an easy and benign solvent-less method for the synthesis of highly pure 1,3-*sn*-diglycerides of lauric, myristic, palmitic, and stearic acids. The process can be commercialized easily.

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