Studies on Organic Fluorine Compounds. LIV.[1] Synthesis of 2,2-Difluoroarachidonic Acid

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2,2-Difluoroarachidonic acid, characterized by the inductively enhanced acidity of the carboxyl group and its biological stability to β-oxidation, was synthesized using a fluorine-containing building block derived from ethyl bromodifluoroacetate and a carbon-chain extension reaction.

Keywords 2,2-difluoroarachidonic acid; fluorine substituent; fluorine-containing building block; Reformatsky reaction; ethyl bromodifluoroacetate

The substituent effect caused by fluorine atom(s) with minimal steric disturbance contributes to the importance of fluorinated molecules in biochemistry.[2] Owing to the high electronegativity of the fluorine atom, the fluorine substituent can influence the degree of chemical reactivity of a neighboring functional group. The C–F bond is strong compared to the C–H bond, enabling it to be generally biologically stable in a fluorinated molecule. These characteristic features of the fluorine substituent have prompted the synthesis of many fluorinated bioactive compounds.[3] Of current interest in this field is the synthesis and biotransformation of fluorinated arachidonic acid, carried out by Fried *et al.*[4] and our group.[5] As an extension of our synthetic study on this series, the synthesis of 2,2-difluoroarachidonic acid (2,2-F_2AA, **1a**) was conducted. 2,2-F_2AA is characterized by the inductively enhanced acidity of the carboxyl group and its biological stability to β-oxidation.[6] The present paper describes a method of the synthesis of 2,2-F_2AA (**1a**) *via* Reformatsky reaction of ethyl bromodifluoroacetate ($BrCF_2COOEt$) and a carbon-chain extension reaction.

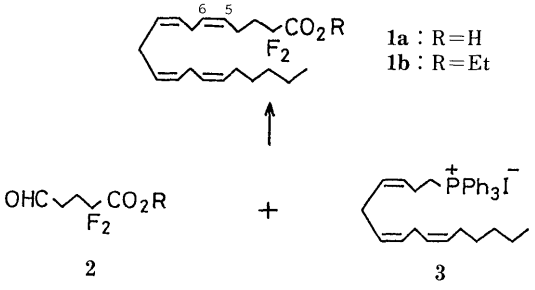
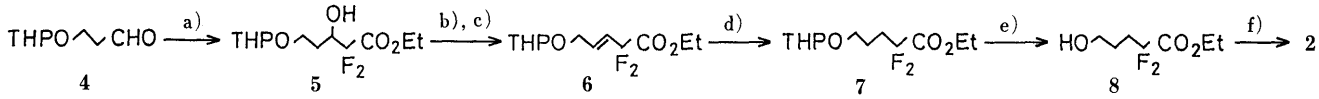


Chart 1

According to Chart 1, our approach to the construction of the 2,2-F_2AA skeleton requires the production of the α,α-difluorocarboxylic acid derivative (**2**, C_1—C_5 segment) as a fluorine-containing building block and the phosphonium salt (**3**, C_6—C_{20} segment) by convenient methods.

The synthetic route leading to **2** is shown in Chart 2. Monotetrahydropyranylation of propane-1,3-diol followed by oxidation with pyridinium chlorochromate (PCC) by the usual method gave the aldehyde (**4**), which was used for preparing both the C_3—C_5 and C_6—C_8 segments of 2,2-F_2AA. Introduction of a carboxydifluoromethyl moiety into **4** was achieved by Reformatsky reaction of $BrCF_2COOEt$.[7] Thus, the zinc-promoted reaction of $BrCF_2COOEt$ with **4** in tetrahydrofuran (THF) gave the adduct (**5**) in 57% yield. Dehydroxylation of **5** to obtain **7** was carried out by a three-step sequence: 1) activation of the hydroxyl group as its triflate by the reaction with triflic anhydride (64% yield); 2) β-elimination with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (89% yield); 3) catalytic hydrogenation with hydrogen and Pd–C catalyst (80% yield). β-Elimination of the hydroxyl group of **5** through the corresponding methanesulfonate was not effective due to the neighboring fluorine substitution. Catalytic hydrogenation of the allyl alcohol derivative of **6** afforded a low yield of **8** accompanied with the formation of a complex mixture. In the catalytic hydrogenation of **6**, the monofluoro ester, derived *via* partial hydrogenolysis of one C–F bond, was also isolated in 14% yield. Deprotection of the tetrahydropyranyl (THP) group of **7** followed by oxidation to the aldehyde with PCC gave the desired fluorine-containing building block, ethyl 2,2-difluoro-5-oxopentanoate (**2**, R=Et), in 62% yield.

The requisite phosphonium salt (**3**) for the chain extension of **2** was prepared as shown in Chart 3. Wittig reaction of **4** with the ylide derived from the phosphonium salt[8] (**9**, *n*-BuLi, −78 °C, 1 h) afforded the *cis*-olefin (**10**) in 69% yield as a single stereoisomer. The silyl ether of **10** was deprotected with tetrabutylammonium fluoride to give an alcohol that was subsequently converted to the phosphonium salt (**12**) by the following sequence: 1) reaction with methanesulfonyl chloride and triethylamine; 2) reaction with sodium iodide; 3) reaction with triphenylphosphine. (3*Z*)-3-Nonen-1-al (**13**), the component corresponding to the C_{12}—C_{20} segment of 2,2-F_2AA, was obtained from (4*Z*)-1,2-dihydroxy-4-decene-1,2-acetonide by a known route [1) HCl–MeOH, 2) $Pb(OAc)_4$–CH_2Cl_2].[9] The ylide derived from **12** [lithium diisopropylamide (LDA), −78 °C, 1 h] was treated with **13** [THF–hexamethylphosphoramide



a) $BrCF_2COOEt$, Zn b) $(CF_3SO_2)_2O$, iso-Pr_2EtN c) DBU d) H_2, Pd-C e) *p*-TsOH, EtOH f) PCC

Chart 2

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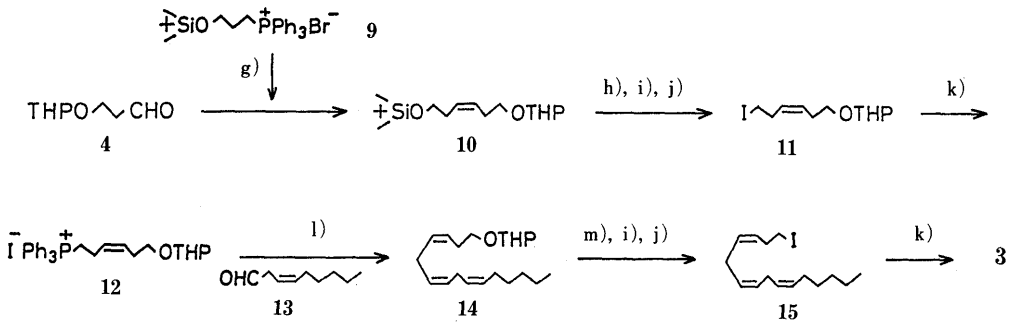

g) *n*-BuLi h) *n*-Bu_4NF i) CH_3SO_2Cl, Et_3N
j) NaI k) Ph_3P l) LDA m) *p*-TsOH, MeOH

Chart 3

(HMPA), −78°C for 5 min and 0 °C for 1.5 h] to give, following an extractive work-up and filtration through a short silica gel column, the triene (**14**) in 46% yield. Although proton nuclear magnetic resonance (^{1}H-NMR) analysis of this crude product showed the minor component of the olefinic isomer (about 10%), the triene thus obtained was used in the next step without further purification (*vide infra*). The transformation of **14** into the phosphonium salt (**3**) was effected by deprotection reaction and using the similar method described above [1) removal of the THP group, 2) mesylation, 3) iodination, 4) treatment with Ph_3P]. Prior to the iodination step, the contaminating minor olefinic isomer was removed from the mixture by silica gel column chromatography to obtain the homogeneous all-*cis*-triene. The complete carbon skeleton of the tetraene was constructed by Wittig reaction of the ylide from **3** (LDA, −78°C, 45 min) with **2** under *cis*-selective olefination conditions to give the ester (**1b**) in 75% yield. Compound (**1b**) was saponified to 2,2-F_2AA (**1a**) with 10 eq of 1 N potassium hydroxide in MeOH at room temperature for 30 min (78% yield).

In summary, the synthesis of 2,2-F_2AA from a readily available fluorine-containing building block was achieved by a practical method. The synthetic procedure described here is applicable to the synthesis of the 2,2-difluoro analogs of other polyunsaturated fatty acids. We have already synthesized 2,2-difluorolinoleic acid and 2,2-difluorolinolenic acid in the same way.[10] The enzymatic transformation of 2,2-F_2AA is now being attempted.

Experimental

^{1}H-NMR spectra were taken on a Brucker AM400 or a Varian EM-390 L spectrometer in $CDCl_3$. Chemical shifts are reported as parts per million (ppm) relative to tetramethylsilane as the internal standard. ^{19}F-NMR spectra were taken on a Varian EM-360L spectrometer in $CDCl_3$, and chemical shifts are reported as ppm relative to benzotrifluoride as the internal standard. Infrared spectra (IR) were recorded on a Jasco A302 infrared spectrophotometer. Mass spectra (MS) were obtained on a Hitachi M-80. All air-sensitive reactions were conducted under an argon atmosphere. Unless otherwise noted, the term "standard work-up" means the addition of ether, sequential washing with the aqueous solutions indicated in parenthesis, drying over $MgSO_4$, and concentration *in vacuo*. Column chromatography was carried out on silica gel (Wakogel C-200), with the solvent indicated in parenthesis as an eluent.

Ethyl 2,2-Difluoro-3-hydroxy-5-(tetrahydropyranyloxy)pentanoate (5) To a mixture of zinc powder (2.31 g, 35.35 mg atom) and THF (30 ml) was added dropwise a solution of **4** (4 g, 25.32 mmol) and ethyl bromodifluoroacetate (5.67 g, 28.04 mmol) in THF (33 ml) at refluxing temperature, and the whole was heated under reflux for 3 h with stirring. After addition of ether and aqueous NH_4Cl to the reaction mixture, the precipitate was removed by filtration through celite and the filtrate was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and purified by flash column chromatography on silica gel (Merck 9385, hexane–AcOEt, 5:1—2:1) to give **5** (4.07 g, 57% yield). ^{1}H-NMR δ: 1.35 (3H, t, J=7.5 Hz, CH_3), 1.2—2.1 (8H, m, $CH_2\times4$), 2.1 (1H, s, OH), 3.4—4.2 (5H, m, $OCH_2\times2$ and OCH), 4.4 (2H, q, J=7.5 Hz, OCH_2), 4.7 (1H, br, OCHO). ^{19}F-NMR δ: −50.9 and −51.1 (1F, each dd, J=259.4, 7.5 Hz), −61.2 and −61.8 (1F, each dd, J=259.4, 6.8 Hz). IR (CCl_4): 3510, 2950, 2880, 1780, 1763 cm^{-1}. MS *m/z*: 283 (M^++1).

Ethyl 2,2-Difluoro-5-(tetrahydropyranyloxy)pentanoate (7) A mixture of **5** (2.49 g, 8.83 mmol), *N*-ethyldiisopropylamine (2.3 g, 17.8 mmol) and trifluoromethanesulfonic anhydride (2.74 g, 9.7 mmol) in CH_2Cl_2 (30 ml) was stirred at −78 °C for 5 h. Standard work-up (cold diluted HCl, aqueous $NaHCO_3$, and brine) and column chromatography (hexane–AcOEt, 10:1—2:1) gave the corresponding triflate (2.328 g, 64% yield). A mixture of the triflate (1.896 g, 4.58 mmol) and DBU (837.3 mg, 5.5 mmol) in CH_2Cl_2 (15 ml) was stirred at 40°C for 4 h. Standard work-up (diluted HCl, aqueous $NaHCO_3$, and brine) and column chromatography (hexane–AcOEt, 10:1) gave the olefinic compound (*trans*-**6**, 1.07 g, 89% yield). The hydrogenation was carried out in a low-pressure catalytic hydrogenation apparatus. Compound (**6**, 311.5 mg, 1.18 mmol), 5% Pd–C (catalytic amount), and ethanol (3 ml) were placed in a bottle, which was filled with hydrogen (3.0 kg/cm^2) and shaken for 5 h. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (hexane–AcOEt, 30:1—20:1) to give **7** (250.2 mg, 80% yield) and the corresponding monofluoro derivative (41.2 mg, 14% yield). **7**: TLC: *Rf* 0.325 (Merck 5715, hexane–AcOEt, 5:1). ^{1}H-NMR δ: 1.3 (3H, t, J=7.5 Hz, CH_3), 1.2—2.5 (10H, m, $CH_2\times5$), 3.3—4.0 (4H, m, $OCH_2\times2$), 4.3 (2H, q, J=7.5 Hz, OCH_2), 4.6 (1H, br s, OCHO). ^{19}F-NMR δ: −43.0 (2F, t, J=17.0 Hz). MS *m/z*: 265 (M^+−1), 237, 181, 165, 137, 117, 101, 85. Monofluoro derivative [ethyl 2-fluoro-5-(tetrahydropyranyloxy)pentanoate]: TLC: *Rf* 0.263 (Merck 5715, hexane–AcOEt, 5:1). ^{1}H-NMR δ: 1.31 (3H, t, J=7.16 Hz, CH_3), 1.42—1.85 (4H, m, $CH_2\times2$), 1.88—2.11 (4H, m, $CH_2\times2$), 2.16—2.21 (2H, m, CH_2), 3.44 (1H, ddd, J=12.4, 9.83, 5.95 Hz, OCH), 3.50 (1H, m, OCH), 3.78 (1H, ddd, J=12.4, 9.8, 6.45 Hz, OCH), 3.84 (1H, m, OCH), 4.26 (2H, q, J=7.16 Hz, OCH_2), 4.58 (1H, m, OCHO), 4.94 (1H, ddd, J=49.2, 7.76, 4.27 Hz, CFH). ^{19}F-NMR δ: −129.0 (dt, J=49.2, 24.5 Hz).

Ethyl 2,2-Difluoro-5-oxopentanoate (2) A mixture of **7** (486 mg, 1.83 mmol) and *p*-toluenesulfonic acid (*p*-TsOH, 53 mg, 0.28 mmol) in ethanol (5 ml) was stirred at room temperature for 4.5 h. The reaction mixture was neutralized with solid $NaHCO_3$, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexane–AcOEt, 5:1—3:1) to give **8** (300.1 mg, 90% yield). ^{1}H-NMR δ: 1.35 (3H, t, J=7.5 Hz, CH_3), 1.5—2.5 (4H, m, $CH_2\times2$), 2.35 (1H, s, OH), 3.7 (2H, t, J=6 Hz, OCH_2), 4.3 (2H, q, J=7.5 Hz, OCH_2). ^{19}F-NMR δ: −43.3 (2F, t, J=17.0 Hz). EI-MS *m/z*: 165 (M^+−OH). CI-MS *m/z*: 183 (M^++1). To a mixture of PCC (152 mg, 0.71 mmol) and AcONa (17.2 mg, 0.21 mmol) in CH_2Cl_2 (1.0 ml) was added a solution of **8** (113.5 mg, 0.62 mmol) in CH_2Cl_2 (3 ml) at 0 °C. After being stirred for 1.5 h at room temperature, PCC (76.0 mg, 0.35 mmol) was further added to the reaction mixture. Stirring was continued for 3 h. The reaction mixture was directly subjected to column chromatography (hexane–AcOEt, 15:1—10:1) to give **2** (77 mg, 69% yield). ^{1}H-NMR δ: 1.36 (3H, t, J=7.15 Hz, CH_3), 2.42 (2H,

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tt, $J=16.97$, 7.46 Hz, CH_2CF_2), 2.74 (2H, t, $J=7.46$ Hz, $OHCCH_2$), 4.33 (2H, q, $J=7.15$ Hz, OCH_2), 9.80 (1H, s, CHO).

(3*Z*)-1-Iodo-6-(tetrahydropyranyloxy)hex-3-ene(11) A mixture of the phosphonium salt (**9**, 10.27 g, 19.94 mmol) and *n*-BuLi (1.21 M solution in hexane, 18.0 ml, 21.8 mmol) in THF (160 ml) was stirred for 1 h at −78 °C. To the reaction mixture was added HMPA (12.8 ml) and a solution of the aldehyde (**4**, 3 g, 19.0 mmol) in THF(10 ml), and the whole was stirred for 10 min at −78°C, then for 1 h at 0°C. Standard work-up (cold diluted HCl, aqueous $NaHCO_3$, and brine) and column chromatography (hexane–AcOEt, 20 : 1) gave **10** (*cis*-selective, 4.09 g, 69% yield). To a solution of **10** (4.0 g, 12.74 mmol) in THF (60 ml) was added a *n*-Bu_4NF (1 M solution in THF, 31.9 ml, 31.9 mmol) at 0 °C and the reaction mixture was stirred at room temperature for 2 h. Standard work-up (brine) gave the alcohol derivative, which was used in the next reaction without purification. To a solution of the residue and triethylamine (1.93 g, 19.11 mmol) in CH_2Cl_2 (56 ml) was added a solution of methanesulfonyl chloride (1.68 g, 14.65 mmol) in CH_2Cl_2 (6 ml) at 0°C and the reaction mixture was stirred for 1.5 h at the same temperature. Standard work-up (cold diluted HCl, aqueous $NaHCO_3$ and brine) and column chromatography (hexane–AcOEt, 3 : 1—2 : 1) gave the mesylate (3.15 g, 81% yield). ^{1}H-NMR δ: 1.50—1.86 (6H, m, $CH_2\times3$), 2.37 (2H, ddd, $J=7.26$, 6.85, 6.75 Hz, allylic H), 2.54 (2H, dt, $J=7.31$, 6.85 Hz, allylic H), 3.00 (3H, s, CH_3), 3.42 (1H, dt, $J=9.57$, 6.75 Hz, OCH_2), 3.76 (1H, dt, $J=9.57$, 6.85 Hz, OCH), 3.50 (1H, m, OCH), 3.86 (1H, m, OCH), 4.22 (2H, t, $J=6.85$ Hz, OCH_2), 4.58 (1H, dd, $J=4.45$, 2.79 Hz, OCHO), 5.46 (1H, dtt, $J=10.82$, 7.26, 1.52 Hz, olefinic H), 5.63 (1H, dtt, $J=10.82$, 7.31, 1.45 Hz, olefinic H). A mixture of the mesylate (975.9 mg, 3.51 mmol) and sodium iodide (895 mg, 5.97 mmol) in acetone (8 ml) was stirred for 11 h at room temperature. Standard work-up (brine) and flash column chromatography on silica gel (Merck 9385, hexane–AcOEt, 50 : 1) gave **11** (871.3 mg, 80% yield). ^{1}H-NMR δ: 1.43—1.86 (6H, m, $CH_2\times3$), 2.35 (2H, m, allylic H), 2.66 (2H, m, allylic H), 3.15 (2H, t, $J=7.28$ Hz, CH_2I), 3.42—3.87 (4H, m, $OCH_2\times2$), 4.59 (1H, dd, $J=4.39$, 2.72 Hz, OCHO), 5.43 (1H, dtt, $J=10.79$, 7.18, 1.51 Hz, olefinic H), 5.58 (1H, dtt, $J=10.79$, 7.30, 1.33 Hz, olefinic H). MS *m/z*: 311 ($M^+ + 1$), 209, 208, 183, 155, 101, 85.

Phosphonium Salt (12) A mixture of **11** (119 mg, 0.38 mmol) and triphenylphosphine (120.8 mg, 0.46 mmol) in CH_3CN (3 ml) was refluxed for 13 h. After the removal of the solvent, the residue was washed with ether several times and dried over P_2O_5 *in vacuo* to give **12** (quantitative yield). ^{1}H-NMR δ: 1.34—1.72 (6H, m, $CH_2\times3$), 2.15 (2H, m, allylic H), 2.47 (2H, m, allylic H), 3.34—3.87 (6H, m, $OCH_2\times2$ and PCH_2), 4.49 (1H, dd, $J=5.31$, 2.65 Hz, OCHO), 5.46—5.51 (1H, m, olefinic H), 5.68—5.74 (1H, m, olefinic H), 7.71—7.86 (15 H, m, aromatic H).

(3*Z*,6*Z*,9*Z*)-1-(Tetrahydropyranyloxy)pentadeca-3,6,9-triene (14) A mixture of the phosphonium salt (**12**, 4.1 g, 7.18 mmol) and LDA (8.88 mmol) in THF (37 ml) was stirred for 1 h at −78 °C. To the reaction mixture was added HMPA (4.3 ml) and a solution of (3*Z*)-3-nonen-1-al (**13**, 1.11 g, 7.96 mmol) in THF (17 ml), and the whole was stirred for 5 min at −78 °C, then for 1.5 h at 0 °C. Standard work-up (brine) and filtration of the crude product through a short silica gel column (hexane–AcOEt, 30 : 1—20 : 1) gave a mixture of the triene (**14**) and the olefinic isomer (*ca.* 9 : 1 by ^{1}H-NMR, 1.00 g, 46% total yield). **14**: ^{1}H-NMR δ: 0.89 (3H, t, $J=7.02$ Hz, CH_3), 1.25—1.87 (12H, m, $CH_2\times6$), 2.05 (2H, dt, $J=6.97$, 6.97 Hz, allylic H), 2.39 (2H, m, allylic H), 2.83 (4H, m, allylic H), 3.39—3.90 (4H, m, $OCH_2\times2$), 4.60 (1H, dd, $J=4.01$, 2.90 Hz, OCHO), 5.30—5.51 (6H, m, olefinic H). MS *m/z*: 220 ($M^+ - THP - H$), 183, 85.

(3*Z*,6*Z*,9*Z*)-1-Iodopentadeca-3,6,9-triene (15) A mixture of **14** (1.0 g, 3.27 mmol) and *p*-TsOH (31.2 mg, 0.16 mmol) in methanol (10 ml) was stirred at room temperature for 5 h. The reaction mixture was neutralized with solid $NaHCO_3$, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexane–AcOEt, 7 : 1—5 : 1) to give the alcohol derivative (550 mg, 76% yield). In the same procedure described for the synthesis of **11**, 550 mg of the alcohol derivative was used. The yield of the mesylate was 661 mg (89%). ^{1}H-NMR δ: 0.89 (3H, t, $J=6.89$ Hz, CH_3), 1.29—1.36 (6H, m, $CH_2\times3$), 2.06 (2H, m, allylic H), 2.54 (2H, m, allylic H), 2.82 (4H, m, allylic H), 3.00 (3H, s, CH_3), 4.23 (2H, t, $J=6.80$ Hz, OCH_2), 5.31—5.43 (5H, m, olefinic H), 5.57 (1H, dtt, $J=10.71$, 7.35, 1.49 Hz, olefinic H). The yield of the iodide (**15**) was 479.8 mg (66%). ^{1}H-NMR δ: 0.89 (3H, t, $J=6.88$ Hz, CH_3), 1.26—1.40 (6H, m, $CH_2\times3$), 2.06 (2H, m, allylic H), 2.67 (2H, m, allylic H), 2.81 (4H, m, allylic H), 3.15 (2H, t, $J=7.25$ Hz, CH_2I), 5.30—5.44 (5H, m, olefinic H), 5.53 (1H, dtt, $J=10.67$, 7.34, 1.40 Hz, olefinic H). MS *m/z*: 332 (M^+), 234, 205, 150, 79. High-resolution MS *m/z*: Calcd for $C_{15}H_{25}I$: 332.1000. Found: 332.0996.

Phosphonium Salt (3) In the same procedure described for the synthesis of **12**, the iodide (**15**, 479 mg, 1.44 mmol) was reacted with triphenylphosphine (417.3 mg, 1.59 mmol) in CH_3CN (5 ml) for 24 h to give the phosphonium salt (**3**) in quantitative yield. ^{1}H-NMR δ: 0.88 (3H, t, $J=6.92$ Hz, CH_3), 1.21—1.37 (6H, m, $CH_2\times3$), 1.99 (2H, dt, $J=6.99$, 6.92 Hz, allylic H), 2.45—2.53 (2H, m, allylic H), 2.59 (2H, dd, $J=7.24$, 7.24 Hz, allylic H), 2.64 (2H, dd, $J=7.21$, 7.21 Hz, allylic H), 3.86 (2H, dt, $J=11.90$, 8.01 Hz, PCH_2), 5.17—5.44 (5H, m, olefinic H), 5.64 (1H, dt, $J=10.6$, 7.04 Hz, olefinic H), 7.69—7.89 (15H, m, aromatic H).

2,2-Difluoroarachidonic Acid Ethyl Ester (1b) A mixture of the phosphonium salt (**3**, 198.6 mg, 0.33 mmol) and LDA (0.32 mmol) in THF (1.9 ml) was stirred for 45 min at −78 °C. To the reaction mixture was added HMPA (0.38 ml) and a solution of the aldehyde (**2**, 67 mg, 0.37 mmol) in THF (2.5 ml), and the whole was stirred for 5 min at −78°C, then for 1 h at 0°C. Standard work-up (brine) and column chromatography (hexane–AcOEt, 60 : 1) gave the ester (**1b**, 91.0 mg, 75% yield). ^{1}H-NMR δ: 0.89 (3H, t, $J=6.91$ Hz, CH_3), 1.27—1.38 (6H, m, $CH_2\times3$), 1.35 (3H, t, $J=7.14$ Hz, CH_3), 2.03—2.30 (6H, m, allylic H and CH_2CF_2), 2.80—2.85 (6H, m, allylic H), 4.32 (2H, q, $J=7.14$ Hz, OCH_2), 5.30—5.47 (8H, m, olefinic H). ^{19}F-NMR δ: −43.5 (2F, t, $J=16.9$ Hz). IR (CCl_4): 3020, 2960, 2940, 2860, 1775, 1760 cm^{-1}. MS *m/z*: 368 (M^+). High-resolution MS *m/z*: Calcd for $C_{22}H_{34}F_2O_2$: 368.2524. Found: 368.2511.

2,2-Difluoroarachidonic Acid (1a) A mixture of the ester (**1b**, 20 mg, 0.054 mmol) and 1 N KOH in MeOH (0.54 ml, 0.54 mmol) was stirred for 30 min at room temperature. Standard work-up (5% HCl and brine) and column chromatography (CH_2Cl_2–Et_2O, 2 : 1) gave the acid as a yellow oil (**1a**, 14.2 mg, 78% yield). ^{1}H-NMR δ: 0.89 (3H, t, $J=6.89$ Hz, CH_3), 1.26—1.40 (6H, m, $CH_2\times3$), 1.95—2.40 (6H, m, allylic H and CH_2CF_2), 2.83 (6H, m, allylic H), 5.31—5.48 (8H, m, olefinic H), 6.58 (1H, br, COOH). IR (CCl_4): 3020, 2960, 2940, 2860, 1755 cm^{-1}. MS *m/z*: 340 (M^+). High-resolution MS *m/z*: Calcd for $C_{20}H_{30}F_2O_2$: 340.2211. Found: 340.2193.

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