Synthesis of Fluorine-Containing Analogues of 1-Lysoglycerophospholipids via Horner-Wadsworth-Emmons Reaction

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Abstract
This article describes an efficient method of synthesizing fluorine-containing analogues of 1-lysoglycerophospholipids (1-LPLs) by introducing a palmitoyl moiety starting from bis(2,2,2-trifluoroethyl)phosphonoacetate (Still-Gennari reagent). Our method effectively employs Horner-Wadsworth-Emmons reagents as masked 1-LPL derivatives to prepare a series of analogues of 1-lysophosphatic acid (1-LPA), 1-lysophosphatidylethanolamine (1-LPE), and 1-lysophosphatidylcholine (1-LPC).

Key words
lysoglycerophospholipid, Horner-Wadsworth-Emmons reaction, fluorine, lysophosphatic acid, lysophosphatidylethanolamine, lysophosphatidylcholine

Lysoglycerophospholipids (LPLs), in which only one acyl chain is attached to the glycerol moiety at the sn-2 position (1-LPL) or sn-1 position (2-LPL), are of considerable current interest as important signaling molecules in living biological systems. Intramolecular acyl chain migration is known to give an equilibrium mixture of 1-LPL and 2-LPL under physiological conditions; the equilibrium generally favors 2-LPL, as shown in Figure 1. On the other hand, fluorine is the most electronegative element of the periodic table and can be considered a reasonable surrogate of a hydroxy group. Thus, replacement of a hydroxy group of 1-LPL by a fluorine atom is an important strategy for blocking the acyl migration of 1-LPL to 2-LPL. In this context, we have been intrigued with sn-2 palmitoyl 1-F-LPA (1), 1-F-LPE (2), and 1-F-LPC (3), which are fluorine-containing analogues of 1-lysophosphatic acid (1-LPA), 1-lysophosphatidylethanolamine (1-LPE), and 1-lysophosphatidylcholine (1-LPC), respectively. However, the literature contains only one report on the synthesis of 1, by Prestwich et al., and there are no reports on the synthesis of 2 or 3.

Recently, we reported a novel approach to synthesizing glycerophospholipids (PLs) based on the Horner-Wadsworth-Emmons (HWE) reaction of easily handled mixed phosphonoacetate, which serves as a masked precursor of PLs. Herein we describe the facile synthesis of fluorine-containing analogues 1-3 using HWE reagent 6 as a key intermediate, which was derived from methyl bis(2,2,2-trifluoroethyl)phosphonoacetate (Still-Gennari reagent, 4) and fluorine-containing chiral alcohol 5 as shown in Figure 1.
In the synthesis of \(5, (S)-2,2\text{-dimethyl-1,3-dioxolan-4-methanol} \) ([S]-solketal, \(7\)\(^{8}\)) was chosen as the starting material (Scheme 1). The \(p\)-methoxybenzylolation of \(7\) with \(p\)-methoxybenzyl chloride (PMBCl) in the presence of sodium hydride in DMF provided \(8\) in 96% yield. Deprotection of the acetonide of \(8\) under acidic conditions afforded diol \(9\) in 99% yield. Selective protection of the primary hydroxy group of diol \(9\) with triphenylchloromethane (TrCl) in the presence of triethylamine and \(N,N\)-dimethylaminopyridine (DMAP) gave secondary alcohol \(10\) in 93% yield. Benzylation of \(10\) with benzyl bromide in the presence of sodium hydride in DMF resulted in the formation of \(11\) in 94% yield. Selective removal of the triphenylmethyl group of \(11\) was easily performed with \(p\)-toluenesulfonic acid in methanol to afford primary alcohol \(12\) in 96% yield. Deoxyfluorination of alcohol \(12\) by a combination of perfluoro-1-butanesulfonyl fluoride (PBSF), triethylamine, and triethylamine trihydrofluoride provided the corresponding fluoride \(13\) in 96% yield.\(^{9}\) The desired chiral alcohol \(5\) was obtained in 93% yield by oxidative cleavage of the PMB ether of \(13\) using 1,2-dichloro-4,5-dicyanobenzoquinone (DDQ) as an oxidant in a dichloromethane/water mixed solvent system.\(^{10}\)

![Scheme 1](image1.png)

**Scheme 1** Synthesis of chiral alcohol \(5\)

Nucleophilic substitution of the chiral alcohol \(5\) at the phosphorus center of Still-Gennari reagent (\(4\)) in the presence of 1.37 equivalent of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and molecular sieves (type 3A) furnished the key intermediate \(6\) as an inseparable diastereomeric mixture (ca. 1:1) in 87% yield as shown in Scheme 2.\(^{2,11}\)

1-F-LPA (\(1\)), the fluorine-containing analogue of 1-lysophosphatidic acid (1-LPA), was prepared using an HWE reaction of mixed phosphonoacetate \(17\) with benzaldehyde as the key reaction as shown in Scheme 3. The nucleophilic substitution of 2-(trimethylsilyl)ethanol (\(14\))\(^{12}\) at the phosphorus center of the key intermediate \(6\) in the presence of excess amounts of \(14\) and DBU gave phosphonoacetate \(15\) in 76% yield. After removal of the benzyl group of \(15\) by hydrogenolysis using a palladium on carbon (Pd-C) catalyst, palmitic acid was incorporated into the resultant secondary alcohol \(16\) with 2-methyl-6-nitrobenzoic anhydride (MNBA)\(^{13,14}\) and DMAP to afford \(17\) in 71% yield (two steps). The HWE reaction of \(17\) with benzaldehyde in the presence of lithium hexamethyldisilazide (LHMDS) provided the expected phosphodiester \(18\), then deprotection of the 2-(trimethylsilyl)ethyl group of the resultant \(18\) furnished 1-F-LPA (\(1\)) in 79% yield (two steps). In the synthetic strategy, HWE reagent \(17\) should be regarded as the masked precursor of sn-2 palmitoyl 1-F-LPA (\(1\)). Compounds \(15-17\) were all obtained as inseparable diastereomeric mixtures (ca. 1:1), similar to the key intermediate \(6\).
1-F-LPE (2), fluorine-containing analogues of 1-lysophosphatidylethanolamine (1-LPE), is shown in Scheme 4. The substitution of tert-butyl (2-hydroxyethyl)carbamate (N-BOC-ethanolamine, 19) instead of 14 at the phosphorus center of 6 afforded phosphonoacetate 20 in 67% yield. Hydrogenolysis of 20 using a Pd-C catalyst, followed by condensation of 21 with palmitic acid in the presence of MNBA and DMAP, gave 22 in 56% yield (two steps). The HWE reaction of 22 with benzaldehyde in the presence of LHMDS, followed by deprotection of the Boc group of the resultant phosphodiester 23 under acidic conditions using hydrogen chloride in 1,4-dioxane, afforded 1-F-LPE (2) as hydrochloride salt in 48% yield (two steps).

Furthermore, Scheme 5 shows the synthesis of 1-F-LPC (3), a fluorine-containing analogue of 1-lysophosphatidylcholine (1-LPC). 2-Bromoethanol (24) was used in the reaction with the key intermediate 6 to afford the corresponding phosphonoacetate 25 in 72% yield in a manner similar to that described for the reaction of 6 with 14 and 19. After hydrogenolysis of 25 using a Pd-C catalyst, condensation of the resultant 26 with palmitic acids using MNBA and DMAP provided 27 in 72% yield (two steps). The HWE reaction of 27 with benzaldehyde in the presence of LHMDS gave phosphodiester 28, then amination of the resultant 28 in the presence of excess amounts of trimethylamine in ethanol furnished 1-F-LPC (3) in 65% yield (two steps).15

In conclusion, we have described a novel and efficient method of synthesizing sn-2 palmitoyl 1-F-LPA (1), 1-F-LPE (2), and 1-F-LPC (3) as 1,2-acyl migration-blocked analogues of 1-LPLs. Considering the operational ease based on the use of HWE reagents as fluorine-containing masked analogues of 1-LPLs via the common key intermediate 6, we believe this synthetic strategy will be valuable for the chemistry and biochemistry of phospholipids classified as glycerophospholipids (PLs) and sphingophospholipids (SPLs).

**Scheme 4** Synthesis of 1-F-LPE (2)

**Scheme 5** Synthesis of 1-F-LPC (3)

The experimental section has no title; please leave this line here.

All melting points were determined on a Yanagimoto micro melting point apparatus and uncorrected. IR spectra were obtained using a JASCO FT/IR-6200 IR Fourier transform spectrometer. 1H NMR (500 MHz) and 13C NMR (125 MHz) spectra were recorded on a Bruker AV500 spectrometer. Chemical shifts are given in δ values (parts per million) using tetramethylsilane (TMS) as an internal standard. ESI-MS were recorded on a Waters LCT Premier spectrometer. Elemental combustion analyses were performed using a J-SCIENCE LAB J10. Optical rotations were recorded on a P-2200 JASCO digital polarimeter. All reactions were monitored by TLC employing 0.25-mm silica gel plates (Merck 5715; 60 F254). Column chromatography was carried out on silica gel [Silica Gel 60N (Kanto Chemical) or COSMOSIL 75 SL-H-PREP (Nacalai Tesque)]. Anhydrous THF, CH2Cl2, DMF, and toluene were used as purchased from Kanto Chemical. DBU and Et3N were distilled prior to use. All other reagents were used as purchased.

(5)-4-(((4-Methoxybenzyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolane (8)16

To a suspension of NaH (50–72% in mineral oil, 187 mg, 3.90–5.61 mmol) in anhydrous DMF (10 mL) was added 7 (0.5 mL, 4.05 mmol), and
the reaction mixture was stirred at 0 °C for 30 min under argon. After the addition of PMBCl (0.58 mL, 4.28 mmol), the mixture was allowed to warm to r.t. and then stirred for 2 h under argon. H2O (10 mL) was added to the reaction mixture, and then extracted with EtOAc-n-hexane (1:1) (50 mL x 3). The oily layer was dried (anhyd MgSO4), filtered, and concentrated in vacuo. The oily residue was purified by column chromatography [Silica Gel 60N: n-hexane–EtOAc (4:1)] to afford B (986 mg 96%) as a colorless oil; [α]D25 +17.8 (c 1.23, CHCl3).

IR (neat): 3060, 3031, 2931, 2868, 1612, 1513, 1449, 1248 cm⁻¹.

1H NMR (500 MHz, CDCl3): δ = 7.28–7.24 (m, 2H), 6.90–6.88 (m, 2H), 4.52 (d, J = 11.7 Hz, 1H), 4.48 (d, J = 11.7 Hz, 1H), 2.48 (quint, J = 6.2 Hz, 1H), 4.04 (dd, J = 8.3, 6.4 Hz, 1H), 3.80 (s, 3H), 3.72 (dd, J = 8.3, 6.3 Hz, 1H), 3.53 (dd, J = 9.8, 5.6 Hz, 1H), 3.42 (dd, J = 9.8, 5.7 Hz, 1H), 1.41 (s, 3H), 1.36 (s, 3H).

13C NMR (125 MHz, CDCl3): δ = 159.3, 130.1, 129.3, 113.8, 109.4, 74.8, 73.2, 70.8, 67.0, 53.3, 26.8, 25.4.


(5)-[[2-(Benzyloxy)-3-(4-methoxybenzyl)oxy]propoxy]methanetrimethyltrihexene (11)

To a solution of 10 (1.70 g, 3.74 mmol) and benzoyl chloride (533 μL, 4.48 mmol) in anhydrous DMF (8 mL) was added NaN (50–72% in mineral oil; washed with several portions of anhydrous n-pentane, 179 mg, 7.46 mmol) at 0 °C under argon. The mixture was stirred at r.t. for 18 h under argon. Then, H2O (10 mL) was added to the reaction mixture and extracted with EtOAc-n-hexane (1:1) (50 mL x 3). The oily layer was washed with H2O (30 mL x 2), dried (anhyd MgSO4), filtered, and concentrated in vacuo. The oily residue was purified by column chromatography [Silica Gel 60N: n-hexane–EtOAc (8:1 to 10:1)] to afford 11 (1.91 g, 94%) as a yellow oil; [α]D23 +3.22 (c 0.88, CHCl3).

IR (neat): 3060, 3031, 2931, 2868, 1612, 1513, 1449, 1248 cm⁻¹.

1H NMR (500 MHz, CDCl3): δ = 7.45–7.42 (m, 6H), 7.36–7.15 (m, 16H), 6.85–6.81 (m, 2H), 4.66 (d, J = 12.0 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.44 (d, J = 11.7 Hz, 1H), 4.42 (d, J = 11.7 Hz, 1H), 3.77 (s, 3H), 3.79–3.72 (m, 2H), 3.63 (dd, J = 10.2, 4.6 Hz, 1H), 3.59 (dd, J = 10.2, 5.8 Hz, 1H), 3.29–3.22 (m, 2H).

13C NMR (125 MHz, CDCl3): δ = 159.1, 144.1, 138.7, 130.5, 129.1, 128.7, 128.3, 127.7, 127.4, 112.9, 71.7, 70.9, 67.7, 72.9, 72.2, 72.8, 63.6, 55.2.

(5)-2-(Benzyloxy)-3-fluoropropan-1-ol (5)

To a solution of 13 (1.40 g, 4.60 mmol) in CH₂Cl₂ (47 mL)-H₂O (3 mL) was added DBBT (1.15 g, 5.07 mmol) at 0 °C. The reaction mixture was stirred at rt for 8 h. Then, aq sat. Na₂CO₃ (10 mL) was added to the reaction mixture and extracted with CHCl₃ (50 mL x 3). The organic layer was dried (anhyd MgSO₄), filtered, and concentrated in vacuo. The oily residue was purified by column chromatography [Silica Gel 60N: n-hexane-EtOAc (3:1)] to afford 5 (791 mg, 93%) as a colorless oil; [α]D⁻²⁴ +14.8 (c 1.01, CHCl₃).

IR (neat): 3416, 2935, 2885, 1455, 1348, 1209, 1119, 1060 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.38–7.27 (m, 5H), 4.72 (d, J = 11.7 Hz, 1H), 4.62 (d, J = 11.7 Hz, 1H), 4.53 (dd, J₁H₂ = 47.2 Hz, J₂H₂ = 9.9 Hz, J₃H₂ = 4.4 Hz, 1H), 4.51 (dd, J₁H₂ = 47.3 Hz, J₂H₂ = 9.9 Hz, J₃H₂ = 5.2 Hz, 1H), 3.78–3.70 (m, 2H), 3.67–3.60 (m, 1H), 2.12 (br s, 1H).

¹³C NMR (125 MHz, CDCl₃): δ = 137.9, 128.6, 128.0, 127.9, 82.8 (d, J = 170 Hz). 77.9 (d, J = 19.1 Hz), 72.5, 61.4 (d, J = 7.4 Hz).


Methyl 2-((S)-(2-Benzyloxy)-3-fluoroproxy)phenylacetate (6)

A solution of alcohol 5 (607 mg, 3.30 mmol) in anhydrous toluene (120 mL) was added to a solution of methyl benzyl(2,2,2-trifluoroethoxy)phenylacetate (4) (773 mL, 3.62 mmol), DBU (673 mL, 4.51 mmol), and molecular sieves 3A (1.28 g) in anhydrous toluene (44 mL) at rt under argon. After the reaction mixture was stirred at rt for 1.5 h, aq 1 M HCl (10 mL) was added to it and then extracted with CHCl₃ (50 mL x 3). The organic layer was dried (anhyd MgSO₄), filtered, and concentrated in vacuo. The oily residue was purified by column chromatography [Silica Gel 60N: n-hexane-EtOAc (3:2)] to afford 6 (diastereomeric mixture, 1.46 g, 87%) as a colorless oil.

¹H NMR (500 MHz, CDCl₃): δ = 7.38–7.28 (m, 9H), 4.70 (dd, J = 11.6, 1.5 Hz), 4.67 (dd, J = 11.6, 2.3 Hz, 1H), 4.53 (dd, J₁H₂ = 46.9 Hz, J₂H₂ = 9.9 Hz, J₃H₂ = 4.4 Hz, 1H), 4.51 (dd, J₁H₂ = 46.9 Hz, J₂H₂ = 9.9 Hz, J₃H₂ = 5.2 Hz, 1H), 4.43–4.31 (m, 3H), 4.25–4.15 (m, 1H), 3.89–3.81 (m, 1H), 3.74/3.73 (s x 2, 3H), 3.08 (br dd, 0.94H for one diastereomer), 70.3, 70.23, 70.2, 70.18, 70.13, 70.07, 70.0, 65.7, 65.6, 63.33, 63.28, 63.22, 52.6, 34.14, 34.11 (d, J = 136.1 Hz for one diastereomer), 34.07 (d, J = 154.5 Hz for one diastereomer), 319, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 24.8, 22.7, 19.83, 19.82, 19.79, 19.77, 14.1, -1.51.


(5)-1-Fluoro-3-((2-methoxy-2-oxoethyl)phenyl)(oxoxy)propan-2-yl Palmitate (17)

A mixture of 15 (43 mg, 0.102 mmol) and 10% Pd-C (21 mg, 0.197 mmol) in MeOH (1 mL) was stirred at rt for 30 min under H₂ atmosphere. The reaction mixture was filtered and concentrated in vacuo to afford 16. A solution of 16 in anhydrous CH₂Cl₂ (3 mL) was added to a solution palmitic acid (52 mg, 0.203 mmol), 2-methyl-6-nitrobenzoic anhydride (70 mg, 0.203 mmol), and DMAP (37 mg, 0.303 mmol) in anhydrous CH₂Cl₂ (10 mL) at rt under argon. The reaction mixture was stirred for 40 min. Aq 1 M HCl (2 mL) was added to the reaction mixture and then extracted with CHCl₃ (10 mL x 3). The organic layer was dried (anhyd MgSO₄), filtered, and concentrated in vacuo. The residue was purified by column chromatography [Silica Gel 60N: n-hexane-EtOAc (3:2)] to afford 17 (diastereomeric mixture, 41 mg, 71%, two steps) as a colorless oil.

¹H NMR (500 MHz, CDCl₃): δ = 5.26–5.16 (m, 1H), 4.64–4.60 (m, 1H), 4.55–4.51 (m, 1H), 4.38–4.46 (m, 4H), 3.74 (s, 3H), 3.00 (d, J = 21.6 Hz, 1H for one diastereomer), 2.98 (d, J₁H₂ = 21.5 Hz, 1H for one diastereomer), 2.37 (br td, 2H), 1.67–1.59 (m, 2H), 1.34–1.24 (m, 22H), 1.11 (t, J = 8.6 Hz, 2H), 0.88 (t, J = 7.1 Hz, 3H), 0.04/0.05 (s x 2, 9H).

¹³C NMR (125 MHz, CDCl₃): δ = 172.83, 172.82, 165.9 (d, J₁C₂ = 6.2 Hz), 80.8 (d, J₁C₂ = 178.2 Hz for one diastereomer), 80.7 (d, J₁C₂ = 173.4 Hz for one diastereomer), 70.3, 70.23, 70.18, 70.13, 70.07, 70.0, 65.7, 65.6, 63.33, 63.28, 63.22, 52.6, 34.14, 34.11 (d, J = 136.1 Hz for one diastereomer), 34.47 (d, J = 154.5 Hz for one diastereomer), 319, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 24.8, 22.7, 19.83, 19.82, 19.79, 19.77, 14.1, -1.51.

Methyl 2-[[2-(Benzylxoy)-3-fluoropropoxy]][2-[(tert-butylcarbonyl)amino][ethoxy]phosphoryl]acetate (25)

To a solution of 6 (50.8 mg, 0.124 mmol), 2-bromoethanol (24) (13 μL, 0.186 mmol), and molecular sieves 3A (50 mg) in anhydrous toluene (0.8 mL) was added DBU (28 μL, 0.186 mmol) at 0 °C under argon. After being stirred at 0 °C for 7 h, the reaction mixture was added with 1/15 M phosphate buffer (pH 7.4, 3 mL), filtered, and then extracted with CHCl₃ (10 mL x 3). The organic layer was filtered through column chromatography [Silica Gel 60N: n-hexane-EtOAc (1:1 to 1:2)] to afford 25 (diastereomeric mixture, 38.4 mg, 72%) as a colorless oil.


Methyl 2-[[2-(Benzyloxy)-3-fluoropropoxy][2-bromoethoxy]phosphoryl]acetate (26)

A mixture of 22 (6 g, 0.113 mmol) and 10% Pd/C (30 mg, 0.282 mmol) in MeOH (1 mL) was stirred at r.t. for 15 min under H₂ atmosphere. The reaction mixture was filtered and concentrated in vacuo to afford 26, which was used in the next reaction without further purification. To a solution of 26 (62.2 mg, 0.143 mmol) and 10% Pd/C (30 mg, 0.282 mmol) in MeOH (1 mL) was stirred at r.t. for 15 min under H₂ atmosphere. The reaction mixture was filtered and concentrated in vacuo to afford 26, which was used in the next reaction without further purification. To a solution of 26 (62.2 mg, 0.143 mmol) and 10% Pd/C (30 mg, 0.282 mmol) in MeOH (1 mL) was stirred at r.t. for 15 min under H₂ atmosphere. The reaction mixture was filtered and concentrated in vacuo to afford 26, which was used in the next reaction without further purification.


(2S)-1-[[2-(Aminoethoxy)[hydroxy]phosphoryl]oxy]-3-fluoropropan-2-yl Malonate (27)

A mixture of 22 (69.2 mg, 0.113 mmol) in anhydrous THF (1 mL) was added LHMDS (1.02 mL; n-hexane, 133 μL, 0.136 mmol) and the solution was stirred at 0 °C for 5 min under argon. After adding benzaldehyde (139 μL, 1.36 mmol), the mixture was allowed to warm to r.t. and stirred for 15 min under argon. 1/15 M phosphate buffer (pH 7.4, 3 mL) was added to the reaction mixture, and then concentrated in vacuo. The residue was purified by column chromatography [COSMOSIL 75 SI-H-PREP: CHCl₃-MeOH (100:1 to 2:1)] to afford 23, which was used in the next reaction without further purification.


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60N: n-hexane–EtOAc (1:1) twice to afford 27 (diastereomeric mixture, 59.6 mg. 72% two steps) as a colorless oil.

1H NMR (500 MHz, CDCl3): δ = 5.27–5.17 (m, 1H), 4.64–4.61 (m, 1H), 4.55–4.51 (m, 1H), 4.45–4.42 (m, 4H), 3.76 (s, 3H), 3.55/3.54 (t x 2, f = 62.6 Hz, 2H), 3.06 (d, f = 19.5 Hz, 1H for one diastereomer), 3.05 (d, f = 19.5 Hz, 1H for one diastereomer). 3.27 (t, f = 7.6 Hz, 2H), 1.68–1.59 (m, 2H), 1.35–1.20 (m, 2H). 0.88 (t, f = 7.1 Hz, 3H).

13C NMR (125 MHz, CDCl3): δ = 172.9, 165.7 (d, f = 5.4 Hz), 80.7 (d, f = 173.3 Hz for one diastereomer), 80.6 (d, f = 172.9 Hz for one diastereomer). 70.12, 70.08, 70.06, 70.02, 69.95, 69.91, 69.86, 66.0, 65.97, 65.95, 65.92, 63.7, 61.63, 65.38, 65.33, 65.3, 63.4, 52.8, 34.14, 34.12, 33.94 (d, f = 138.7 Hz for one diastereomer). 33.89 (d, f = 138.2 Hz for one diastereomer). 31.9, 29.7, 29.69, 29.66, 29.65, 29.62, 29.5, 29.4, 29.3, 29.1, 24.8, 22.7, 14.1.


(3)-3-Fluoro-2-(palmitoyloxy)propyl [2-(Trimethylammonio)ethyl] Phosphat [1-F-PC(3)]

To a solution of 27 (68.6 mg, 0.119 mmol) in anhydrous THF (1 mL) were added LHMDS (1.02 mol/L in n-hexane, 140 μL, 0.143 mmol) and benzaldehyde (14.6 μL, 0.143 mmol) at 0 °C under argon. The mixture was stirred for 15 min under argon. 1/15 M phosphate buffer (pH 7.4, 3 mL) was added to the reaction mixture, and then concentrated in vacuo. The residue was purified by column chromatography [CH2Cl2/MeOH (100:1 to 1:1) to afford 28 which was used in the next reaction without further purification. A mixture of 28 and trimethylphosphate (ca. 3 mol/L in EtOH, 2 mL, ca. 0.6 mmol) was stirred at r.t. for 5 d. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography [SiO2 Gel 60N: CHCl3/MeOH (3:1) to CHCl3/MeOH-H2O (5:5:1)] to afford 1-F-LPC (3) (38.7 mg, 65% yield) as a white solid; mp 65–67 °C; [α]217.919 ± 9.8 (c 0.19, CHCl3).

IR (KBr): 2918, 2850, 1737, 1468, 1247, 1093 cm

29.5, 29.4, 29.3, 29.1, 24.8, 22.7, 14.1.

References


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$^1$H and $^{13}$C NMR spectra
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