# Synthesis of δ-Stearolactone from Oleic Acid

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**ABSTRACT:** δ-Stearolactone was prepared from oleic acid using concentrated sulfuric acid under various conditions in the presence of polar, nonparticipating solvents. δ-Stearolactone was formed in as high as 15:1 ratios over the thermodynamic product, γ-lactone, in the presence of methylene chloride, 100% wt/vol, at room temperature with two equivalents of sulfuric acid for 24 h. This procedure is applicable to other olefinic fatty acids such as estolides and fatty acid methyl esters. Temperature plays a role in the regioselectivity of the cyclization for δ-lactone, as lower temperatures (20°C) gave higher δ/γ ratios. At higher temperatures (50°C) in the presence of sulfuric acid and methylene chloride the yield of lactone was 75% but with a δ/γ ratio of only 0.3:1. Cyclization of oleic acid to lactone also occurred with other acids. Oleic acid underwent reaction with perchloric acid, one equivalent, in the absence of solvent at 50°C, which yielded δ-lactone in a modest yield with a 3.1 δ/γ ratio. The same temperature effect was observed with perchloric acid that was observed in the case of sulfuric acid. Because δ-stearolactone is much more reactive than the corresponding fatty acid, fatty acid ester, or γ-lactone, we believe that it will be a useful synthon for many new industrial products including new biodegradable detergents.

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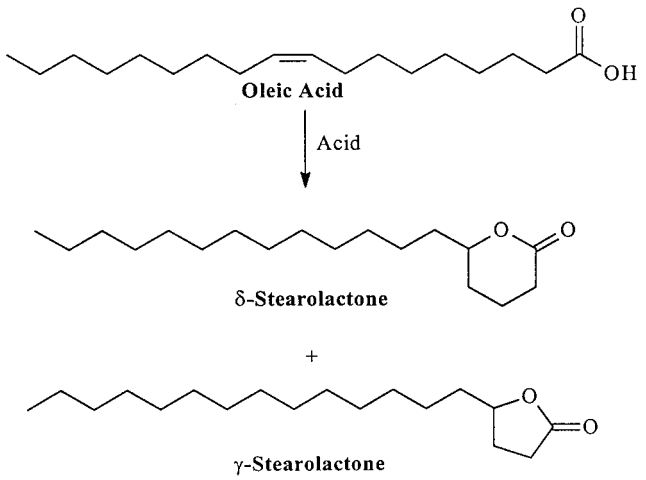
**KEY WORDS:** Acid catalyzed, lactone, oleic acid, perchloric acid, regioselective, δ-stearolactone, sulfuric acid.

Fatty acid lactones are formed from an intramolecular cyclization of a fatty acid carboxylate group with a carbocation located in the 4- or 5-position on the fatty acid backbone. Lactonizations reported by Ansell and Palmer (1) demonstrated that the formation of γ-lactones from short-chain fatty acids, typically with large excesses of acid (sulfuric or trifluoroacetic acids at elevated temperatures, 150°C) was possible. Isbell and Plattner (2) utilized the position of the double bond in the cyclization of a meadowfoam fatty acid, 5-eicosenoic acid, to the corresponding δ-lactone with the use of perchloric acid under various reaction conditions. The C-18 lactone, stearolactone, was more of a challenge because of the position of the double bond in the fatty acid (Scheme 1). There are many reports of the synthesis of the γ-lactone with various acids, such as ion exchange resins (3), *p*-toluenesulfonic acid (4), and sulfuric acid. Sulfuric acid-catalyzed isomerization of oleic acid to yield γ-stearolactone originally dated back to the early 1900s and was restudied by Clutterbuck in 1924 (5).




**SCHEME 1**

Showell *et al.* (6) synthesized γ-stearolactones from an isomerization reaction of oleic with perchloric acid to give high yields of γ-lactone with little or no δ-stearolactone. Their methodology required vigorous reaction conditions to achieve the necessary isomerization of the Δ9 double bond of oleic acid to the Δ4 position before ring closure resulted in the γ-lactone (Scheme 1). Shepherd and Showell (7) confirmed the mechanism proposed by Showell *et al.* (6) for double bond migration prior to lactonization.

Fujita *et al.* (8) studied the stabilized cyclization of 5-methyl-4-hexenoic acid with sulfuric acid, which gave a high yield of δ-lactone. The alkene underwent protonation to yield the tertiary carbocation, which was captured by the carboxyl group to form δ-lactone. In all other cases involving the C-18 lactones, the γ-stearolactone product was detected in high regioselectivity and yield due to the thermodynamic stability of the five-membered ring (9). Ansell and Palmer (1,10) investigated a series of short-chain acids with sulfuric and trifluoroacetic acids. In particular, 5-hexenoic acid, when treated with trifluoroacetic acid for 2 h, gave δ- to γ-lactone ratios of 7:3, however, in low yield.

δ-Lactones from oleic acid were reported in the literature, but the yields were low and reaction conditions were vigorous. One such example was reported by Nakano and Foglia (4), where oleic acid was treated with six equivalents of

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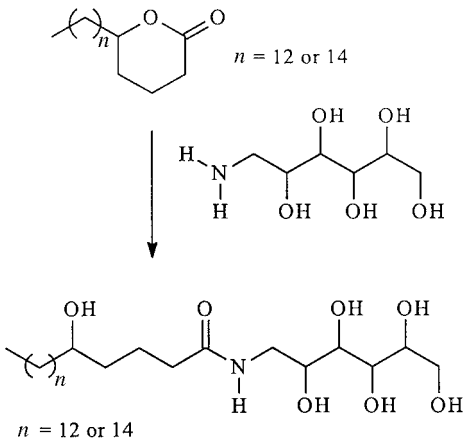



**SCHEME 2**

methanesulfonic acid in the presence of an alkylbenzene at room temperature to obtain γ- and δ-lactones in 15 and 35% yields, respectively. A method that produces a high yield of δ-stearolactone has not been reported.

Lactones are an interesting class of compounds that have many possibilities as industrial intermediates. The γ- and δ-lactones have different rates of reaction in the formation of amides from amines (11). This process enables the δ-lactone, the more reactive lactone, to selectively undergo reaction over the γ-lactone to provide the desired 5-hydroxy amides in high yields. By using this technology, the C-18 and C-20 δ-lactones recently have been converted to their amides in the synthesis of new biodegradable detergents (12) (Scheme 2). This technology has also been utilized for making short-chain fatty acid glucamides as new biodegradable detergents (13). Oleic acid is a desirable starting material because it is readily available from a number of agricultural sources, is relatively inexpensive, and is soon to become abundant from genetically engineered high-oleic crops. We have explored alternative methods and reagents to synthesize δ-stearolactone in higher yields than reported to date (14). In this paper, we report the synthesis of δ-stearolactone, building on knowledge that was gained from meadowfoam lactone research (2).

## EXPERIMENTAL PROCEDURES

*Materials*. Estolide and methyl oleate samples were obtained by a technique developed previously in our laboratory (15). Oleic acid (90%), perchloric acid (70%), and *p*-toluenesulfonic acid were purchased from Aldrich Chemical Co. (Milwaukee, WI). Concentrated sulfuric acid (98%) and potassium hydroxide were obtained from J.T. Baker Chemical Co. (Phillipsburg, NJ). Filter paper was obtained from Whatman (Clifton, NJ). Ethyl acetate and hexanes (for extractions) and acetone [for high-performance liquid chromatography (HPLC)] were obtained from Fisher Scientific Co. (Fairlawn, NJ). Methylene chloride, chloroform, acetonitrile, and monobasic phosphate were obtained from EM Science (Gibbstown, NJ). The fatty acid methyl ester (FAME) standard mixtures were obtained from Alltech Associates, Inc. (Deerfield, IL). Solvents for chromatography or extraction were HPLC or an equivalent grade and were used without further purification.

*Instrumentation*. Gas chromatography (GC) was performed with a Hewlett-Packard 5890 Series II gas chromatograph (Palo Alto, CA), equipped with a flame-ionization detector and an autosampler/injector. Analyses were conducted on two columns: SP 2380, 30 m × 0.25 mm i.d. (Supelco, Bellefonte, PA) and a SGE BP-1 30 m × 0.22 mm i.d. (Scientific Glass Engineering Pty. Ltd., Austin TX). Saturated $C_{10}$–$C_{30}$ FAME provided standards for calculating equivalent chain length (ECL) values, which were used to make fatty acid and lactone assignments.

The SP 2380 analysis: column flow 3.3 mL/min with helium head pressure of 15 psi; split ratio 22:1; programmed ramp 120 to 135°C at 10°C/min, 135 to 175°C at 3°C/min, 175 to 265°C at 10°C/min, hold 10 min at 265°C; injector and detector temperatures set at 250°C. Retention times for eluted peaks (ECL values in parentheses): methyl oleate 9.8 min (18.57), γ-stearolactone 21.64 min (29.73), and δ-stearolactone 22.3 min (30.94).

The BP-1 analysis: column flow 2.2 mL/min with helium head pressure of 25 psi; split ratio 39.2:1; programmed ramp 175 to 265°C at 3°C/min, hold 3 min at 265°C; injector and detector temperatures set at 250°C. Retention times for eluted peaks (ECL values in parentheses): methyl oleate 8.73 min (17.67), γ-stearolactone 12.85 min (19.62), and δ-stearolactone 13.53 min (19.93).

*GC–mass spectrometry (GC–MS)*. GC–MS was performed on a Hewlett-Packard 5890A GC with a 30 m × 0.20 mm i.d. SPB1 column (Supelco) and a Hewlett-Packard 5970 mass selective detector. GC conditions: helium head pressure 3 psi; split ratio 50:1; injector temperature set at 250°C; transfer line temperature set at 250°C; programmed ramp from 170 to 270°C at 3°C/min. MS conditions: mass range 50 to 550 amu; electron multiplier 200 volts relative.

*HPLC*. HPLC analyses were performed on a Thermo Separations (Fremont, CA) spectra system AS1000 autosampler/injector with a P2000 binary gradient pump coupled to a Varex evaporative light-scattering detector (ELSD) III (Alltech Associates). A C-8 reversed-phase analysis was carried out with a Dynamax column (250 × 4.5 mm, 5 μ particle size) from Rainin Instrument Co. (Woburn, MA) and was used to separate reaction mixtures by using the following gradient elution at a flow rate of 1 mL/min: 0 to 4 min 80% acetonitrile 20% acetone; 6 to 10 min 100% acetone; 11 to 16 min 80% acetonitrile 20% acetone. The ELSD drift tube was set at 55°C, with the nebulizer set at 20 psi $N_2$ to provide a flow rate of 2.0 standard liters per minute (SLPM). Retention times for eluted peaks: estolides, 9.8–13.0 min; methyl oleate, 6.3 min; oleic acid, 5.1 min; lactones, 4.8 min; and hydroxy acids 4.1 min.

*Nuclear magnetic resonance (NMR)*. $^{1}H$ and $^{13}C$ NMR spectra were obtained on a Bruker ARX-400 (Karlsruhe, Germany) with a 5-mm dual proton/carbon probe (400 MHz $^{1}H$/100.61 MHz $^{13}C$), using $CDCl_3$ as a solvent in all experiments.

*Methods*. Lactonization reactions conducted without solvent or below the solvent's boiling point were carried out in a three-neck round-bottom flask maintained at ±0.1°C of the desired set point. Higher temperature reactions were run at the solvent's boiling point in a three-neck round-bottom flask fitted with a reflux condenser. Mixing of the reactants was maintained by magnetic stirring throughout the course of the reaction. The product distribution was monitored by HPLC, GC, and/or GC–MS, as described above. All reactions were performed either with fatty acid 10.0 g (35.4 mmoles), methyl oleate 10.0 g (33.7 mmoles), estolides 10.0 g (8.90 mmoles), or triolein 10.0 g (11.3 mmoles) with described conditions or as outlined in the tables. Completed reactions were quenched by the addition of base, either KOH or NaOH. The addition of base resulted in a color change from black to yellow/red which coincided with the neutralization of the acid present in the reaction mixture. The pH was adjusted to 5.3–6.0 with the aid of pH 5 buffer ($NaH_2PO_4$, 519 g/4 L). A pH > 6.0 resulted in the soaping of the material and pH < 5.0 resulted in dehydration during the distillation. Purification of the lactone was accomplished by wiped film distillation (160°C at 0.1–0.5 mm Hg) to give a white crystalline product, mp 50.6–52.0°C.

$^1$H NMR of δ-stearolactone: δ 4.25–4.22 (*m*, 1H, –O–C*H*–$CH_2CH_2CH_2$C=O), 2.57–2.51 (*m*, 1H, –O–CH-$CH_2CH_2CH_aH_b$C=O), 2.44–2.41 (*m*, 1H, –O–CHC$H_2$-$CH_2CH_aH_b$C=O), 1.89–1.83 (*m*, 3H, –O–CHC$H_aH_b$C$H_2$-$CH_2$C=O), 1.71–1.64 (*m*, 1H, –O–CHC$H_aH_b$C$H_2CH_2$C=O), 1.55–1.47 (*m*, 4H, –$CH_2CH_2CH_2$–HCO–), 1.28–1.22 (*m*, 20H, –C$H_2$–) and 0.94 ppm (*t*, *J* = 7.0 Hz, 3H, –C$H_3$). $^{13}$C NMR of δ-stearolactone: δ 171.9 (*s*, *C*=O), 80.6 (*d*, –*C*H–O–C=O), 35.8 (*t*), 31.9 (*t*), 29.6 (*t*), 29.6 (*t*), 29.5 (*t*), 29.5 (*t*), 29.4 (*t*), 29.4 (*t*), 29.3 (*t*), 27.8 (*t*), 24.9 (*t*), 22.6 (*t*), 18.5 (*t*) and 14.1 ppm (*q*, –*C*$H_3$). δ- Stearolactone retention time 15.1 min, MS: *m/z* 282 ($M^+$, 1%), 264 ($M^+$ – 18, 5%) and 99 ($C_5H_7O_2$, 100%).

$^1$H NMR of γ-stearolactone: δ 4.43–4.38 (*m*, 1H, –O–C*H*–$CH_2CH_2$C=O), 2.48–2.19 (*m*, 2H, –O–$CHCH_2$-C$H_2$C=O), 2.28–2.27 (*m*, 1H, –O–CHC$H_aH_b$C$H_2$C=O), 1.83–1.21 (*m*, 1H, –O–CHC$H_aH_b$C$H_2$C=O), 1.69–1.62 (*m*, 1H, –$CH_2$C$H_aH_b$–HCO–), 1.56–1.47 (*m*, 1H, –$CH_2CH_a$-$H_b$–HCO–), 1.43–1.23 (*m*, 24H, –C$H_2$–), and 0.79 ppm (*t*, *J* = 3.2 Hz, 3H, –C$H_3$). $^{13}$C NMR of γ-stearolactone: δ 177.2 (*s*, *C*=O), 80.9 (*d*, –*C*H–O–C=O), 35.4 (*t*), 31.8 (*t*), 29.5 (*t*), 29.5 (*t*), 29.5 (*t*), 29.4 (*t*), 29.3 (*t*), 29.2 (*t*), 28.7 (*t*), 27.8 (*t*), 25.1 (*t*), 22.5 (*t*), and 13.9 ppm (*q*, –*C*$H_3$). γ-Stearolactone retention time 14.4 min, MS: *m/z* 282 ($M^+$, 1%), 264 ($M^+$ – 18, 3%), and 85 ($C_4H_5O_2$, 100%).

*Methyl ester synthesis*. Methyl esters of fatty acids were prepared by heating a 10-mg sample in 2 mL of 1 M $H_2SO_4$/MeOH to reflux on a heating block for 30 min in a sealed vial. The solution was poured into a separatory funnel with 3 mL of 1:1 hexane/ethyl acetate solution and washed with 2 × 2 mL of saturated NaCl solution, then dried over $Na_2SO_4$, filtered, placed in a sealed GC vial, and injected into the GC and/or GC–MS.

Trimethylsilyl (*TMS) derivatization of hydroxy fatty esters*. Hydroxy fatty acid esters (~10 mg) were dissolved in 0.1 mL of pyridine and 0.05 mL TMS acetamide. This solution was then placed in a sealed vial for 10 min at 100°C. After this time, hexane (1 mL) was added, and the resulting solution was then filtered though a silica plug and placed in a sealed GC vial and injected onto the GC and/or GC–MS.

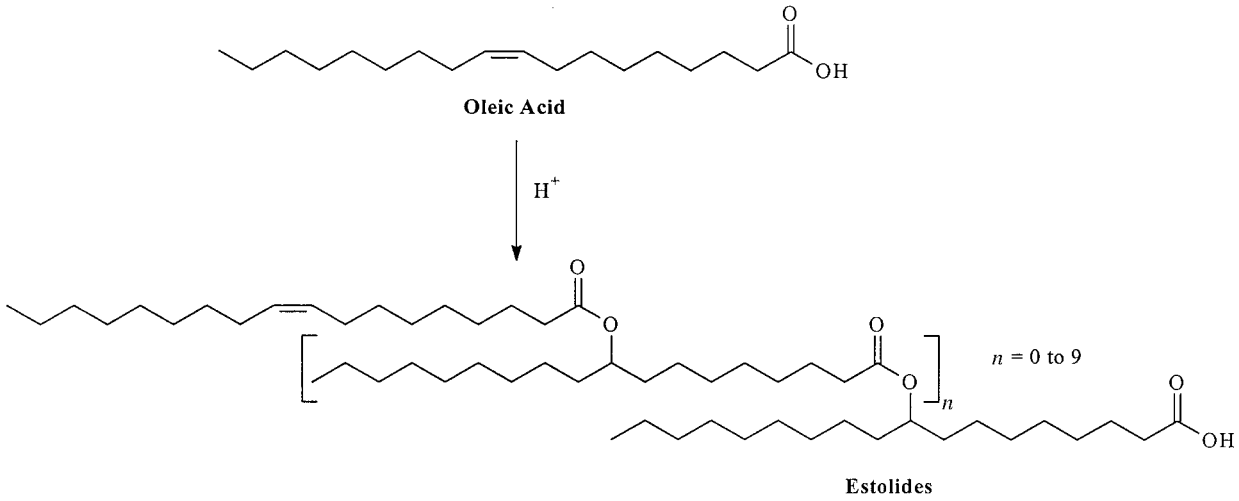
## RESULTS AND DISCUSSION

Brown *et al.* (9) showed that γ-lactones are the most thermodynamically stable lactone ring and that reaction conditions had to be revised to obtain the kinetically controlled product, δ-lactone. Table 1 outlines a series of reactions that explores the formation of δ-stearolactone. Initial reactions were run in

**TABLE 1**
**Lactonization of Oleic Acid with Sulfuric Acid[a]**

| Entry | Mole equivalent | Solvent | % Solvent (wt/vol) | Temp. (°C) | δ/γ[b] | Lactones[c] (%) | Estolides[c] (%) | Fatty acid[c] (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | 2 | None | 0 | 40 | 3.4 | 25.9 | 60.6 | 13.8 |
| 2 | 2 | $CH_2Cl_2$ | 500 | 40 | 4.2 | 52.9 | 36.9 | 10.2 |
| 3 | 3 | $CH_2Cl_2$ | 500 | 40 | 4.3 | 60.6 | 25.7 | 13.8 |
| 4 | 4 | $CH_2Cl_2$ | 500 | 40 | 2.1 | 61.0 | 39.0 | 0.0 |
| 5 | 2 | $CH_2Cl_2$ | 100 | 40 | 13.2 | 57.2 | 24.6 | 8.0 |
| 6 | 3 | $CH_2Cl_2$ | 100 | 40 | 13.1 | 61.2 | 32.9 | 5.9 |
| 7 | 2 | $CH_2Cl_2$ | 100 | rt | 15.0 | 85.2 | 10.6 | 4.2 |
| 8 | 2 | Hexane | 100 | rt | 5.2 | 62.3 | 27.5 | 10.2 |
| 9 | 2 | $CHCl_3$ | 100 | 50 | 1.0 | 68.7 | 26.7 | 4.6 |
| 10 | 2 | $CHCl_3$ | 100 | 60 | 0.3 | 75.2 | 22.0 | 2.8 |
| 11 | 2 | EtOAc[d] | 100 | rt | — | 0.0 | 3.2 | 96.8 |

[a]Reactions were run for 24 h with magnetic stirring.
[b]Ratios determined on the crude reaction mixture by gas chromatography (GC) (30 m × 0.25 mm i.d.; SP 2380; Supelco, Bellefonte, PA).
[c]Yield determined on the crude reaction mixture by high-performance liquid chromatography (HPLC) (C-8 reversed-phase analysis on Dynamax column, Rainin Instrument Co., Woburn, MA; 250 × 4.5 mm, 5 µ).
[d]EtOAc, ethyl acetate; rt, room temperature.




**SCHEME 3**

the absence of solvent, but only a small amount of lactones was formed, as seen in entry 1. The major products were estolides, which are of interest for other applications (Scheme 3) (16). The estolides are postulated as coming from a protonation mechanism to give a carbocation. The carbocation undergoes nucleophilic addition by another fatty acid to give estolides. This condensation can continue resulting in oligomeric compounds, however, the average extent of oligomerization is two estolide units ($n$ = 2, Scheme 3) (17). We assume that estolide and lactone formation are in equilibrium at the γ- and δ-positions in a classic ring- chain equilibrium typical of other lactones such as caprolactone (1). The equilibrium is likely to favor γ-lactone over estolide formation because the γ-lactone is a very stable ring, but the δ-lactone ring–chain equilibrium probably is shifted more easily toward estolide depending on stabilization of the intermediates. The situation is further complicated in that estolides formed at other chain positions do not form stable rings. The distribution of carbon positions for estolides ranges from positions 5–13 where the original Δ9 and Δ10 positions have the largest abundances (Table 2). A set of reaction conditions that minimized estolide formation was needed. Upon addition of solvent, estolide formation decreased and lactone formation increased (Table 1, compare entries 1, 2 and 5).

As the amount of acid was increased (Table 1, compare entries 2–4) the amount of lactone observed increased, but the δ/γ ratio decreased to only 2.1. Decreasing the solvent from 500 to 100% (wt/vol) gave a slight increase in the yield of lactone, but, more importantly, increased the δ/γ ratio from 4.2:1 to 13.2:1 (Table 1, entries 2 and 5). This helped eliminate the use of large amounts of solvent.

*Temperature effects*. The lower amount of solvent was used in the study of the effect of temperature. As the temperature was decreased from 50°C to room temperature, the lactone yield increased and the δ/γ-lactone ratio also increased (Table 1, entries 9, 5 and 7). In reactions where the temperature was greater than 40°C, a higher boiling solvent was employed (chloroform). Entries 9 and 10 demonstrate that as the temperature increases, the lactone yields increases at the expense of the δ/γ ratios. Entries 7 and 8 demonstrate the effect of solvent; as the polarity decreases the yield of lactone also decreases. These results were consistent with the work done by Isbell and Plattner (2) on the δ-eicosanolactone. Therefore, optimal reaction conditions were determined to be room temperature in $CH_2Cl_2$ at 100% wt/vol of oleic acid (entry 7).

*Other acids*. A number of other acid catalysts were explored with oleic acid (Table 3). The most interesting reactions studied were the cases involving perchloric acid (entries 6–11). As Showell *et al.* (6) demonstrated, γ-lactones were synthesized at higher temperatures with perchloric acid

**TABLE 2**
**Estolide Position as Determined by Gas Chromatography–Mass Spectrometry (GC–MS) of Trimethylsilyl Ether of Alkali-Hydrolyzed Estolide**

| Estolide fraction from | Hydroxy position | MS fragments | | Total abundance |
|---|---|---|---|---|
| | | Carbonyl | Alkyl | |
| Table 1 Entry (7) | 5 | 203 | 285 | 1 |
| | 6 | 217 | 271 | 10 |
| | 7 | 231 | 257 | 16 |
| | 8 | 245 | 243 | 27 |
| | 9 | 259 | 229 | 43 |
| | 10 | 273 | 215 | 41 |
| | 11 | 287 | 201 | 23 |
| | 12 | 301 | 187 | 1 |
| | 13 | 315 | 173 | 1 |
| Table 1 Entry (10) | 5 | 203 | 285 | 2 |
| | 6 | 217 | 271 | 9 |
| | 7 | 231 | 257 | 18 |
| | 8 | 245 | 243 | 28 |
| | 9 | 259 | 229 | 41 |
| | 10 | 273 | 215 | 39 |
| | 11 | 287 | 201 | 22 |
| | 12 | 301 | 187 | 11 |
| | 13 | 315 | 173 | 1 |

**TABLE 3**
**Lactonization of Oleic Acid with Other Acids[a]**

| Entry | Acid | Mole equivalent | Solvent | % Solvent (wt/vol) | Temp. (°C) | δ/γ[b] | Lactones (%) | Estolides[c] (%) | Fatty acids[c] (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3SO_3H$ | 2.0 | None | 0 | 40 | — | 0.0 | 0.0 | 100.0 |
| 2 | $CH_3SO_3H$ | 2.0 | $CH_2Cl_2$ | 100 | 42 | 7.3 | 9.0 | 88.0 | 4.0 |
| 3 | $CF_3SO_3H$ | 0.5 | $CH_2Cl_2$ | 100 | 40 | 8.0 | 6.2 | 86.3 | 7.5 |
| 4 | $CF_3SO_3H$ | 1.0 | $CH_2Cl_2$ | 100 | 40 | 8.4 | 46.7 | 44.0 | 9.3 |
| 5 | $CF_3SO_3H$ | 2.0 | $CH_2Cl_2$ | 100 | 40 | 8.2 | 2.9 | 61.6 | 35.5 |
| 6 | $HClO_4$ | 1.0 | None | 0 | 50 | 3.1 | 51.8 | 41.8 | 6.4 |
| 7 | $HClO_4$ | 1.0 | None | 0 | 40 | 8.2 | 3.7 | 81.1 | 15.2 |
| 8 | $HClO_4$ | 2.0 | None | 0 | 50 | 1 | 76.1 | 23.0 | 0.9 |
| 9 | $HClO_4$ | 1.0 | $CH_2Cl_2$ | 100 | 42 | 1.5 | 2.3 | 86.2 | 11.5 |
| 10 | $HClO_4$ | 2.0 | $CH_2Cl_2$ | 100 | rt | 21.3 | 2.3 | 93.2 | 4.5 |
| 11[d] | $HClO_4$ | 1.0 | None | 0 | 85 | <0.1 | 88.2 | 11.8 | 0.0 |
| 12 | Amberlyst-15 | 10.0 | None | 0 | 42 | — | 0.0 | 0.0 | 100.0 |
| 13 | Amberlyst-15 | 10.0 | $CH_2Cl_2$ | 100 | 42 | — | 0.0 | 0.0 | 100.0 |
| 14 | *p*-TSA[e] | 1.0 | $CH_2Cl_2$ | 100 | 40 | — | 0.0 | 0.0 | 100.0 |

[a]Reactions were run for 24 h with magnetic stirring.
[b]Ratios determined on the crude reaction mixture by GC (SP 2380, 30 m × 0.25 mm i.d.).
[c]Yield determined on the crude reaction mixture by HPLC (C-8 250 mm × 4.5 mm, 5 µ).
[d]Reaction time 8.5 h with magnetic stirring.
[e]*p*-TSA, *p*-toluenesulfonic acid; for other abbreviations see Table 1.

(Table 3, entry 11). As we decreased the temperature to 50°C (with 1 equivalent of acid), the lactone yield decreased, the δ/γ ratio increased to 3.1, and estolide formation jumped from 11.8 to 41.8% (Table 3, entry 11 vs. 6). This was very interesting when compared to the sulfuric case (Table 1, entry 1), where the major product was estolide. The reactions were carried out in the absence of solvent, but the perchloric acid gave a higher yield of lactone and about the same δ/γ ratios. Thus, perchloric acid appears to favor ring formation over estolide formation at 24 h. With a 10°C drop in temperature to 40°C, less than 4% lactone was observed (Table 3, entry 7) and the δ/γ ratio was 8.2 but estolide conversion was 81.1%. The optimal conditions with sulfuric acid were tested on the perchloric case (Table 3, entry 10), with only 2.3% lactone observed, although the δ/γ ratio improved dramatically to >20. This suggests that the use of perchloric acid at lower temperatures with or without solvent improves the ratios of δ-lactone.

Estolide samples from Table 3, entries 7 and 10 were hydrolyzed in 0.5 M KOH/MeOH, then esterified with 1 M $H_2SO_4$/MeOH to give the corresponding hydroxy and fatty esters. The isolated hydroxy fatty esters were then silylated and analyzed by GC–MS (18). The main mass spectral features were *m/z* 371 ($M^+$ –15, 1.2%), 73 ($TMS^+$, 100%) and a Gaussian fragment representing cleavage at the silyloxy positions (masses 173 to 315). The fragments and abundances are summarized in Table 2 relative to their respective positions on the fatty ester backbone. The estolide position is distributed from positions 5–13 with the original Δ9 and Δ10 positions having the largest abundances in the mass spectrum. These results suggest that the cationic shift needs a higher temperature to isomerize the olefin to Δ5 and thus obtain lactone in the cases involving perchloric acid. This is also confirmed by the data in Table 3. Reactions with perchloric acid show that at lower temperatures estolide is the major product while at higher temperatures (50°C) lactones are the major product.

The other acid catalysts tested showed no real improvement over two equivalents of sulfuric acid in the overall yield of δ-stearolactone, and a few of the acids gave no lactone. The *p*-toluenesulfonic acid had solubility problems, whereas Amberlyst-15 gave no lactone. Amberlyst is known to yield γ-lactones at higher temperatures (3). The trifluoro- and methanesulfonic acids did give decent δ/γ ratios, but the yield of lactones was no greater than 46.7% after 24 h.

*Oleic esters*. Methyl oleate was examined as a possible starting material intended to help eliminate estolide formation (Table 4). Methyl oleate, under similar conditions to sulfuric acid, displayed results comparable to the oleic case (entry 1). When methyl oleate was combined with acid and no solvent was used (Table 4, entry 2), there was an unexpected increase in the lactone yield as compared to the oleic acid case (Table 1, entry 1).

In an attempt to determine the reaction pathway for the formation of lactones from the ester, estolides were combined under acidic conditions. Small amounts of lactone were synthesized from the estolides. This suggests that the estolide reaction is reversible and under the appropriate conditions could yield larger amounts of lactone. The reaction of estolides with perchloric acid (entry 7) gave the best δ/γ ratios but with <3% lactone formation. Reaction of estolides with sulfuric acid (entry 8) gave the best lactone conversion from estolide, but with γ-lactone as the major lactone.

*Stability and analysis of lactones*. Owing to the reactivity of the ring, purification and analysis of the lactone proved to be very challenging in this investigation. The lactone is very sensitive to distillation, especially in the presence of residual acids. Under these conditions, the lactone undergoes dehydration to the unsaturated fatty acids.

GC analysis of the lactones is straightforward and provides normal fatty acid separation on both polar and nonpolar columns. The ECL values were used for identifying the lac-

**TABLE 4**
**Lactonization of Oleic Esters with Acids[a]**

| Entry | Esters | Acid | Mole equivalent | Solvent | % Solvent (wt/vol) | Temp. (°C) | δ/γ[b] | Lactones[c] (%) | Estolides[c] (%) | Fatty acids[c] (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Oleate[d] | $H_2SO_4$ | 2 | $CH_2Cl_2$ | 100 | 40 | 13.1 | 57.6 | 40.1 | 2.3 |
| 2 | Oleate[d] | $H_2SO_4$ | 2 | None | 0 | 40 | 2.3 | 42.8 | 44.0 | 13.2 |
| 3 | Oleate[d] | $HClO_4$ | 1 | $CH_2Cl_2$ | 100 | 42 | 8.2 | 9.0 | 63.0 | 24.0 |
| 4 | Triolein | $H_2SO_4$ | 6 | $CH_2Cl_2$ | 100 | 40 | — | 43.5 | 6.7 | 50.8 |
| 5 | Estolides[f] | $HClO_4$ | 1 | $CH_2Cl_2$ | 100 | 42 | 2.4 | 5.0 | >94 | <1 |
| 6[e] | Estolides[f] | $HClO_4$ | 2 | None | 0 | 50 | 1.3 | 36.6 | 59.8 | 3.6 |
| 7 | Estolides[f] | $HClO_4$ | 2 | $CH_2Cl_2$ | 100 | rt | 8.9 | 2.9 | 96.1 | 1.0 |
| 8 | Estolides[f] | $H_2SO_4$ | 2 | $CH_2Cl_2$ | 100 | rt | 0.8 | 54.4 | 39.9 | 5.7 |

[a]Reactions were run for 24 h with magnetic stirring.
[b]Ratios determined on the crude reaction mixture by GC (SP 2380, 30 m × 0.25 mm i.d.).
[c]Yield determined on the crude reaction mixture by HPLC (C-8 250 mm × 4.5 mm, 5 μ).
[d]Methyl oleate.
[e]Reaction was run for 48 h with magnetic stirring.
[f]Position of hydroxide groups comparable to those listed in Table 2. For abbreviation see Table 1.

tones, and the corresponding separation enabled us to determine the δ/γ ratios for all experiments by running the crude reaction mixtures on the GC. To determine the amount of additional hydroxy fatty acid in the reaction mixture, the methyl esters were prepared with $H_2SO_4$/methanol. Other hydroxy fatty acids present in the mixture are possible because of the migration of the double bond. The lactones were opened to the hydroxy methyl esters, but it has been reported by Tulloch (19) that upon injection into the hot injection port these compounds undergo spontaneous ring closure. Isbell and Plattner (2) also found this to be true in the synthesis of δ-eicosanolactone derivatives, but with our procedures the δ-stearolactone did not undergo complete ring closure. Our procedures were tested with authentic δ-eicosanolactone samples provided by Isbell and Plattner (2), and we were able to detect the 4- and 5-hydroxyeicosanoic acids by GC, thus our findings were confirmed.

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