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Highly fluorinated C18 fatty acids: synthesis and interfacial properties

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Abstract

A fluorinated oleic acid **1**-**Z** containing a perfluorooctyl group and its analogues (*E*-isomer **1**-**E**, alkyne type **2** and saturated type **3**) were synthesized in good yields. In these syntheses, it was found that a key compound **5** could be converted to each of **1**-**Z**, **1**-**E** and **2**. Furthermore, equilibrium spreading pressures of their monolayers at the air–water interface were measured in order to demonstrate how the degree of unsaturation in the hydrophobic chain, the geometric isomerization, and the presence of F-atoms influence the monolayer stability. Irrespective of the structural alteration in the hydrophobic chains, the fluorinated fatty acids formed more stable monolayers with high spreading pressures as compared to their hydrocarbon counterparts.

Keywords: Fluorocarbon; Fluorinated fatty acid; Oleic acid; Elaidic acid; Stearic acid; Equilibrium spreading pressure; Monolayer

1. Introduction

Fluorinated compounds have attracted much attention from the viewpoint of their unique characteristics such as thermal and chemical stability, surface tension lowering ability, hydrophobicity and lipophobicity [1–3]. The synthesis and characterization of a variety of fluorinated fatty acids have been described by many authors [4–9]. So far, only Buchanan et al. have studied the synthesis of oleic acid containing perfluorohexyl group [7,9]. They reported synthesis and assignment by ^{19}F NMR spectrum of the compound [9].

In this paper, we report the synthesis of a highly fluorinated oleic acid **1**-**Z** in which a fluorocarbon moiety is bonded directly to a C–C double bond. We have also achieved synthesis of the analogues of **1**-**Z** (*E*-isomer **1**-**E**, alkyne type **2** and saturated type **3**) in good yields (Fig. 1). In these reactions, we obtained the key compound **5** that could be converted to each of **1**-**Z**, **1**-**E** and **2**. Furthermore, we measured equilibrium spreading pressures (π_es) of their monolayers at the air–water interface, in order to demonstrate how the degree of unsaturation in the hydrophobic chain, the geometric isomerization, and the presence of F-atoms influence the monolayer stability.

2. Results and discussion

We planned to develop new kinds of lipids containing a fluorocarbon group. As the first step, we have synthesized highly fluorinated C18 fatty acids.

(*Z*)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-9-octadecenoic acid **1**-**Z** as a derivative of oleic acid, and *E*-isomer **1**-**E** as a derivative of elaidic acid were synthesized by the following procedures.

9-Decyn-1-ol **4** was prepared using the Zipper reaction [10] from 3-decyn-1-ol in 91% yield. Perfluorooctyl iodide reacted with **4** in the presence of $Na_2S_2O_4$ as a free radical initiator [5,11] to give alkenyl iodide **5** in 70% yield as *E*/*Z* mixture (*E*:*Z* = 77:23). **5** was easily separated into *E*-isomer **5**-**E** and *Z*-isomer **5**-**Z** using a column chromatography. Each configuration was determined from ^{1}H and ^{19}F NMR spectra (Scheme 1).

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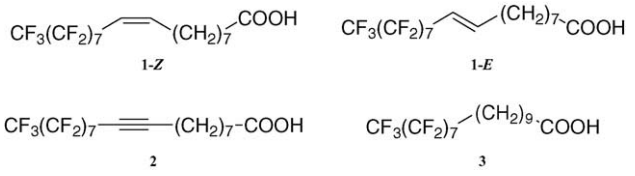
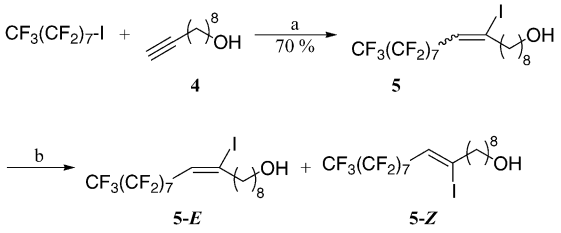
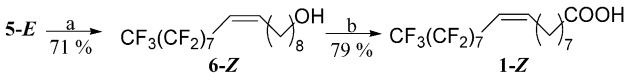


Fig. 1. Synthesized fluorinated C18 fatty acids.



Scheme 1. Synthesis and separation of **5**-**E** and **5**-**Z**. (a) $Na_2S_2O_4$, $NaHCO_3$/CH_3CN, H_2O, rt, 4 h; (b) silica gel column (EtOAc:hexane = 1:3, **5**-**E**:**5**-**Z** = 77:23).



Scheme 2. Synthesis of a fluorinated oleic acid **1**-**Z**. (a) *n*-BuLi/ether, −78 °C, 4 h; (b) Jones reagent/acetone.

5-**E** was treated with *n*-BuLi for 4 h at −78 °C to give *Z*-isomeric olefin **6**-**Z** in 71% yield [12]. **6**-**Z** was oxidized by the Jones reagent, and successively purified with a column chromatography and a recrystallization to give **1**-**Z** in 79% yield (Scheme 2). *E*-isomer **1**-**E** was prepared similarly in 54% yield for two steps from **5**-**Z**.

11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluoro-9-octadecynoic acid **2** was synthesized from *E*/*Z* mixture iodide **5** by the following procedures. We tried the synthesis in two routes for the alkynyl alcohol **7** (as the precursor of **2**). In one route, when **5** was treated with *t*-BuOK [4,11] directly, **7** was obtained in 51% yield (Scheme 3, route A). In another route, **5** was protected by a tetrahydropyranyl group at first, and was continuously treated with *t*-BuOK, and was finally deprotected to give **7** in 75% overall yield (Scheme 3, routes a–c). **7** was oxidized by the Jones reagent, and successively purified with a column chromatography to give **2** in 83% yield (Scheme 3).

Thus, we found that **5** was a key compound that could be converted to each of **1**-**Z**, **1**-**E** and **2**.

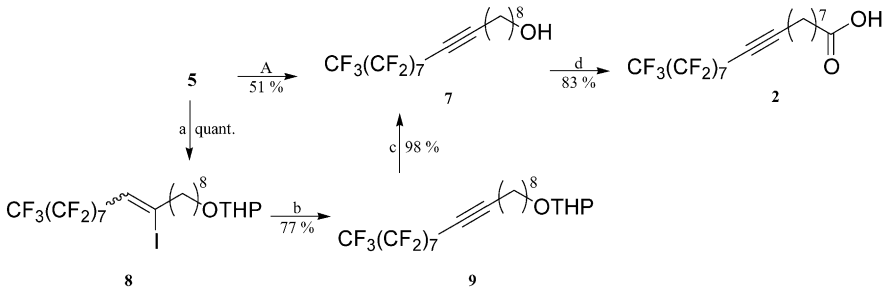
Finally, 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluorooctadecanoic acid **3** as a derivative of stearic acid was synthesized by following procedure. Perfluorooctyl iodide reacted with 9-decen-1-ol in the presence of $Na_2S_2O_4$ to give alkyl iodide **10**. **10** was deiodinated with Zn to give **11** in the presence of catalytic amount of $NiCl_2{\cdot}6H_2O$. **11** was oxidized by the Jones reagent, and successively purified to give **3** (Scheme 4).

The equilibrium spreading pressures (π_es) of each fatty acid are listed in Table 1. At the experimental temperature (25 °C), **1**-**Z** rapidly spread on the water surface and exhibited the highest π_e value among the fatty acids examined. On the other hand, **3** gradually (over 30 min) spread to the π_e of 30 mN/m. The obtained π_es for hydrocarbon counterparts, oleic acid (31.4 mN/m) and elaidic acid (13.6 mN/m) were in agreement with the literature data [13]. The π_es for the hydrocarbon counterparts, 9-octadecynoic acid and stearic acid have been reported as 9.7 and <0.1 mN/m at 25 °C, respectively [13]. As the π_e is suggested as a criterion for monolayer stability [14,15], it is obvious that fluorinated fatty acids form more stable monolayers with higher spreading pressures at the air–water interface as compared to their hydrocarbon counterparts. The interfacial properties of fatty acids vary considerably depending on the position and degree of unsaturation in the hydrophobic chain, geometric isomerization, and the presence of heteroatoms [13,16]. In

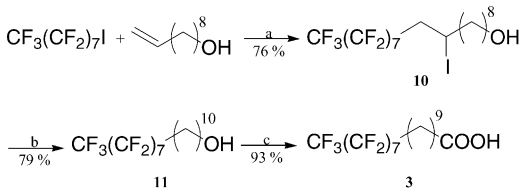
Table 1
Equilibrium spreading pressures (π_es) of fluorinated fatty acids and their hydrocarbon counterparts[a]

Fluorinated fatty acid	π_e (mN/m)	Fatty acid	π_e (mN/m)
1-**Z**	45.4	Oleic acid	31.4
1-**E**	33.2	Elaidic acid	13.6
2	43.7	9-Octadecynoic acid[b]	9.7
3	29.8	Stearic acid[b]	<0.1

[a] On pure water (pH ~6); 25 °C.
[b] Ref. [13].



Scheme 3. Synthesis of a fluorinated alkynoic acid **2**. (a) DHP, PPTS/CH_2Cl_2, rt, overnight; (b) *t*-BuOK/ether, −20 °C, 1 h, then 0 °C, 2 h; (c) PPTS/EtOH, 55 °C, 1 h; (d) Jones reagent/acetone; (A) *t*-BuOK/ether, −20 °C, 1 h, then 0 °C, 2 h.



Scheme 4. Synthesis of a fluorinated stearic acid **3**. (a) $Na_2S_2O_4$, $NaHCO_3$/CH_3CN, H_2O, rt, 4 h; (b) Zn, $NiCl_2$/THF, H_2O, rt, overnight; (c) Jones reagent/acetone.

particular, partially fluorinated fatty acids are known to be extremely surface-active and extremely hydrophobic [17], therefore, they are expected to form stable insoluble monolayers at the air–water interface.

The π_e strongly depends on several conditions, e.g., the temperature of the subphase and the state of the bulk lipid phase. In cases of simple fatty acids, the maximal spreading pressures are observed at their bulk melting points, and the temperature coefficient of the spreading pressure can be well correlated with the heat of fusion of fatty acid crystals [16]. Among the fluorinated fatty acids used in this study and their hydrocarbon counterparts, **1**-**Z**, **2**, and oleic acid (mp 13.3 °C, [18]) are in a liquid form at 25 °C and the others, **1**-**E** (mp 57–58 °C), **3** (mp 72–79 °C), elaidic acid (mp 44.5 °C [18]), 9-octadecynoic acid (mp 47–48 °C [19]), stearic acid (mp 69.7 °C [18]) are in a solid form. Therefore, it is reasonable that the high spreading pressures could be observed for a liquid **1**-**Z** and a liquid **2**. As a rule, melting point is a measure of the cohesive force in the fatty acid crystals. Judging from the melting points of *E*-monoene acids (elaidic acid and **1**-**E**) and saturated acids (stearic acid and **3**) except monoyne acids (9-octadecynoic acid and **2**), the replacement of the C_8H_{17} tail in the C_{18} fatty acids by the C_8F_{17} one appears to enhance the crystallinity of the fatty acids in solid form. The spreading pressures of the fatty acids below their melting points are strongly temperature-dependent and considerably low as compared to liquid fatty acids [16]. However, the π_es of the solid fluorinated fatty acids are much higher than those of their hydrocarbon counterparts as described above. This suggests the intermolecular interactions of the fluorinated fatty acids in the crystals might be weaker and/or the fatty acid–water interactions might be stronger than those of the hydrocarbon counterparts. Based on the observations that the low polarizability of the F-atom results in the low intermolecular van der Waals forces and the low cohesive energy densities in liquid fluorocarbons [17], it is likely that the interactions between hydrophobic chains of fluorinated fatty acids in crystals are much weaker than hydrocarbon counterparts leading to higher spreading pressures, although a definite conclusion awaits further studies on the temperature-dependent spreading pressure measurements of fluorinated fatty acid monolayers. It should be noted here that **3** used in this study exhibited a broad melting point (72–79 °C), suggesting the existence of impurities in the main product, and these impurities might contribute to a certain extent to the spreading pressure of **3**. Even if there might be some influences of the impurities on the interfacial behavior of **3**, it is reasonable to assume that the spreading pressure of **3** itself is higher than that of stearic acid.

In summary, we successfully synthesized highly fluorinated fatty acids **1**-**Z**, **1**-**E**, **2** and **3** in good yields. Their equilibrium spreading pressures (π_es) **3** were much higher than those of their hydrocarbon counterparts, indicating that the highly fluorinated fatty acids formed more stable monolayers with high spreading pressures.

3. Experimental

3.1. Instruments

^{1}H NMR spectra were measured with a JEOL JNM-LA 500 FT NMR system (500 MHz) using TMS as an internal standard. ^{19}F NMR spectra were measured with a JEOL JNM-LA 500 FT NMR system (500 MHz) or a JEOL JNM-LA 300 (300 MHz) using benzotrifluoride (BTF) as an internal standard. FT-IR spectra were measured with a JASCO FT/IR-680 plus. Mass spectra (ESI-MS) were measured with a JEOL JMS-700T Tandem MStation. Column chromatography purifications were carried out using silica gel 60 (Merck 7734).

3.2. Materials

Fluorinated fatty acids **1**-**E**, **1**-**Z**, **2** and **3** were synthesized by the following procedures. Perfluorooctyl iodide was purchased from DAIKIN Finechemical Laboratory and its purity was over 95% (GC). 3-Decyn-1-ol and 9-decen-1-ol were purchased from Tokyo Kasei Kogyo Co. and their purities were over 96% (GC) and 95% (GC), respectively. Oleic acid and elaidic acid were purchased from Sigma Co. and their purities were approximately 99%. The water used was prepurified with a homemade purification system (RO membrane, ion-exchange column, and 0.22 μm filter) and was further purified with a Milli-Q Labo system (Millipore Corp., Bedford, MA) and distillation in an all-glass still. Its resistivity was higher than 18 MΩ cm.

3.2.1. 9-Decyn-1-ol (*4*)

To sodium hydride (60% in oil) (19.90 g, 0.50 mol) at an ice bath was added 1,3-diaminopropane (175 mL). The suspension was heated gradually to 80 °C over a period of 2 h with stirring, was cooled to 10 °C, and 3-decyn-1-ol (25.0 mL, 0.14 mol) was added gradually over a period of 5 min, successively. The mixture was heated gradually to 100 °C over 40 min, and stirred for 80 min at 100 °C. The mixture was cooled in an ice bath, and cautiously poured into crushed ice, and then extracted with *n*-hexane. The organic layers were washed with H_2O, satd $NaHCO_3$ aq, and satd NaCl aq, successively, and then dried over $MgSO_4$.

After filtration and evaporation of the solvent, the residue was distilled to give 9-decyn-1-ol (**4**) (20.02 g, 91.4%) [91.5–92.0 °C/4 mmHg].

^{1}H NMR ($CDCl_3$) δ: 1.20–1.43 (8H, m, H3–H6), 1.43–1.63 (4H, m, H2, H7), 1.94 (2H, t, J = 2.75 Hz, H10), 2.18 (2H, dt, J = 7.16, 2.81 Hz, H8), 3.64 (2H, t, J = 6.70 Hz, H1).

*3.2.2. (E)- and (Z)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-9-iodo-octadec-9-en-1-ol (**5**-**E**, **5**-**Z**)*

To a solution of **4** (2.00 g, 0.13 mol) in CH_3CN (18 mL) and deionized H_2O (9 mL) was added perfluorooctyl iodide (8.50 g, 0.16 mol), $NaHCO_3$ (545 mg, 6.48 mmol) and 80% $Na_2S_2O_4$ (1.41 g, 6.48 mmol) at 0 °C, and then the mixture was stirred for 4 h at room temperature. The mixture was diluted with deionized H_2O, and then extracted with Et_2O. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 25%) to give (*E*)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-9-iodooctadec-9-en-1-ol (**5**-**E**) (4.88 g, 53.6%) and *Z*-isomer **5**-**Z** (1.47 g, 16.1%). *E*:*Z* = 77:23.

5-**E**: ^{1}H NMR ($CDCl_3$) δ: 1.27–1.45 (8H, m, H3–H6), 1.50–1.65 (4H, m, H2, H7), 2.63 (2H, dd, J = 7.46 Hz, H8), 3.65 (2H, t, J = 6.71 Hz, H1), 6.32 (1H, t, J = 14.47 Hz, H10). ^{19}F NMR ($CDCl_3$) ppm: −18.02 (3F, t, J = 10.80 Hz, F18), −42.62 (1F, q, J = 15.18 Hz, F11), −58.70 (2F, bs, F12), −59.16, −59.97, −60.50 (2F, 4F, 2F, bs, bs, bs, F13–F16), −63.37 (2F, bs, F17).

5-**Z**: ^{1}H NMR ($CDCl_3$) δ: 1.15–1.29 (8H, m, H3–H6), 1.52–1.65 (4H, m, H2, H7), 2.66 (2H, dd, J = 7.46 Hz, H8), 3.65 (2H, t, J = 6.69 Hz, H1), 6.24 (1H, t, J = 13.10 Hz, H10). ^{19}F NMR ($CDCl_3$) ppm: −18.05 (3F, t, J = 10.80 Hz, F18), −45.70 (1F, q, J = 10.80 Hz, F11), −58.67 (2F, bs, F12), −58.58 to −59.53, −59.60 to −60.01, −60.20 (2F, 4F, 2F, m, m, bs, F13–F16), −63.40 (2F, bs, F17).

*3.2.3. (Z)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadec-9-en-1-ol (**6**-**Z**)*

1.6 M *n*-BuLi/hexane (0.88 mL, 1.37 mmol) was dropped to a solution of **5**-**E** (200 mg, 0.29 mmol) in dry THF (3 mL) at −78 °C. The mixture was stirred for 4 h, and then quenched with pre-cooled (−78 °C) methanol (0.88 mL). After being warmed to 0 °C, the mixture was poured into satd NH_4Cl aq (6 mL), and was extracted with EtOAc. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 15%) to give (*Z*)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluorooctadec-9-en-1-ol (**6**-**Z**) (116.6 mg, 71.0%).

^{1}H NMR ($CDCl_3$) δ: 1.20–1.39 (8H, m, H3–H6), 1.39–1.50 (2H, m, H2), 1.52–1.63 (2H, m, H7), 2.25–2.37 (2H, m, H8), 3.64 (2H, t, J = 6.54 Hz, H1), 5.48 (1H, dd, J = 15.37, 12.78 Hz, H10), 6.11 (1H, dtt, J = 11.88, 7.77, 2.21 Hz, H9). ^{19}F NMR ($CDCl_3$) ppm: −18.00 (3F, t, J = 10.04 Hz, F18), −43.85 (2F, q, J = 13.17 Hz, F11), −58.72 (2F, bs, F12), −58.94 to −59.54, −59.98, −60.56 to −61.14 (2F, 4F, 2F, m, bs, m, F13–F16), −63.14 to −63.62 (2F, m, F17).

*3.2.4. (E)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadec-9-en-1-ol (**6**-**E**)*

6-**E** was prepared from **5**-**Z**, similarly (68.9%).

^{1}H NMR ($CDCl_3$) δ: 1.28–1.44 (8H, m, H3–H6), 1.44–1.52 (2H, m, H2), 1.57 (2H, dq, J = 7.12 Hz, H7), 2.15–2.25 (2H, m, H8), 3.64 (2H, t, J = 5.84 Hz, H1), 5.59 (1H, dd, J = 15.22, 12.78 Hz, H10), 6.38 (1H, dtt, J = 15.73, 6.81, 2.15 Hz, H9). ^{19}F NMR ($CDCl_3$) ppm: −18.02 (3F, t, J = 9.07 Hz, F18), −48.48 (2F, q, J = 12.08 Hz, F11), −58.74 (2F, bs, F12), −59.23, −59.99, −60.81 (2F, 4F, 2F, bs, bs, bs, F13–F16), −63.39 (2F, bs, F17).

*3.2.5. (Z)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadec-9-enoic acid (**1**-**Z**)*

To **6**-**Z** (129 mg, 0.23 mmol) in acetone (2.5 mL) was added the Jones reagent at room temperature till the color of the chromium ion remained visible for 10 min. The mixture was quenched with 2-propanol. After filtration and evaporation of solvents, the residue was extracted with EtOAc. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was recrystallized in *n*-hexane at −20 °C to give (*Z*)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluorooctadec-9-enoic acid (**1**-**Z**) (105.0 mg, 79.3%).

^{1}H NMR ($CDCl_3$) δ: 1.25–1.38 (6H, m, H4–H6), 1.38–1.48 (2H, m, H3), 1.57–1.70 (2H, m, H7), 2.27–2.40 (2H, m, H8), 2.35 (2H, t, J = 7.46 Hz, H2), 5.48 (1H, dd, J = 12.48, 15.53 Hz, H10), 6.11 (1H, dtt, J = 11.95, 7.65, 2.23 Hz, H9). ^{19}F NMR ($CDCl_3$) ppm: −18.02 (3F, t, J = 10.33 Hz, F18), −43.88 (2F, q, J = 13.17 Hz, F11), −58.70 (2F, bs, F12), −59.19, −60.00, −60.98 (2F, 4F, 2F, bs, bs, bs, F13–F16), −63.38 (2F, bs, F17). IR (cm^{-1}): 1712.48 (C=C). ESI-MS (*m*/*z*): calcd. for $C_{18}H_{17}F_{17}O_2$ $[M]^+$ 588.0957, found 588.0965.

*3.2.6. (E)-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadec-9-enoic acid (**1**-**E**)*

1-**E** was prepared from **6**-**E**, similarly (80.0%).

mp 57.0–57.9 °C. ^{1}H NMR ($CDCl_3$) δ: 1.25–1.39 (6H, m, H4–H6), 1.40–1.51 (2H, m, H3), 1.57–1.74 (2H, m, H7), 2.14–2.25 (2H, m, H8), 2.35 (2H, t, J = 7.46 Hz, H2), 5.59 (1H, dd, J = 15.57, 11.93 Hz, H10), 6.40 (1H, dtt, J = 16.05, 7.03, 2.29 Hz, H9). ^{19}F NMR ($CDCl_3$) ppm: −17.95 (3F, t, J = 10.80 Hz, F18), −48.40 (2F, q, J = 10.80 Hz, F11), −58.63 (2F, bs, F12), −59.15, −59.94, −60.73 (2F, 4F, 2F, bs, bs, bs, F13–F16), −62.99 to −63.97 (2F, m, F17). IR (cm^{-1}): 1699.94 (C=C). ESI-MS (*m*/*z*): calcd. for $C_{18}H_{17}F_{17}O_2$ $[M]^+$ 588.0957, found 588.0959.

3.2.7. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadec-9-yn-1-ol (7) [Scheme 3, route A]

A solution of **5** (2.00 g, 2.86 mmol) in anhydrous Et_2O (30 mL) was added to a solution of *t*-BuOK (801 mg, 7.14 mmol) in anhydrous Et_2O (20 mL), and this mixture was stirred for 1 h at −20 °C, and then was stirred at 0 °C, continuously. The mixture was quenched with 2 M HCl (30 mL), and then was extracted with Et_2O. The organic layers were washed with satd NaCl aq, and dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 20%) to give 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluorooctadec-9-yn-1-ol (**7**) (794 mg, 51.3%).

^{1}H NMR ($CDCl_3$) δ: 1.28–1.47 (8H, m, H3–H6), 1.50–1.64 (4H, m, H2, H7), 2.35 (2H, dd, J = 6.10, 12.50 Hz, H8), 3.65 (2H, t, J = 6.10 Hz, H1). ^{19}F NMR ($CDCl_3$) ppm: −18.00 (3F, t, J = 9.71 Hz, F18), −33.21 to −33.72 (2F, m, F11), −58.15 to −58.49 (2F, m, F12), −58.85 to −59.48, −59.68 to −60.24 (4F, 4F, m, F13–F16), −63.15 to −63.55 (2F, m, F17).

3.2.8. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluoro-9-iodo-1-tetrahydropyranyloxyoctadec-9-ene (8) [Scheme 3, route a]

To a solution of **5** (*E*/*Z* mixture: 2.20 g, 3.14 mmol) in CH_2Cl_2 (16 mL) was added 3,4-dihydro-2*H*-pyrane (0.43 mL, 4.71 mmol) and pyridinium *p*-toluenesulfonate (16 mg), and this mixture was stirred overnight at room temperature. The mixture was diluted with CH_2Cl_2. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 5%) to give 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-9-iodo-1-tetrahydropyranyloxyoctadec-9-ene (**8**) (2.44 g, 99.1%).

^{1}H NMR ($CDCl_3$) δ: 1.20–1.67 (16H, m, H2–H7, THP), 1.67–1.77 (1H, m, THP), 1.77–1.90 (1H, m, THP), 2.62 (2H, t, J = 7.33 Hz, H8), 3.39 (1H, dt, J = 6.70, 9.45 Hz, H1), 3.44–3.58 (1H, m, THP), 3.74 (1H, dt, J = 7.03, 9.32 Hz, H1), 3.87 (1H, dt, J = 3.35, 7.95 Hz, THP), 4.58 (1H, dd, J = 4.26, 2.74 Hz, THP), 6.32 (1H, t, J = 14.48 Hz, H10). ^{19}F NMR ($CDCl_3$) ppm: −18.00 (3F, t, J = 9.71 Hz, F18), −42.57 (2F, q, J = 13.60 Hz, F11), −58.29 to −58.89 (2F, m, F12), −58.89 to −59.44, −59.59 to −60.24, −60.24 to −60.64 (4F, 2F, 2F, m, m, m, F13–F16), −63.09 to −63.59 (2F, m, F17).

3.2.9. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluoro-1-tetrahydropyranyloxyoctadec-9-yne (9) [Scheme 3, route b]

A solution of **8** (1.39 g, 1.77 mmol) in anhydrous Et_2O (16 mL) was added to a solution of *t*-BuOK (497 mg, 4.43 mmol) in anhydrous Et_2O (10 mL) at −20 °C, and this mixture was stirred for 1 h at −20 °C, and then was stirred for 2 h at 0 °C, continuously. The mixture was quenched with 2 M HCl (16 mL), and then was extracted with Et_2O. The organic layers were washed with satd NaCl aq, and dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 2%) to give 11,11,12,12,-13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-1-tetrahydropyranyloxyoctadec-9-yne (**9**) (891 mg, 76.7%).

^{1}H NMR ($CDCl_3$) δ: 1.22–1.65 (16H, m, H2–H7, THP), 1.66–1.77 (1H, m, THP), 1.78–1.90 (1H, m, THP), 2.35 (2H, q, J = 6.40 Hz, H8), 3.38 (1H, dt, J = 6.50, 9.72 Hz, H1), 3.43–3.56 (1H, m, THP), 3.73 (1H, dt, J = 6.86, 9.57 Hz, H1), 3.82–3.92 (1H, m, THP), 4.57 (1H, dd, J = 4.45, 2.60 Hz, THP). ^{19}F NMR ($CDCl_3$) ppm: −18.00 (3F, t, J = 9.71 Hz, F18), −33.22 to −33.62 (2F, m, F11), −58.10 to −58.51 (2F, m, F12), −58.87 to −59.47, −59.62 to −60.22 (4F, 4F, m, m, F13–F16), −63.15 to −63.56 (2F, m, F17).

3.2.10. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadec-9-yn-1-ol (7) [Scheme 3, route c]

To a solution of **9** (500 mg, 0.76 mmol) in ethanol (5 mL) was added pyridinium *p*-toluenesulfonate (95.7 mg, 0.38 mmol), and this mixture was stirred for 1 h at 55 °C. The mixture was diluted with EtOAc. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 15–20%) to give **7** (428 mg, 98.1%).

3.2.11. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadec-9-ynoic acid (2)

To a solution of **7** (580 mg, 1.01 mmol) in acetone (6 mL) was added the Jones reagent at room temperature till the color of the chromium ion remained visible for 10 min. The mixture was quenched with 2-propanol. After filtration and evaporation of the solvent, the residue was extracted with EtOAc. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 20–30%), and then was recrystallized in *n*-hexane at −20 °C to give 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluorooctadec-9-ynoic acid (**2**) (492 mg, 83.0%).

mp 73.4–78.6 °C. ^{1}H NMR ($CDCl_3$) δ: 1.52–1.62 (6H, m, H4–H6), 1.52–1.62 (2H, m, H7), 1.62–1.69 (2H, m, H3), 2.29–2.44 (2H, m, H8), 2.35 (2H, t, J = 7.46 Hz, H2). ^{19}F NMR ($CDCl_3$) ppm: −18.00 (3F, t, J = 9.71 Hz, F18), −33.16 to −33.56 (2F, m, F11), −58.06 to −58.56 (2F, m, F12), −58.90 to −59.59, −59.59 to −60.36 (4F, 4F, m, m, F13–F16), −63.06 to −63.58 (2F, m, F17). IR (cm^{-1}): 1713.44 (C≡C). ESI-MS (*m*/*z*): calcd. for $C_{18}H_{15}F_{17}O_2$ $[M]^+$ 588.0801, found 588.0797.

*3.2.12. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluoro-9-iodooctadecan-1-ol (**10**)*

To a solution of 9-decen-1-ol (787 mg, 5.04 mmol) in CH_3CN (5 mL) and deionized H_2O (5 mL) was added perfluorooctyl iodide (3.28 g, 6.00 mmol), $NaHCO_3$ (431 mg, 5.04 mmol) and 85% $Na_2S_2O_4$ (1.03 g, 5.04 mmol) at 0 °C, and then this mixture was stirred for 4 h at room temperature. The mixture was diluted with deionized H_2O, and then extracted with CH_2Cl_2. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 30%) to give 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-9-iodooctadecan-1-ol (**10**) (2.76 g, 76.2%).

^{1}H NMR ($CDCl_3$) δ: 1.16–1.48 (10H, m, H3–H7), 1.48–1.68 (2H, m, H2), 1.70–1.90 (2H, m, H8), 2.68–2.83, 2.83–3.00 (1H, 1H, m, m, H10), 3.65 (2H, t, J = 6.71 Hz, H1), 4.33 (1H, tt, J = 4.41, 8.88, 17.60 Hz, H9). ^{19}F NMR ($CDCl_3$) ppm: −18.03 (3F, t, J = 9.71 Hz, F18), −48.25 to −48.78, −49.20 to −49.74, −51.00 to −51.19, −52.20 to −52.70 (2F, m, m, m, m, F11), −58.55 to −59.00 (2F, m, F12), −59.00 to −59.50, −59.75 to −60.28, −60.60 to −61.20 (4F, 2F, 2F, m, m, m, F13–F16), −63.20 to −63.64 (2F, m, F17).

*3.2.13. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadecan-1-ol (**11**)*

10 (2.76 g, 3.84 mmol) was added to a mixture of Zn powder (507 mg, 7.75 mmol) and $NiCl_2{\cdot}6H_2O$ (97.5 mg, 0.77 mmol) in dry THF (5.8 mL) and deionized H_2O (10 drops). This mixture was stirred for 4 h at room temperature. The mixture was quenched with satd $NaHCO_3$ aq, and was extracted with CH_2Cl_2. The organic layers were washed with satd NaCl aq, and then was dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by a column chromatography (EtOAc/*n*-hexane, 30%) to give 11,11,12,12,13,13,-14,14,15,15,16,16,17,17,18,18,18-heptadecafluorooctadecan-1-ol (**11**) (1.54 g, 78.8%).

^{1}H NMR ($CDCl_3$) δ: 1.26–1.45 (10H, m, H3–H8), 1.52–1.65 (4H, m, H2, H9), 2.05 (2H, tt, J = 8.24, 18.87 Hz, H10), 3.65 (2H, tt, J = 4.03, 6.46 Hz, H1). ^{19}F NMR ($CDCl_3$) ppm: −18.00 (3F, t, J = 10.04 Hz, F18), −51.71 (2F, m, J = 16.03 Hz, F11), −58.72 to −59.57, −59.79 to −60.17, −60.65 to −61.10, (6F, 2F, 2F, m, m, m, F12–F16), −63.20 to −63.36 (2F, m, F17).

*3.2.14. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptadecafluorooctadecanoic acid (**3**)*

To a solution of **11** (206 mg, 0.36 mmol) in acetone (4 mL) was added the Jones reagent at room temperature till the color of the chromium ion remained visible for 10 min. The mixture was quenched with 2-propanol. After filtration and evaporation of the solvent, the residue was extracted with EtOAc. The organic layers were washed with satd NaCl aq, and then dried over $MgSO_4$. After filtration and evaporation of the solvent, the residue was recrystallized in *n*-hexane at −20 °C to give 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluorooctadecanoic acid (**3**) (197 mg, 93.3%).

^{1}H NMR ($CDCl_3$) δ: 1.24–1.42 (10H, m, H4–H8), 1.53–1.70 (4H, m, H3, H9), 1.98–2.12 (2H, m, H10), 2.35 (2H, t, J = 7.46 Hz, H2). ^{19}F NMR ($CDCl_3$) ppm: −18.00 (3F, t, J = 12.91 Hz, F18), −51.65 (2F, m, J = 17.38 Hz, F11), −58.99 (2F, bs, F12), −59.10 to −59.70, −60.03 to −61.35 (4F, 2F, 2F, m, m, m, F13–F16), −62.75 to −63.80 (2F, m, F17). ESI-MS: (*m*/*z*) calcd. for $C_{18}H_{19}F_{17}O_2$ $[M]^+$ 590.1113, found 590.1114.

3.2.15. Equilibrium spreading pressure measurements

A fatty acid sample was sprinkled onto the clean surface of pure water (pH ∼6) in a thermostated Teflon vessel as one or more visible droplets or powders remained on the surface. The surface pressure was monitored by Wilhelmy technique using a sandblasted platinum plate attached to a KSV electronic balance (pressure sensitivity: 0.01 mN/m; KSV Instruments, Helsinki, Finland) at 25.0 ± 0.2 °C. This set-up was housed in a clean box to reduce any contaminations. The equilibrium spreading pressures, π_es were reproduced within ±0.5 mN/m.

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