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ORIGINAL PAPER

Condensation of the dianion of ethyl acetoacetate with perfluoroalkyl iodides. Application to the synthesis of 3-perfluoroalkylsalicylic acids

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Abstract 3-Perfluoroalkylsalicylic esters and acids were prepared based on the condensation of the dianion of ethyl acetoacetate with various perfluoroalkyl iodides.

Keywords Dianions · Condensation · Organofluorine compounds · Arenes · Cyclizations · Regioselectivity

Introduction

Perfluoroalkyl-substituted compounds are of considerable importance in medicinal chemistry, as liquid crystals, and as ligands and organocatalysts in fluorous biphase systems [1–15]. Previously, (perfluoroalkyl)arenes have been prepared by reaction of iodoarenes with (perfluoroalkyl)-cuprates [16]. Portella et al. reported the synthesis of *ortho*-perfluoroalkylphenones from hemifluorinated enones [17]. Perfluoroalkylated heterocycles have been prepared by reactions of perfluoroketene dithioacetals, perfluorodithiocarboxylic acid derivatives [18], and γ-ketothioesters [19]. In addition, the cyclocondensation of carboxylic acid dianions with perfluoroketene dithioacetals has been demonstrated [20]. Haufe and coworkers reported the synthesis of polyfluoroalkyl-containing pyrones, pyridines, and pyrido [1,2-*a*]benzazoles from fluorinated β-alkoxyenones [21]. They also applied fluoroalkyl-substituted enones as dienophiles in Diels–Alder reactions [22]. In recent years, we developed a synthesis path to trifluoromethyl and perfluoroalkyl substituted arenes based on cyclization reactions of (non-fluorinated) 1,3-bis(trimethylsilyloxy)-1,3-butadienes, masked 1,3-dicarbonyl dianions (for a review of 1,3-bis(silyl enol ethers), see [23–25], for a review of [3 + 3] cyclizations of 1,3-bis(silyl enol ethers), see: [26]), with trifluoromethyl and perfluoroalkyl substituted enones, respectively (for a review of the synthesis of fluorinated molecules based on cyclization reactions of 1,3-bis(silyl enol ethers), see [27]). We also reported cyclization reactions of 1-trifluoromethyl- and 1-perfluoroalkyl-1,3-bis(trimethylsilyloxy)-1,3-butadienes derived from the corresponding 1,3-diketones [28, 29]. Due to the low nucleophilicity of these dienes, the cyclizations were restricted to the use of highly electrophilic oxalyl chloride. Herein, we report what are, to the best of our knowledge, the first condensations of 1,3-dicarbonyl dianions with perfluoroalkyl iodides to give novel perfluoroalkylated β-ketoester. The latter were transformed to 1-methoxy-4-perfluoroalkyl-1,3-bis(trimethylsilyloxy)-1,3-butadienes, which are structurally new as they contain the perfluoroalkyl group at a different position as compared to our previously reported 1-perfluoroalkyl-1,3-bis(trimethylsilyloxy)-1,3-butadienes [29].

Results and discussion

The reaction of the dianion of ethyl acetoacetate (**1**), generated by means of two equivalents of lithium

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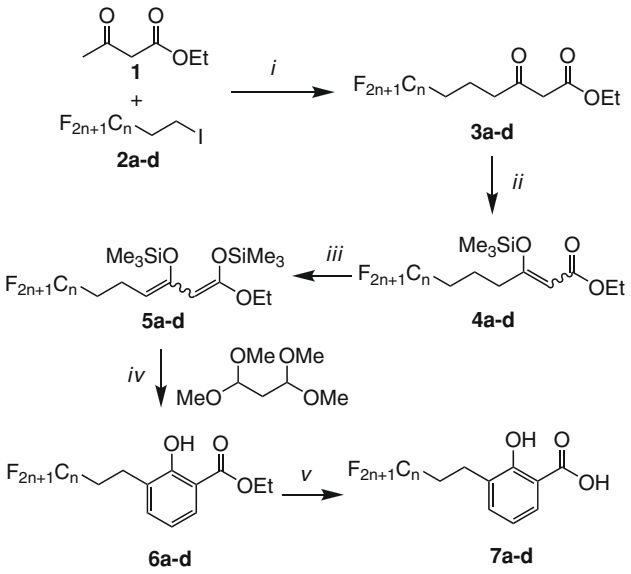
diisopropylamide (LDA), with 1-iodo-1*H*,1*H*,2*H*,2*H*-perfluoralkanes **2a**–**2d** afforded the perfluoroalkylated *β*-ketoesters **3a**–**3d** (Scheme 1). The ethylene spacer of **2a**–**2d** was necessary because completely perfluorinated iodalkanes do not undergo nucleophilic displacement reactions due to the electron withdrawing effect of fluorine [30–32]. The silylation of **3a**–**3d** produced mono-silylated enol ethers **4a**–**4d**, which were subsequently transformed to dienes **5a**–**5d**. The latter were directly subjected to the $TiCl_4$ mediated cyclization with 1,1,3,3-tetramethoxypropane. While the cyclizations of dienes **5a**–**5c** afforded the desired salicylates **6a**–**6c**, the employment of **5d**, containing the longest perfluoroalkyl group, proved to be unsuccessful due to its low solubility and precipitation in CH_2Cl_2 at −78 °C. After aqueous workup, only unknown by-products were isolated. Hydrolysis of **6b** and **6c** afforded salicylic acids **7b** and **7c**, respectively (Table 1).

In conclusion, we have reported a new strategy for the synthesis of 3-perfluoroalkylsalicylic esters and acids based on the condensation of the perfluoroalkyl-functionalized dianion of ethyl acetoacetate.

Experimental

^1H and ^{13}C NMR spectra were measured in $CDCl_3$ at 250, 300, and 500 MHz, respectively. Chemical shifts are reported in parts per million using the solvent internal standard (chloroform, 7.26 ppm for ^1H and 77.0 ppm for ^{13}C). Infrared spectra were recorded on a FT-IR spectrometer. Mass spectrometric data (MS) were obtained by electron impact ionization (EI, 70 eV). Chromatographic separations were carried out with Merck silica gel 60 (63–200 mesh) and analytical TLC was made using Merck silica gel 60 F254 sheets with visualization under UV light ($\lambda = 254$ nm). All cyclization reactions were carried out in Schlenk tubes under an argon atmosphere using dried solvents. The appropriate enol ethers were prepared as described in the literature [23, 24].

Scheme 1



i: LDA, THF, -78 to 20 °C; *ii*: Me_3SiCl, NEt_3, *n*-pentane, 20 °C; *iii*: 1) LDA, THF, -78 °C, 1 h, 2) Me_3SiCl; *iv*: $TiCl_4$, tetramethoxypropane, CH_2Cl_2, -78 to 20 °C; *v*: NaOH, H_2O, EtOH, 20 °C.

Table 1 Products and yields

3–7	*n*	3/%[a]	6/%[a]	7/%[a]
a	4	47	33	–
b	6	63	60	61
c	8	63	74	45
d	10	46	–[b]	–

[a] Yields of isolated products

[b] Low solubility of the starting material

General procedure for the synthesis of β-ketoesters ***3a–3d***

A tetrahydrofuran (THF) solution of LDA was prepared by addition of *n*-butyllithium (2.3 equiv., 2.5 M in *n*-hexane) to a solution of diisopropylamine (2.3 equiv.) in THF. To this solution we added ethyl acetoacetate (1 equiv.) at 0 °C. The deep yellow, clear solution was stirred at 0 °C for 1 h. We then added the alkyl halide (1 equiv.) at −78 °C. The solution was allowed to rise to ambient temperature over 14 h and the solution was stirred at room temperature for 2 h. Hydrochloric acid (200 cm^3, 10 %) was added to the solution and the mixture was extracted with diethyl ether (4 × 250 cm^3). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc = 20:1 → 10:1) to give **3a**–**3d**.

Ethyl 7,7,8,8,9,9,10,10,10-nonafluoro-3-oxodecanoate (**3a**, $C_{12}H_{13}F_9O_3$)

Starting with 3.11 g of diisopropylamine (30.8 mmol), 12.3 cm^3 of *n*-butyllithium (2.5 M, 30.8 mmol), 1.91 g of ethyl acetoacetate (14.7 mmol), and 5.00 g of 1,1,1,2,2,3,3,4,4-nonafluoro-6-iodohexane (13.4 mmol), **3a** was isolated after column chromatography as a colorless oil (2.34 g, 47 %). $R_f = 0.37$ (*n*-heptane/EtOAc = 1:1); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 4.20$ (q, 2H, $^3J = 7.1$ Hz, $OC\underline{H}_2CH_3$), 3.44 (s, 2H, H-2), 2.69 (t, 2H, $^3J = 6.7$ Hz, H-4), 1.84–2.25 (m, 4H, H-5, H-6), 1.28 (t, 3H, $^3J = 7.1$ Hz, $OCH_2C\underline{H}_3$) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 201.3$ (C-3), 167.0 (C-1), 61.5 ($O\underline{C}H_2CH_3$), 49.2 (C-2), 41.4 (C-4), 29.6 (t, $^3J_{C,F} = 21.9$ Hz, C-6), 14.3 (t, $^4J_{C,F} = 4.3$ Hz,

C-5), 13.9 ($OCH_2\underline{C}H_3$) ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -81.0$ (CF_3), -114.6 ($CH_2\underline{C}F_2$), -121.8, -124.4 (CF_2), -126.1 ($C\underline{F}_2CF_3$) ppm; IR (neat): $\bar{\nu} = 1{,}746$ (COOEt), 1,720 (C=O) cm^{-1}; MS (EI, 70 eV): *m/z* = 376 (M^+), 330 (M^+-OCH_2CH_3); HRMS (EI): calcd. for $C_{12}H_{13}F_9O_3$ (M^+) 376.0716, found 376.0709.

Ethyl 7,7,8,8,9,9,10,10,11,11,12,12,12-tridecafluoro-3-oxododecanoate (**3b**, $C_{14}H_{13}F_{13}O_3$)

Starting with 2.46 g of diisopropylamine (24.3 mmol), 15.2 cm^3 of *n*-butyllithium (1.6 M, 24.3 mmol), 1.37 g of ethyl acetoacetate (10.5 mmol), and 5.00 g of 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-8-iodooctane (10.5 mmol), **3b** was isolated after column chromatography as a colorless oil (3.17 g, 63 %). $R_f = 0.53$ (*n*-heptane/EtOAc = 1:1); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 4.20$ (q, 2H, $^3J = 7.0$ Hz, $OC\underline{H}_2CH_3$), 3.44 (s, 2H, H-2), 2.69 (t, 2H, $^3J = 6.7$ Hz, H-4), 1.85–2.24 (m, 4H, H-5, H-6), 1.28 (t, 3H, $^3J = 7.0$ Hz, $OCH_2C\underline{H}_3$) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 201.5$ (C-3), 167.1 (C-1), 61.7 ($O\underline{C}H_2CH_3$), 49.4 (C-2), 41.6 (C-4), 29.9 (t, $^3J_{C,F} = 22.3$ Hz, C-6), 14.7 (C-5), 14.4 ($OCH_2\underline{C}H_3$) ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.7$ (CF_3), -114.3 ($CH_2\underline{C}F_2$), -121.8, -122.8, -123.4 (CF_2), -126.0 ($C\underline{F}_2CF_3$) ppm; IR (neat): $\bar{\nu} = 1{,}744$ (COOEt), 1,719 (C=O)cm^{-1}; MS (EI, 70 eV): *m/z* = 476 (M^+), 431 (M^+-OCH_2CH_3), 389 (M^+-$CH_2C(O)OCH_2CH_3$).

Ethyl 7,7,8,8,9,9,10,10,11,11,12,12,13,13,14,14,14-heptadecafluoro-3-oxotetradecanoate (**3c**, $C_{16}H_{13}F_{17}O_3$)

Starting with 2.03 g of diisopropylamine (20.0 mmol), 8.0 cm^3 of *n*-butyllithium (1.6 M, 19.8 mmol), 1.13 g of ethyl acetoacetate (8.71 mmol), and 5.00 g of 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluoro-10-iododecane (8.71 mmol), **3c** was isolated after column chromatography as a colorless solid (3.17 g, 63 %). M.p.: 32.5 °C; $R_f = 0.53$ (*n*-heptane/EtOAc); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 4.19$ (q, 2H, $^3J = 7.1$ Hz, $OC\underline{H}_2CH_3$), 3.43 (s, 2H, H-2), 2.69 (t, 2H, $^3J = 6.7$ Hz, H-4), 1.84–2.24 (m, 4H, H-5, H-6), 1.27 (t, 3H, $^3J = 7.1$ Hz, $OCH_2C\underline{H}_3$) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 201.5$ (C-3), 167.1 (C-1), 61.7 ($O\underline{C}H_2CH_3$), 49.4 (C-2), 41.6 (C-4), 29.9 (t, $^3J_{C,F} = 22.3$ Hz, C-6), 14.5 (C-5), 14.1 ($OCH_2\underline{C}H_3$) ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.7$ (CF_3), -114.3 ($CH_2\underline{C}F_2$), -121.8, -122.6, -123.3 (CF_2), -126.0 ($C\underline{F}_2CF_3$) ppm; IR (neat): $\bar{\nu} = 1{,}742$ (COOEt), 1,713 (C=O) cm^{-1}; MS (EI, 70 eV): *m/z* = 576 (M^+), 531 (M^+-OCH_2CH_3); HRMS (EI): calcd. for $C_{16}H_{13}F_{17}O_3$ (M^+) 576.0588, found 576.0579.

Ethyl 7,7,8,8,9,9,10,10,11,11,12,12,13,13,14,14,15,15,16,16,16-henicosafluoro 3-oxo-hexadecanoate (**3d**, $C_{18}H_{13}F_{21}O_3$)

Starting with 1.73 g of diisopropylamine (17.1 mmol), 6.83 cm^3 of *n*-butyllithium (2.5 M, 17.1 mmol), 1.06 g of ethyl acetoacetate (8.2 mmol), and 5.00 g of 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-henicosafluoro-12-iodododecane (7.42 mmol), **3d** was isolated after column chromatography as a colorless solid (2.33 g, 46 %). M.p.: 56 °C; $R_f = 0.39$ (*n*-heptane/EtOAc = 1:1); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 4.20$ (q, 2H, $^3J = 7.2$ Hz, $OC\underline{H}_2CH_3$), 3.44 (s, 2H, H-2), 2.69 (t, 2H, $^3J = 6.7$ Hz, H-4), 1.84–2.25 (m, 4H, H-5, H-6), 1.28 (t, 3H, $^3J = 7.2$ Hz, $OCH_2C\underline{H}_3$) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 201.5$ (C-3), 167.1 (C-1), 61.7 ($O\underline{C}H_2CH_3$), 49.4 (C-2), 41.6 (C-4), 29.9 (t, $^3J_{C,F} = 22.3$ Hz, C-6), 14.5 (t, $^3J_{C,F} = 22.3$ Hz, C-5), 14.1 ($OCH_2\underline{C}H_3$) ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.5$ (CF_3), -114.2 ($CH_2\underline{C}F_2$), -121.4, -122.4, -123.2 (CF_2), -125.8 ($C\underline{F}_2CF_3$) ppm; IR (Nujol): $\bar{\nu} = 1{,}744$ (COOEt), 1,713 (C=O) cm^{-1}; MS (EI, 70 eV): *m/z* = 676 (M^+), 631 (M^+-OEt); HRMS (EI): calcd. for $C_{18}H_{13}F_{21}O_3$ (M^+) 676.0524, found 676.0521.

General procedure for the synthesis of silyl enol ethers ***4a–4d***

To a pentane solution of *β*-ketoester **3a–3d** (1.0 equiv.) we added NEt_3 (1.5 equiv.). After stirring for 1 h at 20 °C, TMSCl (1.5 equiv.) was then added dropwise at 20 °C. After stirring for 48 h, the precipitated salts were filtered and the filtrate was concentrated in vacuo to give **4a–4d**. Due to their lability, the products were directly used without purification and characterization for the next step.

General procedure for the synthesis of 1,3-bis(silyl enol ethers) ***5a–5d***

To a THF solution of LDA, prepared by addition of *n*-butyllithium (1.5 equiv., 1.6 M in hexane) to a THF solution of diisopropylamine (1.5 equiv.) at 0 °C and stirring for 20 min, we added a THF solution of **4a–4d** (1.0 equiv.) at −78 °C. After stirring for 1 h at −78 °C, we then added TMSCl (1.5 equiv.). The solution was allowed to rise to ambient temperature over 2 h and was then stirred for 1 h at 20 °C. The solvent was removed in vacuo and *n*-hexane was added to the residue. The precipitated lithium chloride was removed by filtration under inert conditions and the solvent of the filtrate was removed in vacuo to give **5a–5d**. Due to their lability, the products were directly used without purification and characterization for the next step.

General procedure for the synthesis of ***6a–6d***

To a CH_2Cl_2 solution of 1,3-bis(silyl enol ether) **5a–5d** (1 equiv.) and 1,1,3,3-tetramethoxypropane (1.03 equiv.) we added $TiCl_4$ (1 equiv.) at −78 °C under argon atmosphere. The temperature of this mixture was allowed to rise to 20 °C over 14 h. Afterwards, we added aqueous HCl solution (10 %, 10 cm^3), separated out the organic layer,

and extracted the residue with CH_2Cl_2 (3 × 10 cm^3). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-heptane/EtOAc = 50:1 → 20:1).

Ethyl 3-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)salicylate (**6a**, $C_{15}H_{13}F_9O_3$)

Starting with 0.14 cm^3 of 1,1,3,3-tetramethoxypropane (0.84 mmol), 312 mg of **5a** (0.6 mmol), and 0.07 cm^3 of $TiCl_4$ (0.6 mmol), **6a** was isolated as a colorless oil (81 mg, 33 %). $R_f = 0.55$ (*n*-heptane/EtOAc = 1:1); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 11.18$ (s, 1H, OH), 7.78 (dd, 1H, $^3J_{5,6} = 8.1$ Hz, $^4J_{4,6} = 1.6$ Hz, H-6), 7.34 (dd, 1H, $^3J_{4,5} = 7.5$ Hz, $^4J_{4,6} = 1.6$ Hz, H-4), 6.83 (dd, 1H, $^3J_{4,5} = 7.5$ Hz, $^3J_{5,6} = 8.1$ Hz, H-5), 4.41 (q, 2H, $^3J = 7.3$ Hz, $OC\underline{H}_2CH_3$), 2.96 (dt, 2H, H-1'), 2.30–2.55 (m, 2H, H-2'), 1.42 (t, 3H, $^3J = 7.3$ Hz, $OCH_2C\underline{H}_3$) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 170.6$ (C=O), 160.0 (C-2), 136.0 (C-4), 128.8 (C-6), 127.6 (C-3), 118.9 (C-5), 112.5 (C-1), 61.7 ($O\underline{C}H_2CH_3$), 30.5 (t, $^2J_{C,F} = 22.0$ Hz, C-2'), 21.7 (t, $^3J_{C,F} = 4.4$ Hz, C-1'), 14.3 ($OCH_2\underline{C}H_3$) ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.8$ (CF_3), −114.7 ($CH_2\underline{C}F_2$), −124.3 (CF_2), −125.8 ($C\underline{F}_2CF_3$) ppm; IR (neat): $\bar{\nu} = 3{,}139$ (OH), 1,674 (C=O) cm^{-1}; MS (EI, 70 eV): *m/z* = 412 (M^+), 366 (M^+-HOEt); HRMS (EI): calcd. for $C_{15}H_{13}F_9O_3$ (M^+) 412.07155, found 412.072366.

Ethyl 3-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)salicylate (**6b**, $C_{17}H_{13}F_{13}O_3$)

Starting with 130 mg of 1,1,3,3-tetramethoxypropane (0.8 mmol), 390 mg of **5b** (0.8 mmol), and 0.69 cm^3 of $TiCl_4$ (6.3 mmol), we isolated **6b** as a colorless solid (245 mg, 60 %). M.p.: 41 °C; $R_f = 0.8$ (*n*-heptane/EtOAc = 2:3); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 11.19$ (s, 1H, OH), 7.78 (dd, 1H, $^3J_{5,6} = 8.0$ Hz, $^4J_{4,6} = 1.5$ Hz, H-6), 7.34 (dd, 1H, $^3J_{4,5} = 7.3$ Hz, $^4J_{4,6} = 1.5$ Hz, H-4), 6.83 (dd, 1H, $^3J_{4,5} = 7.3$ Hz, $^3J_{5,6} = 8.0$ Hz, H-5), 4.41 (q, 2H, $^3J = 7.0$ Hz, $OC\underline{H}_2CH_3$), 2.96 (dt, 2H, H-1'), 2.30–2.55 (m, 2H, H-2'), 1.42 (t, 3H, $^3J = 7.0$ Hz, $OCH_2C\underline{H}_3$) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 170.6$ (C=O), 160.0 (C-2), 136.0 (C-4), 128.8 (C-6), 127.6 (C-3), 118.9 (C-5), 112.7 (C-1), 61.7 ($O\underline{C}H_2CH_3$), 30.6 (t, $^2J_{C,F} = 21.7$ Hz, C-2'), 21.7 (t, $^3J_{C,F} = 4.7$ Hz, C-1'), 14.3 ($OCH_2\underline{C}H_3$) ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.5$ (CF_3), −114.5 ($CH_2\underline{C}F_2$), −121.6, −122.6, −123.3 (CF_2), −125.9 ($C\underline{F}_2CF_3$) ppm; IR (Nujol): $\bar{\nu} = 3{,}194$ (OH), 1,679 (C=O) cm^{-1}; MS (70 eV): *m/z* = 512 (M^+), 466 (M^+-HOEt).

Ethyl 3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)salicylate (**6c**, $C_{19}H_{13}F_{17}O_3$)

Starting with 227 mg of 1,1,3,3-tetramethoxypropane (1.38 mmol), 1.00 g of **5c** (1.38 mmol), and 0.15 cm^3 of $TiCl_4$ (1.38 mmol), we isolated **6c** as a colorless solid (627 mg, 74 %). M.p.: 57 °C; $R_f = 0.85$ (*n*-heptane/EtOAc = 2:3); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 11.19$ (s, 1H, OH), 7.78 (dd, 1H, $^3J_{5,6} = 7.9$ Hz, $^4J_{4,6} = 1.7$ Hz, H-6), 7.34 (dd, 1H, $^3J_{4,5} = 7.3$ Hz, $^4J_{4,6} = 1.4$ Hz, H-4), 6.83 (dd, 1H, $^3J_{4,5} = 7.3$ Hz, $^3J_{5,6} = 7.9$ Hz, H-5), 4.41 (q, 2H, $^3J = 7.0$ Hz, $OC\underline{H}_2CH_3$), 2.92–3.00 (m, 2H, H-1'), 2.30–2.55 (m, 2H, H-2'), 1.42 (t, 3H, $^3J = 7.0$ Hz, $OCH_2C\underline{H}_3$) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 170.6$ (C=O), 160.0 (C-2), 136.0 (C-4), 128.8 (C-6), 127.7 (C-3), 118.9 (C-5), 112.7 (C-1), 61.6 ($O\underline{C}H_2CH_3$), 30.6 (t, $^2J_{C,F} = 22.9$ Hz, C-2'), 21.8 (t, $^3J_{C,F} = 4.4$ Hz, C-1'), 14.3 ($OCH_2\underline{C}H_3$) ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.5$ (CF_3), −114.5 ($CH_2\underline{C}F_2$), −121.7, −122.5, −123.3, (CF_2), −125.9 ($C\underline{F}_2CF_3$) ppm; IR (Nujol): $\bar{\nu} = 3{,}199$ (OH), 1,685 (C=O) cm^{-1}; MS (70 eV): *m/z* = 612 (M^+), 566 (M^+-HOEt).

3-(3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluorooctyl)salicylic acid (**7b**, $C_{15}H_9F_{13}O_3$)

A solution of 259 mg **6b** (0.51 mmol) and 70 mg NaOH (1.75 mmol) in 20 cm^3 of EtOH were stirred under reflux for 4–5 h. After cooling to room temperature, the solution was acidified to pH 1 by addition of conc. hydrochloric acid. We added 10 cm^3 of water to the solution and extracted the mixture using diethyl ether (3 × 20 cm^3). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc = 1:1) to give **7b** as a colorless solid (150 mg, 61 %). M.p.: 120 °C; $R_f = 0.2$ (*n*-heptane/EtOAc = 2:3); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 10.72$ (s, 1H, OH), 7.86 (dd, 1H, $^3J_{5,6} = 8.1$ Hz, $^4J_{4,6} = 1.7$ Hz, H-6), 7.43 (dd, 1H, $^3J_{4,5} = 7.3$ Hz, $^4J_{4,6} = 1.7$ Hz, H-4), 6.90 (t, 1H, $^3J_{4,5} = 7.3$ Hz, $^3J_{5,6} = 8.1$ Hz, H-5), 2.92–3.03 (m, 2H, H-1'), 2.31–2.56 (m, 2H, H-2') ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 174.6$ (C=O), 160.5 (C-2), 137.4 (C-4), 129.8 (C-6), 128.0 (C-3), 119.5 (C-5), 111.3 (C-1), 30.6 (t, $^2J_{C,F} = 22.3$ Hz, C-2'), 21.7 (t, $^3J_{C,F} = 4.7$ Hz, C-1') ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.5$ (CF_3), −114.5 ($CH_2\underline{C}F_2$), −121.6, −122.6, −123.3 (CF_2), −125.8 ($C\underline{F}_2CF_3$) ppm; IR (Nujol): $\bar{\nu} = 3{,}200$ (OH), 1,645 (C=O) cm^{-1}; MS (70 eV): *m/z* = 484 (M^+), 466 (M^+-H_2O).

3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)salicylic acid (**7c**, $C_{15}H_9F_{17}O_3$)

The synthesis was carried out following the procedure given for the synthesis of **7b**. Starting with 300 mg **6c** (0.49 mmol) and 70 mg NaOH (1.75 mmol) in 20 cm^3 of EtOH, we isolated **7c** as a colorless solid (130 mg, 45 %). M.p.: 138 °C; $R_f = 0.1$ (*n*-heptane/EtOAc = 2:3); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 10.72$ (s, 1H, OH), 7.72 (d, 1H, $^3J_{5,6} = 7.9$ Hz, H-6), 7.26 (d, 1H, $^3J_{4,5} = 7.5$ Hz, H-4), 6.75 (t, 1H, $^3J_{4,5} = 7.5$ Hz, $^3J_{5,6} = 7.9$ Hz, H-5),

2.80–2.93 (m, 2H, H-1'), 2.21–2.47 (m, 2H, H-2') ppm; ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 172.8$ (C=O), 160.0 (C-2), 135.7 (C-4), 129.4 (C-6), 127.1 (C-3), 118.7 (C-5), 30.5 (t, $^{2}J_{C,F} = 22.3$ Hz, C-2'), 21.5 (C-1') ppm; ^{19}F NMR (235 MHz, $CDCl_3$): $\delta = -80.8$ (CF_3), -114.7 (CH_2CF_2), -121.8, -122.6, -123.4 (CF_2), -126.1 (CF_2CF_3) ppm; IR (Nujol): $\bar{\nu} = 3{,}169$ (OH), 3,110 (OH), 1,666 (C=O) cm^{-1}; MS (70 eV): $m/z = 584$ (M^+), 566 (M^+-H_2O); HRMS (EI): calcd. for $C_{17}H_9F_{17}O_3$ (M^+) 584.0275, found 584.0260.

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