Electronic Supplementary Information for:

Tuning the mesomorphic properties of phenoxy-terminated smectic liquid crystals: the effect of fluoro substitution

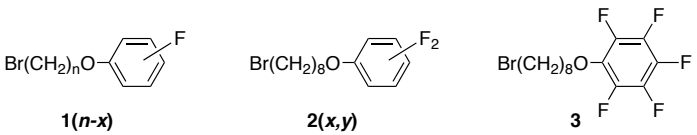
Matthew Thompson,[a] Carolyn Carkner,[a] Nicholas J. Mosey,[a] Nadia Kapernaum[b] and Robert P. Lemieux[,a]*

[a] Chemistry Department, Queen's University, Kingston, Ontario, Canada
[b] Institute of Physical Chemistry, Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart, Germany

email: lemieux@chem.queensu.ca

EXPERIMENTAL

General. ^{1}H and ^{13}C NMR spectra were recorded using Bruker Avance 300 and 400 spectrometers; chemical shifts (δ) are reported in parts per million (ppm) relative to TMS. Mass spectra were recorded using Waters/Micromass GC-TOF (low- and high-resolution) and Applied Biosystems/MDS Sciex QSTAR XL QTOF (low-resolution) instruments in electron ionization (EI) mode. Differential scanning calorimetry (DSC) analyses were performed using a TA Instruments Q2000 instrument with a scanning rate of 5 K min^{-1}. Texture analyses were performed using a Nikon Eclipse E600 POL polarized microscope fitted with a Linkam LTS 350 hot stage and TMS 93 temperature controller. Optical tilt angles were measured as a function of temperature by polarized microscopy as half the rotation between the two extinction positions corresponding to opposite signs of an applied electric field using mixtures of liquid crystal and the chiral dopant (*R,R*)-2-(4-*n*-octylphenyl)-5-(2,3-difluorooctyloxy)pyrimidine (**MDW797**, 2-5 mol%). The mixtures were introduced into ITO glass cells with a low pretilt polyimide alignment substrate (< 1°, parallel rubbing, 4 μm spacing, E.H.C. Co,, Japan), and aligned by slow cooling from the isotropic phase to the chiral SmC* phase. Small-angle X-ray scattering experiments were performed on a SAXSess system from Anton Paar GmbH. Unaligned samples (filled into Hilgenberg Mark capillary tubes of 0.7 mm diameter) were mounted in a temperature controlled sample holder unit (TSC 120). The X-ray beam from a ceramic tube generator was focused by a bent multilayer mirror and shaped by a line collimation block. The X-ray scattering was recorded with a CCD detector (Princeton Instruments SCX-TE-4300K/2) and processed and analysed using the SAXSquant 3.5 software. Chemicals were obtained from commercial sources unless otherwise noted.



1(*n-x*) **2(*x,y*)** **3**

General procedure for the synthesis of 1-bromo-*n*-(*x*-fluorophenoxy)alkanes (1(*n-x*)), 1-bromo-8-(*x,y*-difluorophenoxy)octane (2(*x,y*)) and 1-bromo-8-(2,3,4,5,6-pentafluoro-phenoxy)octane (3). Under a N_2 atmosphere, the appropriate fluorinated phenol (10.6 mmol) was combined with cesium carbonate (5.2 g, 15.9 mmol) in dry acetonitrile (100 mL). After stirring for 5 min, the appropriate dibromoalkane (15.9 mmol) was added to the mixture, which

was heated to reflux overnight. After cooling, the mixture was concentrated, dissolved in EtOAc (40 mL) and washed with 10% aq HCl (50 mL). The aqueous phase was extracted with EtOAc (2 × 40 mL) and the combined organic extracts were washed with sat aq $NaHCO_3$, water, brine, dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography on silica gel (0%-15% EtOAc/Hexane).

1-Bromo-4-(2-fluorophenoxy)butane (1(4-2)). Clear oil, 23% yield: ^{1}H NMR (400MHz , $CDCl_3$) δ 7.01-6.87 (m, 4H), 4.08 (t, J = 6.1 Hz, 2H), 3.51 (t, J = 6.6 Hz, 2H), 2.18-2.06 (m, 2H), 2.04-1.95 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9 (d, J = 246 Hz), 124.3 (d, J = 5 Hz), 121.2 (d, J = 7 Hz), 116.2 (d, J = 18 Hz), 115.0 (d, J = 2 Hz), 115.1 (d, J = 2 Hz), 68.4, 33.4, 29.3, 27.9; LRMS (EI) *m/z* 248 ((M+2, 9), 246 (M+, 9), 137 (65), 134 (66), 112 (100), 92 (13), 83 (18), 64 (11), 57 (10).

1-Bromo-4-(3-fluorophenoxy)butane (1(4-3)). Clear oil, 47% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 6.8 Hz, 1H), 6.74-6.56 (m, 3H), 4.00 (t, J = 6.1 Hz, 2H), 3.51 (t, J = 6.6 Hz, 2H), 2.15-2.03 (m, 2H), 2.0-1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (d, J = 245 Hz), 160.2 (d, J = 11 Hz), 130.1 (d, J = 10 Hz), 110.2 (d, J = 3 Hz), 107.5 (d, J = 21 Hz), 102.1 (d, J = 24 Hz), 67.1, 33.3, 29.4, 27.7; LRMS (EI) *m/z* 248 ((M+2, 16), 246 (M+, 16), 137 (80), 135 (80), 112 (100), 95 (14), 86 (27), 84 (55), 83 (17).

1-Bromo-4-(4-fluorophenoxy)butane (1(4-4)). Clear oil, 36% yield: ^{1}H NMR (400MHz , $CDCl_3$) δ 6.98 (dd, J = 9.3, 8.3 Hz, 2H), 6.87-6.80 (m, 2H), 3.96 (t, J = 6.1 Hz, 2H), 3.50 (t, J = 6.7 Hz, 2H), 2.12-2.02 (m, 2H), 1.99-1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3 (d, J = 238 Hz), 155.1 (d, J = 2 Hz), 115.8 (d, J = 23 Hz), 115.5 (d, J = 8 Hz), 67.5, 33.4, 29.5, 28.0; LRMS (EI) *m/z* 248 (M+2, 14), 246 (M+, 14), 137 (72), 135 (74), 112 (100), 95 (14), 84 (13), 83 (20), 55 (57).

1-Bromo-6-(2-fluorophenoxy)hexane (1(6-2)). Clear oil, 24% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-7.03 (m, 2H), 6.97 (m, 1H), 6.93-6.85 (m, 1H), 4.04 (t, J = 6.4 Hz, 2H), 3.43 (t, J = 6.8 Hz, 2H), 1.93-1.88 (m, 2H), 1.88-1.47 (m, 2H), 1.59-1.47 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7 (d, J = 245 Hz) 147.0 (d, J = 10 Hz) 124.2 (d, J = 4 Hz) 120.8 (d, J = 7 Hz) 116.0 (d, J = 18 Hz) 114.9 (d, J = 2 Hz), 69.1, 33.7, 32.6, 29.0, 27.8, 25.1; LRMS (EI) *m/z* 276 (M+2, 8), 274 (M+, 8), 165 (13), 163 (14), 112 (100), 84 (61), 55(55).

1-Bromo-6-(3-fluorophenoxy)hexane (1(6-3)). Clear oil, 17% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 6.8 Hz, 1H), 6.73-6.59 (m, 3H), 3.96 (t, J = 6.3 Hz, 2H), 3.45 (t, J = 6.8 Hz, 2H), 2.00-1.87 (m, 2H), 1.87-1.78 (m, 2H), 1.59-1.46 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (d, J = 245 Hz), 160.5 (d, J = 11 Hz), 130.2 (d, J = 10 Hz), 110.3 (d, J = 3 Hz), 107.3 (d, J = 21 Hz), 102.1 (d, J = 25 Hz), 68.0, 33.8, 32.7, 29.0, 27.9, 25.3; LRMS (EI) *m/z* 276 (M+2, 16), 274 (M+, 16), 112 (100), 95 (11), 83 (37).

1-Bromo-6-(4-fluorophenoxy)hexane (1(6-4)). Clear oil, 35% yield: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.03-6.92 (m, 2H), 6.88-6.79 (m, 2H), 3.93 (t, J = 6.3 Hz, 2H), 3.44 (t, J = 6.7 Hz, 2H), 2.02-1.83 (m, 2H), 1.83-1.65 (m, 2H), 1.65-1.46 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2 (d, J = 238 Hz), 155.2 (d, J = 2 Hz), 115.8 (d, J = 23 Hz), 115.4 (d, J = 8 Hz), 68.4, 33.8, 32.7, 29.1, 27.9, 25.3; LRMS (EI) *m/z* 276 ((M+2, 12), 274 (M+, 12), 112 (100), 86 (19), 84 (33).

1-Bromo-8-(2-fluorophenoxy)octane (1(8-2)). Clear oil, 15% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11-7.02 (m, 2H), 6.99-6.93 (m, 1H), 6.85-6.92 (m, 1H) 4.03 (t, J = 6.6 Hz, 2H), 3.42 (t, J = 6.9 Hz, 2H), 1.92-1.78 (m, 4H), 1.55-1.30 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7 (d, J = 245 Hz), 147.1 (d, J = 10 Hz), 124.2 (d, J = 4 Hz), 120.8 (d, J = 7 Hz), 116.1 (d, J = 18 Hz), 114.9 (d, J = 2 Hz), 69.3, 33.9, 32.7, 29.2, 29.1, 28.6, 28.1, 25.8; LRMS (EI) *m/z* 304 (M+2, 8), 302 (M+, 8), 112 (100), 86 (30), 84(45), 69 (17), 69 (14).

1-Bromo-8-(3-fluorophenoxy)octane (1(8-3)). Clear oil, 9 % yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 6.9 Hz, 1H), 6.72-6.59 (m, 3H), 3.94 (t, J = 6.4 Hz, 2H), 3.43 (t, J = 6.9 Hz, 2H), 1.93-1.83 (m, 2H), 1.83-1.74 (m, 2H), 1.54-1.43 (m, 4H), 1.42-1.33 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (d, J = 244 Hz), 160.5 (d, J = 11 Hz), 130.0 (d, J = 10 Hz), 110.3 (d, J = 3 Hz), 106.5 (d, J = 21 Hz), 102.0 (d, J = 25 Hz), 68.1, 33.9, 32.7, 29.1, 29.0, 28.6, 28.0, 25.9; LRMS (EI) *m/z* 304 (M+2, 17), 302 (M+, 17), 193 (17), 191 (17), 151 (12), 149 (12), 137 (42), 135 (43), 112 (41), 111 (75), 109 (14), 107 (14), 95 (10), 86 (28), 84 (44), 83 (14), 69 (100), 67 (12), 57 (42), 56 (12), 55 (94), 51 (20).

1-Bromo-8-(4-fluorophenoxy)octane (1(8-4)). Clear oil, 30% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03-6.92 (m, 2H), 6.89-6.78 (m, 2H), 3.92 (t, J = 6.6 Hz, 2H), 3.42 (t, J = 6.9 Hz, 2H), 1.93-1.72 (m, 4H), 1.53-1.29 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1 (d, J = 238 Hz), 155.2 (d, J = 2 Hz), 115.7 (d, J = 23 Hz), 115.4 (d, J = 8 Hz), 68.5, 33.9, 32.7, 29.2, 29.1, 28.6, 28.0, 25.9; LRMS (EI) *m/z* 304 (M+2, 8), 302 (M+, 8), 69 (14).

1-Bromo-8-(2,3-difluorophenoxy)octane (2(2,3)). White solid, 43% yield: mp 27-28 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (m, 1H), 6.80-6.69 (m, 2H), 4.04 (t, J = 6.4 Hz, 2H), 3.42 (t, J = 6.8 Hz, 2H), 1.93-1.78 (m, 4H), 1.54-1.42 (m, 4H), 1.42-1.29 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4 (dd, J = 246, 10 Hz), 148.8 (dd, J = 7, 3 Hz), 141.4 (dd, J = 247, 14 Hz), 123.0 (dd, J = 9, 5 Hz), 109.7 (d, J = 2 Hz), 108.8 (d, J = 18 Hz), 69.7, 33.8, 32.7, 29.0, 28.6, 28.0, 25.7; LRMS (EI) *m/z* 322 (M+2, 28), 320 (M+, 29), 190 (37), 150 (24), 147 (20), 137 (25), 135 (24) 130 (100), 111 (49), 84 (13), 69 (55), 57 (20), 55 (11).

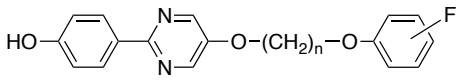
1-Bromo-8-(2,4-difluorophenoxy)octane (2(2,4)). Clear oil, 46% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (ddd, J = 9.1, 7.8, 5.3 Hz, 1H), 6.85 (td, J = 7.6, 4.2 Hz, 1H), 6.77 (td, J = 3.0, 1.8 Hz, 1H), 3.99 (t, J = 6.4 Hz, 2H), 3.41 (t, J = 6.8 Hz, 2H), 1.93-1.84 (m, 2H), 1.83-1.74 (m, 2H), 1.55-1.37 (m, 4H), 1.37-1.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3 (dd, J = 241, 10 Hz), 152.5 (dd, J = 249, 12 Hz), 143.6 (dd, J = 11, 4 Hz), 115.6 (dd, J = 10, 3 Hz), 110.1 (dd, J = 22, 4 Hz), 104.7 (dd, J = 26, 22 Hz), 70.1, 33.8, 32.7, 29.1, 29.0, 28.6, 28.0, 25.7; LRMS (EI) *m/z* 322 (M+2, 17), 320 (M+, 19), 130 (100), 69 (22), 55 (15).

1-Bromo-8-(2,5-difluorophenoxy)octane (2(2,5)). Clear oil, 23% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03-6.95 (m, 1H), 6.72-6.64 (m, 1H), 6.60-6.51 (m,1H), 3.99 (t, J = 6.6 Hz, 2H), 3.41 (t, J = 6.8 Hz, 2H), 1.93-1.75 (m, 4H), 1.55-1.37 (m, 4H), 1.37-1.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7 (dd, J = 242, 2 Hz), 148.9 (dd, J = 241, 3 Hz), 147.8 (dd, J = 12, 10 Hz), 116.0 (dd, J = 21, 10 Hz), 106.1 (dd, J = 24, 7 Hz), 102.5 (dd, J = 28, 2 Hz), 69.4, 33.8, 32.7, 29.0, 28.9, 28.6, 28.0, 25.7; LRMS (EI) *m/z* 322 (M+2, 38), 320 (M+, 36), 192 (29), 190 (31), 150 (25), 148 (30), 137 (21), 135 (24), 130 (100), 111 (43), 69 (63), 57 (20), 55 (14).

1-Bromo-8-(2,6-difluorophenoxy)octane (2(2,6)). Clear oil, 30% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99-6.83 (m, 3H), 4.12 (t, J = 6.4 Hz, 2H), 3.41 (t, J = 6.8 Hz, 2H), 1.91-1.81 (m, 2H), 1.80-1.70 (m, 2H), 1.54-1.40 (m, 4H), 1.40-1.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3 (dd, J = 248, 6 Hz), 135.8 (t, J = 14 Hz), 122.4 (t, J = 9 Hz), 112.0 (dd, J = 17, 7 Hz), 74.6 (t, J = 3 Hz), 33.8, 32.7, 29.8, 29.0, 28.6, 28.0, 25.5; LRMS (EI) *m/z* 322 (M+2, 22), 320 (M+, 25), 192 (38), 190 (43), 150 (21), 148 (21), 137 (31), 135 (29), 130 (100), 111 (55), 85 (40), 83 (63), 69 (56), 57 (20), 55 (13), 51 (15).

1-Bromo-8-(3,4-difluorophenoxy)octane (2(3,4)). Clear oil, 25% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (ddd, J = 10.0, 9.1, 8.7 Hz, 1H), 6.76-6.67 (m, 1H), 6.62-6.55 (m, 1H), 3.89 (t, J = 6.4 Hz, 2H), 3.42 (t, J = 6.9 Hz, 2H), 1.93-1.82 (m, 2H), 1.81-1.71 (m, 2H), 1.52-1.41 (m, 4H), 1.41-1.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4 (dd, J = 8, 2 Hz) 150.4 (dd, J = 247, 14 Hz), 144.8 (dd, J = 239, 12 Hz), 117.1 (dd, J = 19, 2 Hz), 109.7 (dd, J = 6, 4 Hz), 103.9 (d, J = 20 Hz) 68.7, 33.9, 32.7, 29.1, 29.0, 28.6, 28.0, 25.8; LRMS (EI) *m/z* 322 (M+2, 17), 320 (M+, 19), 130 (100), 69 (22), 55 (15).

1-Bromo-8-(3,5-difluorophenoxy)octane (2(3,5)). Clear oil, 20% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45-6.35 (m, 3H), 3.91 (t, J = 6.6 Hz, 2H), 3.41 (t, J = 6.8 Hz, 2H), 1.93-1.82 (m, 2H), 1.81-1.72 (m, 2H), 1.51-1.40 (m, 4H), 1.40-1.31 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (dd, J = 246, 15 Hz), 161.1 (t, J = 14 Hz), 98.2 (dd, J = 21, 8 Hz), 96.0 (t, J = 26 Hz), 68.5, 32.8, 29.8, 29.0, 28.6, 28.0, 25.4; LRMS (EI) *m/z* 322 (M+2, 34), 320 (M+, 34), 192 (40), 190 (29), 150 (23), 148 (24), 137 (23), 135 (26), 130 (100), 111 (43), 69 (67), 57 (22), 55 (16).



4(*n*-*x*)

General procedure for the synthesis of 5-(*n*-(*x*-fluorophenoxy)-1-alkyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(*n*-*x*)). Under a N_2 atmosphere, 2-(4-hydroxyphenyl)pyrimidin-5-ol (0.187 g, 1.0 mmol) was combined with cesium carbonate (0.293 g, 0.9 mmol) in dry acetonitrile (40 mL). After stirring for 5 min, **1(*n*-*x*)** (0.9 mmol) was added to the mixture, which was heated to reflux overnight. After cooling, the mixture was concentrated, dissolved in EtOAc (40 mL) and washed with 10% aq HCl (50 mL). The aqueous phase was extracted with EtOAc (2 × 40 mL) and the combined organic extracts were washed with sat aq $NaHCO_3$, water, brine, then dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (0%-20% EtOAc/Hexane) gave the product, which was recrystallized from acetonitrile and then from hexanes to give a white solid.

5-(4-(2-Fluorophenoxy)-1-butyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(4-2)). White solid, 46% yield: mp 147-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 8.25 (d, J = 8.8 Hz, 2H), 7.12-7.03 (m, 2H), 7.01-6.95 (m, 1H), 6.93-6.88 (m, 3H), 4.20 (t, J = 5.9 Hz, 2H), 4.14 (t, J = 5.7 Hz, 2H), 2.12-1.90 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.6 (d, J = 252 Hz), 150.7, 146.4 (d, J = 10 Hz), 143.9, 143.9, 128.6, 128.2, 124.7 (d, J = 4 Hz), 120.9 (d, J = 7 Hz), 115.9 (d, J = 18 Hz) 115.3, 115.0 (d, J = 2 Hz), 68.2, 68.1, 25.2, 25.1; LRMS (EI) *m/z* 354 (M+, 31), 236 (10), 188 (68), 167 (75), 125 (100), 69 (38), 55 (84).

5-(4-(3-Fluorophenoxy)-1-butyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(4-3)). White solid, 54% yield: mp 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 2H), 8.26 (d, J = 8.6 Hz, 2H), 7.24 (td, J = 8.3, 7.0 Hz, 1H), 6.93 (d, J = 8.3 Hz, 2H), 6.74-6.59 (m, 3H), 4.19 (t, J = 5.9 Hz, 2H), 4.06 (t, J = 5.7 Hz, 2H), 2.12-1.97 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0 (d, J = 244 Hz), 160.1 (d, J = 11 Hz) 159.1, 156.6, 150.7, 144.0, 130.6 (d, J = 10 Hz), 128.7, 128.2, 115.3, 110.8 (d, J = 3 Hz), 107.0 (d, J = 21 Hz), 101.9 (d, J = 25 Hz), 68.1, 67.4, 25.2, 25.0; LRMS (EI) m/z 354 (M+, 37), 188 (54), 167, (88), 125 (100), 55 (52).

5-(4-(4-Fluorophenoxy)-1-butyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(4-4)). White solid, 56% yield: mp 159-161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 2H), 8.25 (d, J = 8.6 Hz, 2H), 7.01-6.94 (m, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.88-6.82 (m, 2H), 4.18 (t, J = 5.9 Hz, 2H), 4.02 (t, J = 5.8 Hz, 2H), 2.09-1.96 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.1, 156.6, 154.9 (d, J = 2 Hz) 156.4 (d, J = 235 Hz), 150.7, 144.0, 128.6, 128.2, 115.7 (d, J = 23 Hz), 115.6 (d, J = 7 Hz), 115.3, 68.2, 67.6, 25.2, 25.0; LRMS (EI) m/z 354 (M+, 57), 188 (53), 167, (71), 125 (100), 69 (17), 55 (61).

5-(6-(2-Fluorophenoxy)-1-hexyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(6-2)). White solid, 18% yield: 126-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.25 (d, J = 8.8 Hz, 2H), 7.11-7.02 (m, 2H), 7.00-6.86 (m, 4H), 4.11 (t, J = 6.4 Hz, 2H), 4.06 (t, J = 6.3 Hz, 2H), 1.92-1.85 (m, 4H), 1.65-1.55 ppm (m, 4H); ^{13}C NMR (100 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 157.9, 157.6, 152.7 (d, J = 245 Hz), 151.1, 147.1 (d, J = 11 Hz), 143.8, 129.8, 129.2, 124.2 (d, J = 4 Hz), 120.8 (d, J = 7 Hz), 116.3, 116.0 (d, J = 18 Hz), 114.9 (d, J = 2 Hz), 69.3, 68.8, 29.2, 29.0, 25.8, 25.7; LRMS (EI) m/z 382 (M+, 42), 270 (19), 188 (100), 132 (10), 119 (16), 112 (15), 83 (17).

5-(6-(3-Fluorophenoxy)-1-hexyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(6-3)). White solid, 52% yield: mp 124-127 °C; ^{1}H NMR (400 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 8.41 (s, 2H), 8.20 (d, J = 8.8 Hz, 2H), 7.14-7.04 (m, 1H), 6.84 (d, J = 8.6 Hz, 2H), 6.58-6.52 (m, 1H), 6.51-6.45 (m, 2H), 4.02 (t, J = 6.3 Hz, 2H), 3.84 (t, J = 6.3 Hz, 2H), 1.81-1.74 (m, 2H), 1.73-1.66 (m, 2H), 1.44-1.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (d, J = 244 Hz), 159.9 (d, J = 11 Hz), 158.6, 157.2, 150.3, 143.2, 129.6 (d, J = 10 Hz), 128.5, 128.4, 115.0, 109.8 (d, J = 3 Hz) 106.6 (d, J = 21 Hz), 101.5 (d, J = 25 Hz), 68.1, 67.4, 28.4, 28.4, 25.2, 25.0; LRMS (EI) m/z 382 (M+, 89), 188 (100), 125 (12), 119 (15), 112 (14), 83 (20), 55 (32).

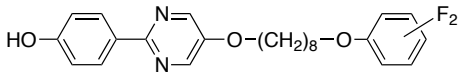
5-(6-(4-Fluorophenoxy)-1-hexyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(6-4)). White solid, 45% yield: mp 108-110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.32 (s, 2H), 8.12 (d, J = 8.6 Hz, 2H), 6.94-6.83 (m, 4H), 6.81-6.70 (m, 2H), 4.01 (t, J = 6.1 Hz, 2H), 3.85 (t, J = 6.1 Hz, 2H), 1.88-1.75 (m, 4H), 1.66-1.22 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 157.5, 157.1 (d, J = 238 Hz), 155.1 (d, J = 2 Hz), 151.1, 143.8, 130.2, 129.3, 115.7 (d, J = 23 Hz), 115.5, 115.4 (d, J = 8 Hz), 68.8, 68.4, 29.2, 29.0, 25.8, 25.7; LRMS (EI) m/z 382 (M+, 100), 188 (97), 125 (13), 112 (13), 83 (27).

5-(8-(2-Fluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(8-2)). White solid, 51% yield: mp 126-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.22 (d, J = 8.6 Hz, 2H), 7.11-7.01 (m, 1H), 7.00-6.93 (m, 3H), 6.93-6.85 (m, 2H), 4.08 (t, J = 6.4 Hz, 2H), 4.04 (t, J = 6.6 Hz, 2H), 1.88-1.78 (m, 4H), 1.56-1.37 (m, 8H); ^{13}C NMR (100 MHz, 1:1

$CDCl_3$/DMSO-d_6) δ 157.59, 157.57, 152.8 (d, J = 246 Hz), 151.2, 147.1 (d, J = 10 Hz), 143.9, 130.1, 129.3, 124.2 (d, J = 4 Hz), 120.9, 116.1 (d, J = 18 Hz), 115.5, 115.0 (d, J = 2 Hz), 69.4, 68.9, 29.7, 29.2, 29.2, 29.1, 25.9, 25.8; LRMS (EI) m/z 410 (M+, 56), 188 (100), 119 (10), 112 (15), 69 (20), 55 (17).

5-(8-(3-Fluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(8-3)). White solid, 60% yield: mp 106-108 °C; ^{1}H NMR (400 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 8.97 (s, 1H), 8.31 (s, 2H), 8.10 (d, J = 8.8 Hz, 2H), 7.17-7.06 (td, J = 8.3, 7.1 Hz, 1H), 6.83 (d, J = 8.8 Hz, 2H), 6.62-6.47 (m, 3H), 3.99 (t, J = 6.4 Hz, 2H), 3.85 (t, J = 6.4 Hz, 2H), 1.79-1.64 (m, 4H), 1.46-1.36 (m, 4H), 1.35-1.27 ppm (m, 4H); ^{13}C NMR (100 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 163.3 (d, J = 244 Hz), 160.2 (d, J = 3 Hz), 158.8, 157.5, 150.6, 143.5, 129.9 (d, J = 10 Hz), 128.8, 128.7, 115.3, 110.0 (d, J = 3 Hz), 106.9 (d, J = 21 Hz), 101.8 (d, J = 26 Hz), 68.6, 67.9, 28.9, 28.8, 25.6, 25.5; LRMS (EI) m/z 410 (M+, 50), 188 (100), 119 (11), 112 (12), 69 (15).

5-(8-(4-Fluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (4(8-4)). White solid, 46% yield: mp 127-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H) 8.22 (d, J = 8.8 Hz, 2H) 7.01-6.93 (m, 2H) 6.89 (d, J = 8.8 Hz, 2H) 6.86-6.80 (m, 2H), 4.08 (t, J = 6.4 Hz, 2H), 3.92 (t, J = 6.4 Hz, 2H), 1.88-1.74 (m, 6H) 1.55-1.37 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 157.6, 157.1 (d, J = 238 Hz), 155.2 (d, J = 2 Hz), 151.2, 143.9, 129.3, 129.0, 115.5, 115.4 (d, J = 7 Hz), 115.7 (d, J = 23 Hz), 68.9, 68.6, 29.2, 29.2, 29.1, 25.9, 25.8; LRMS (EI) m/z 410 (M+, 60), 300 (12), 188 (100), 112 (13), 69 (18).



5(*x,y*)

General procedure for the synthesis of 5-(8-(*x,y*-difluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (5(*x,y*)). The general procedure described for the synthesis of **4(*n-x*)** was repeated with 2-(4-hydroxyphenyl)pyrimidin-5-ol (0.187 g, 1.0 mmol), cesium carbonate (0.293 g, 0.9 mmol) and **2(*x,y*)** (0.290 g, 0.9 mmol) to give the product as a white solid.

5-(8-(2,3-Difluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (5(2,3)). White solid, 35% yield: mp 90-92 °C; ^{1}H NMR (400 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 9.01 (s, 1H), 8.33 (s, 2H), 8.11 (d, J = 8.8 Hz, 2H), 6.96-6.87 (m, 1H), 6.84 (d, J = 8.8 Hz, 2H), 6.71-6.62 (m, 2H), 4.01 (t, J = 6.4 Hz, 2H), 3.97 (t, J = 6.6 Hz, 2H), 1.82-1.71 (m, 4H), 1.49-1.39 (m, 4H), 1.38-1.31 (m, 4H); ^{13}C NMR (100 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 158.8, 157.6, 150.7, 151.1 (dd, J = 246, 10 Hz), 148.5 (dd, J = 8, 3 Hz), 143.5, 141.1 (dd, J = 247, 15 Hz), 128.8, 122.9 (dd, J = 9, 5 Hz), 115.4, 109.6 (d, J = 3 Hz), 108.6 (d, J = 18 Hz) 69.5, 68.6, 28.9, 28.9, 28.8, 28.8, 25.51, 25.49; LRMS (EI) m/z 428 (M+, 68), 188 (100), 130 (13), 119 (10), 69 (14), 55 (12).

5-(8-(2,4-Difluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (5(2,4)). White solid, 40% yield: mp 111-112 °C; ^{1}H NMR (400 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 8.97 (s, 1H), 8.26 (s, 2H), 8.03 (d, J = 8.8 Hz, 2H), 6.77 (d, J = 8.8 Hz, 2H), 6.77-6.60 (m, 3H), 3.95 (t, J = 6.4 Hz, 2H), 3.86 (t, J = 6.8 Hz, 2H), 1.75-1.58 (m, 4H), 1.50-1.34 (m, 4H), 1.32-1.20 (m, 4H); ^{13}C NMR (100 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 159.1, 156.6, 155.4 (dd, J = 239, 11 Hz), 150.8, 151.4 (dd, J = 245, 11 Hz), 143.9, 143.3 (dd, J = 11, 3 Hz), 128.6, 128.2, 115.6 (dd, J = 10, 3

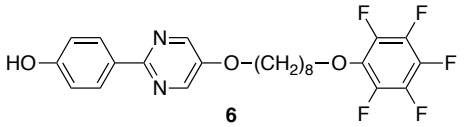
Hz,), 115.3, 110.7 (dd, J = 22, 4 Hz), 104.7 (dd, J = 27, 22 Hz), 69.2, 68.47,, 28.6,, 28.54, 28.50, 25.3, 25.2; LRMS (EI) *m/z* 428 (M+, 77), 188 (100), 69 (13), 55 (10).

5-(8-(2,5-Difluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (5(2,5)). White solid, 39% yield: mp 95-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 2H), 7.89 (d, J = 8.8 Hz, 2H), 6.73 (ddd, J = 10.7, 9.0, 5.6 Hz, 1H), 6.59 (d, J = 8.8 Hz, 2H), 6.41 (ddd, J = 9.9, 6.9, 2.9 Hz, 1H), 6.32-6.25 (m, 1H), 3.80 (t, J = 6.4 Hz, 2H), 3.72 (t, J = 6.4 Hz, 2H), 1.60-1.50 (m, 6H), 1.27-1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 157.7, 158.8 (dd, J = 242, 3 Hz), 151.2, 149.0 (dd, J = 242, 3 Hz), 147.8 (dd, J = 12, 11 Hz), 143.9, 129.4, 129.4, 116.1 (dd, J = 20, 10 Hz), 115.7, 106.3 (dd, J = 24, 7 Hz), 102.6 (dd, J = 28, 2 Hz), 69.5, 69.0, 29.2, 29.05, 28.97, 25.80, 25.75, 21.9; LRMS (EI) *m/z* 428 (M+, 80), 188 (100), 130 (21), 91 (31), 69(37), 55(31).

5-(8-(2,6-Difluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (5(2,6)). White solid, 52% yield: mp 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 2H), 8.19 (d, J = 8.8 Hz, 2H), 7.05-6.85 (m, 5H), 4.15 (t, J = 6.3 Hz, 2H), 4.09 (t, J = 6.8 Hz, 2H), 1.90-1.70 (m, 4H), 1.65-1.55 (m, 4H), 1.53-1.35 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 157.6, 155.9 (dd, J = 248, 5 Hz), 151.2, 143.9, 135.8 (t, J = 14 Hz), 129.7, 129.3, 122.5 (t, J = 9 Hz), 115.6, 112.1 (dd, J = 17, 7 Hz), 74.7 (t, J = 3 Hz), 69.0, 29.9, 29.2, 29.1, 29.0, 25.7, 25.5; MS (EI) *m/z* 428 (M+, 78), 188 (100), 130 (14), 119 (11), 69(19), 55(16).

5-(8-(3,4-Difluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (5(3,4)). White solid, 51% yield: mp 105-108 °C; ^{1}H NMR (400 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 8.87 (s, 1H), 8.33 (s, 2H), 8.11 (d, J = 8.8 Hz, 2H), 6.98 (ddd, J = 19.5, 10.1, 9.1 Hz, 1H), 6.85 (d, J = 8.8 Hz, 2H), 6.63 (ddd, J = 12.2, 6.6, 2.9 Hz, 1H), 6.54-6.48 (m, 1H), 4.01 (t, J = 6.4 Hz, 2H), 3.83 (t, J = 6.8 Hz, 2H), 1.82-1.65 (m, 4H), 1.50-1.30 (m, 8H); ^{13}C NMR (100 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 159.1, 156.6, 155.3 (dd, J = 9, 2 Hz), 150.8, 149.6 (dd, J = 244, 14 Hz), 143.9, 143.8 (dd, J = 238, 12 Hz), 128.6, 128.2, 117.4 (dd, J = 17, 2 Hz), 115.3, 110.6, (dd, J = 6, 3 Hz) 103.9 (d, J = 20 Hz), 68.5, 68.4, 28.6, 28.5, 28.4, 25.3, 25.2; LRMS (EI) *m/z* 428 (M+, 69), 188 (100), 69 (14).

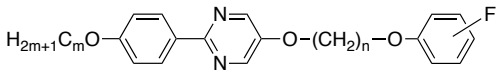
5-(8-(3,5-Difluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (5(3,5)). White solid, 46% yield: mp 110-112 °C; ^{1}H NMR (400 MHz, 1:1 $CDCl_3$/DMSO-d_6) δ 8.92 (s, 1H), 8.31 (s, 2H), 8.09 (d, J = 8.8 Hz, 2H), 6.82 (d, J =8.8 Hz, 2H), 6.38-6.27 (m, 3H), 3.99 (t, J = 6.4 Hz, 2H), 3.83 (t, J = 6.4 Hz, 2 H), 1.80-1.68 (m, 4H), 1.50-1.35 (m, 4H), 1.35-1.27 (m, 4H); ^{13}C NMR (100 MHz, 1:1$CDCl_3$/DMSO-d_6) δ 163.5 (dd, J = 244, 16 Hz), 161.1 (t, J = 12 Hz), 159.1, 157.8, 150.8, 143.7, 129.8.79, 128.76, 115.6, 98.2 (dd, J = 21, 8 Hz), 95.9 (t, J = 26 Hz), 68.8, 68.5, 29.1, 29.1, 29.0, 28.8, 25.8, 25.7; LRMS (EI) *m/z* 410 (M+, 74), 188 (100), 69 (16), 55 (11).



6

5-(8-(2,3,4,5,6-Pentafluorophenoxy)-1-octyloxy)-2-(4-hydroxyphenyl)pyrimidine (6). The general procedure described for the preparation of **4(*n-x*)** was repeated with 2-(4-hydroxyphenyl)pyrimidin-5-ol (0.290 g, 1.54 mmol), cesium carbonate (0.510 g, 0.94 mmol) and **3** (0.353 g, 1.08 mmol) to give **6** (0.30 g, 66% yield) as a white solid: mp 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 2H) 8.15 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 4.14 (t, J =

6.4 Hz, 2H), 4.06 (t, *J* = 6.8 Hz, 2H), 1.90-1.70 (m, 4H), 1.55-1.40 (m, 4H), 1.40-1.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 157.6, 151.0, 143.8, 129.2, 115.5, 114.4, 75.8 (t, *J* = 3 Hz), 69.0, 29.8, 29.1, 29.0, 25.8, 25.5; LRMS (EI) *m/z* 482 (M+, 76), 188 (100), 69 (33), 55 (26).



QL20-*m/n-x*F

General procedure for the synthesis of 2-(4-(1-alkyloxy)phenyl)-5-(*n*-(*x*-fluoro-phenoxy)-1-alkyloxy)pyrimidine (QL20-*m*/*n*-*x*F). Under a N_2 atmosphere, **4(*n*-*x*)** (0.192 mmol) was combined with cesium carbonate (94 mg, 0.29 mmol) in dry acetonitrile (40 mL). After stirring for 5 min, the appropriate 1-bromoalkane (0.29 mmol) was added to the mixture, which was heated to reflux overnight. After cooling, the mixture was concentrated, dissolved in EtOAc (40 mL) and washed with 10% aq HCl (50 mL). The aqueous layer was extracted with EtOAc (2 × 40 mL) and the combined organic extracts were washed with sat aq $NaHCO_3$, water, brine, dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (0%-20% EtOAc/Hexane) gave the product, which was recrystallized from acetonitrile and then from hexanes to give a white solid.

5-(8-(2-Fluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL20-8/8-2F). White solid, 95% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, *J* = 8.8 Hz, 2H), 7.12-7.02 (m, 2H), 7.00-6.94 (m, 3H), 6.91-6.84 (m, 1H), 4.08 (t, *J* = 6.4 Hz, 2H), 4.03 (m, 4H), 1.90-1.75 (m, 6H), 1.58-1.22 (m, 18H), 0.90 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.7, 152.8 (d, *J* = 246 Hz), 151.0, 147.1 (d, *J* = 12 Hz), 143.8, 130.0, 128.9, 124.2 (d, *J* = 4 Hz), 120.8 (d, *J* = 7 Hz), 116.1 (d, *J* = 18 Hz), 114.9 (d, *J* = 2 Hz), 114.4, 69.3, 68.9, 68.1, 31.8, 29.4, 29.3, 29.23, 29.21, 29.18, 29.1, 26.0, 25.9, 25.8, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 188 (46), 69 (18); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$ 522.3257, found 522.3271.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.52; H, 8.21; N, 5.25.

5-(8-(3-Fluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL20-8/8-3F). White solid, 90% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, *J* = 9.1 Hz, 2H), 7.21 (td, *J* = 8.2, 7.1 Hz, 1H), 6.98 (d, *J* = 9.1 Hz, 2H), 6.72-6.57 (m, 3H), 4.09 (t, *J* = 6.4 Hz, 2H), 4.02 (t, *J* = 6.7 Hz, 2H), 3.95 (t, *J* = 6.6 Hz, 2H), 1.92-1.73 (m, 6H), 1.57-1.24 (m, 18H), 0.90 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (d, *J* = 246 Hz), 160.7, 160.5 (d, *J* = 11 Hz), 157.7, 151.0, 143.8, 130.1 (d, *J* = 10 Hz), 130.1, 129.0, 114.4, 110.3 (d, *J* = 3 Hz), 107.2 (d, *J* = 22 Hz), 102.1 (d, *J* = 25 Hz), 68.9, 68.2, 68.1, 31.8, 29.4, 29.26, 29.23, 29.1, 26.04, 25.94, 25.8, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 410 (11), 188 (50); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$ 522.3257, found 522.3245.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.24; H, 8.22; N, 5.31.

5-(8-(4-Fluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL20-8/8-4F). White solid, 73% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, *J* = 8.8 Hz, 2H), 7.01-6.93 (m, 4H), 6.88-6.78 (m, 2H), 4.09 (t, *J* = 6.6 Hz, 2H), 4.02 (t, *J* = 6.6 Hz, 2H), 3.92 (t, *J* = 6.6 Hz, 2H), 1.90-1.72 (m, 6H), 1.56-1.21 (m, 18H), 0.90 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 157.8 (d, *J* = 237.9 Hz), 158.4, 155.9 (d, *J* = 2.2 Hz), 151.7, 144.5, 130.7, 129.6, 115.7 (d, *J* = 23 Hz), 115.4 (d, *J* = 7 Hz), 115.1, 69.5, 69.2, 68.8, 32.5, 30.0, 29.93, 29.91,

29.8, 26.7, 26.6, 26.5, 23.3, 14.8; LRMS (EI) *m/z* 522 (M+, 100), 188 (50), 112 (12), 69 (12); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$ 522.3257, found 522.3243.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.31; H, 8.31; N, 4.98.

2-(4-(1-Decyloxy)phenyl)-5-(6-(2-fluorophenoxy)-1-hexyloxy)pyrimidine (QL20-10/6-2F). White solid, 56% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, J = 9.1 Hz, 2H), 7.11-7.03 (m, 2H), 7.00-6.94 (m, 3H), 6.92-6.85 (m, 1H), 4.10 (t, J = 6.4 Hz, 2H), 4.06 (t, J = 6.4 Hz, 2H), 4.02 (t, J = 6.7 Hz, 2H), 1.93-1.76 (m, 6H), 1.62-1.24 (m, 18H), 0.89 (t, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.7, 152.8 (d, J = 239 Hz), 151.0, 147.1 (d, J = 11 Hz), 143.8, 130.1, 128.9, 124.2 (d, J = 4 Hz), 121.0 (d, J = 7 Hz), 116.2 (d, J = 18 Hz), 115.0 (d, J = 2 Hz), 114.4, 69.2, 68.7, 68.1, 31.9, 29.6, 29.5,, 29.4, 29.3, 29.3, 29.1, 29.0, 26.0, 25.7, 25.6, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 382 (13), 188 (48), 112 (10), 83 (18); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$ 522.3257, found 522.3257.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.77; H, 8.33; N, 4.95.

2-(4-(1-Decyloxy)phenyl)-5-(6-(3-fluorophenoxy)-1-hexyloxy)pyrimidine (QL20-10/6-3F). White solid, 39% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, J = 9.1 Hz, 2H), 7.22 (td, J = 8.2, 7.2 Hz, 1H), 6.98 (d, J = 9.1 Hz, 2H), 6.74-6.58 (m, 3H), 4.10 (t, J = 6.3 Hz, 2H), 4.02 (t, J = 6.6 Hz, 2H), 3.97 (t, J = 6.4 Hz, 2H), 1.93-1.76 (m, 2H), 1.62-1.53 (m, 4H), 1.53-1.20 (m, 18H), 0.89 (t, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 161.4 (d, J = 208 Hz), 160.6 (d, J = 22 Hz), 157.7, 151.0, 143.8, 130.1 (d, J = 10 Hz), 130.0, 129.0, 114.4, 110.3 (d, J = 3 Hz), 107.3 (d, J = 21 Hz), 102.1 (d, J = 26 Hz), 68.7, 68.1, 68.0, 31.9, 29.6, 29.5, 29.4, 29.3, 29.25, 29.1, 29.0, 26.0, 25.8, 25.7, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 382 (33), 188 (80), 83 (23), 55 (26); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$ 522.3258, found 522.3244.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.30; H, 8.33; N, 5.24

2-(4-(1-Decyloxy)phenyl)-5-(6-(4-fluorophenoxy)-1-hexyloxy)pyrimidine (QL20-10/6-4F). White solid, 71% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, J = 8.8 Hz, 2H), 7.02-6.92 (m, 4H), 6.88-6.78 (m, 2H), 4.10 (t, J = 6.3 Hz, 2H), 4.03 (t, J = 6.6 Hz, 2H), 3.94 (t, J = 6.3 Hz, 2H), 1.95-1.75 (m, 6H), 1.59-1.22 (m, 18H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.1 (d, J = 239 Hz), 157.8, 155.2 (d, J = 2 Hz), 151.0, 143.8, 130.0, 129.0, 115.7 (d, J = 23 Hz), 115.4 (d, J = 7 Hz), 114.4, 68.7, 68.4, 68.1, 31.9, 29.6, 29.5, 29.4, 29.3, 29.25, 29.2, 29.1, 26.0, 25.8, 25.7, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 382 (17), 188 (50), 112 (10), 83 (16), 55 (19); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$ 522.3257, found 522.3243.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.93; H, 8.33; N, 4.99.

2-(4-(1-Dodecyloxy)phenyl)-5-(4-(2-fluorophenoxy)-1-butyloxy)pyrimidine (QL20-12/4-2F). White solid, 58% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 8.28 (d, J = 8.8 Hz, 2H), 7.12-7.03 (m, 2H), 7.01-6.95 (m, 3H), 6.94-6.88 (m, 1H), 4.20 (t, J = 5.8 Hz, 2H), 4.14 (t, J = 5.8 Hz, 2H), 4.03 (t, J = 6.6 Hz, 2H), 2.13-2.01 (m, 4H), 1.86-1.77 (m, 2H), 1.53-1.42 (m, 2H), 1.42-1.10 (m, 16H), 0.89 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.8, 152.8 (d, J = 245 Hz), 150.9, 146.9 (d, J = 10 Hz), 143.8, 130.0, 129.0, 124.3 (d, J = 4 Hz), 121.2 (d, J = 7 Hz), 116.2 (d, J = 18 Hz), 115.0 (d, J = 2 Hz), 114.4, 68.8, 68.4, 68.1, 31.9, 29.7,

29.6, 29.6, 29.56, 29.4, 29.33, 29.25, 26.0, 25.8, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 188 (28), 167 (80), 125 (48); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$, 522.3257, found 522.3257.

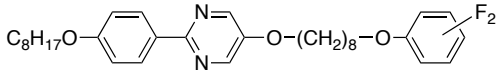
Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.81; H, 8.38; N, 5.05.

2-(4-(1-Dodecyloxy)phenyl)-5-(4-(3-fluorophenoxy)-1-butyloxy)pyrimidine (QL20-12/4-3F). White solid, 38% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 8.28 (d, J = 8.8 Hz, 2H), 7.23 (td, J = 8.3, 7.0 Hz, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.73-6.57 (m, 3H), 4.18 (t, J = 5.8 Hz, 2H), 4.07-3.99 (m, 4H), 2.10-1.96 (m, 6H), 1.88-1.74 (m, 6H), 1.53-1.19 (m, 12H), 0.89 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (d, J = 245 Hz), 160.8, 160.3 (d, J = 11 Hz), 157.9, 150.9, 143.8, 130.2 (d, J = 10 Hz), 130.0, 129.0, 114.5, 110.3 (d, J = 3 Hz), 107.6 (d, J = 22 Hz), 102.2 (d, J = 25 Hz), 68.4, 68.1, 67.6, 31.9, 29.7, 29.63, 29.60, 29.57, 29.4, 29.3, 29.3, 26.04 (s), 25.99, 25.7, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 188 (16), 167 (80), 125 (43); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$, 522.3257, found 522.3271.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.28; H, 7.98; N, 5.30.

2-(4-(1-Dodecyloxy)phenyl)-5-(4-(4-fluorophenoxy)-1-butyloxy)pyrimidine (QL20-12/4-4F). White solid, 82% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 8.28 (d, J = 8.8 Hz, 2H), 7.01-6.95 (m, 4H), 6.87-6.81 (m, 2H), 4.18 (t, J = 5.9 Hz, 2H), 4.05-4.00 (m, 4H), 2.10-1.95 (m, 4H), 1.86-1.76 (m, 2H), 1.54-1.24 (m, 18H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 157.9, 157.3 (d, J = 238 Hz), 155.0 (d, J = 2 Hz), 150.9, 143.8, 130.0, 129.0, 115.8 (d, J = 23 Hz), 115.4 (d, J = 7 Hz), 114.5, 68.5, 68.1, 67.9, 31.9, 29.7, 29.63, 29.60, 29.57, 29.41, 29.34, 29.27, 26.04, 26.02, 25.8, 22.7, 14.1; LRMS (EI) *m/z* 522 (M+, 100), 188 (20), 167 (94), 125 (53); HRMS (EI) *m/z* calcd for $C_{32}H_{43}FN_2O_3$ 522.3257, found 522.3243.

Anal. calcd for $C_{32}H_{43}FN_2O_3$: C, 73.53; H, 8.29; N, 5.36. Found: C, 73.73; H, 7.97; N, 5.21.



QL22-8/8-*x,y*F_2

General procedure for the synthesis of 5-(8-(*x,y*-difluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL22-8/8-*x,y*F_2). The general procedure described for the synthesis of **QL20-*m*/*n*-*x*F** was repeated with **5(*x,y*)** (82 mg, 0.192 mmol), cesium carbonate (94 mg, 0.29 mmol) and 1-bromooctane (56 mg, 0.29 mmol) to give the product as a white solid.

5-(8-(2,3-Difluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL22-8/8-2,3F_2). White solid, 58% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 8.29 (d, J = 8.8 Hz, 2H), 6.97-6.94, (m, 3H), 6.81-6.71 (m, 2H), 4.10 (t, J = 6.4 Hz, 2H), 4.07-4.01 (m, 4H), 1.91-1.78 (m, 6H), 1.58-1.47 (m, 6H), 1.46-1.26 (m , 12H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.7, 151.1, 151.5 (dd, J = 247, 10 Hz), 148.9 (dd, J = 8, 3 Hz), 143.8, 141.5 (dd, J = 247, 14 Hz), 130.1, 129.0, 123.1 (dd, J = 9, 5 Hz), 114.4, 109.9 (d, J = 3 Hz), 109.0 (d, J = 18 Hz), 69.8, 68.9, 68.1, 31.8, 29.4, 29.28, 29.25, 29.2, 29.13, 29.11, 26.06, 25.84, 25.81, 22.7, 14.1; LRMS (EI) *m/z* 540 (M+, 100), 428 (13), 188 (31), 69 (12); HRMS (EI) *m/z* calcd for $C_{32}H_{42}F_2N_2O_3$ 540.3164, found, 540.3160.

Anal. calcd for $C_{32}H_{42}F_2N_2O_3$: C, 71.08; H, 7.83; N, 5.18. Found: C, 71.03; H, 7.81; N, 5.08.

5-(8-(2,4-Difluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL22-8/8-2,4F$_2$). White solid, 60% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 6.94-6.82 (m, 2H), 6.80-6.74 (m, 1H), 4.08 (t, J = 6.4 Hz, 2H), 4.03 (t, J = 6.8 Hz, 2H), 4.00 (t, J = 6.8 Hz, 2H), 1.91-1.75 (m, 6H), 1.57-1.24 (m, 18H), 0.93 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.7, 156.4 (dd, J = 242, 10 Hz), 152.6 (dd, J = 250, 12 Hz), 151.0, 143.8, 143.7 (dd, J = 11, 4 Hz), 130.1, 129.0, 115.8 (dd, J = 10, 4 Hz), 114.4, 110.2 (dd, J = 23, 4 Hz), 104.8 (dd, J = 27, 23 Hz), 70.3, 68.9, 68.1, 31.8, 29.4, 29.3, 29.22, 29.20, 29.1, 26.0, 25.83, 25.78, 22.6, 14.1; LRMS (EI) m/z 540 (M+, 100), 428 (13), 188 (58), 130 (51), 69 (33), 55 (30); HRMS (EI) m/z calcd for $C_{32}H_{42}F_2N_2O_3$ 540.3164, found 540.3173.

Anal. calcd for $C_{32}H_{42}F_2N_2O_3$: C, 71.08; H, 7.83; N, 5.18. Found: C, 71.20; H, 7.91; N, 5.07.

5-(8-(2,5-Difluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL22-8/8-2,5F$_2$). White solid, 78% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.27 (d, J = 8.8 Hz, 2H), 7.05-6.95 (m, 3H), 6.69 (ddd, J = 9.9, 6.8, 3.0 Hz, 1H), 6.52-6.61 (m, 1H), 4.09 (t, J = 6.4 Hz, 2H), 4.03 (t, J = 6.8 Hz, 2H), 4.00 (t, J = 6.6 Hz, 2H), 1.89-1.77 (m, 6H), 1.55-1.25 (m, 18H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 158.8 (dd, J = 242, 2 Hz), 157.7, 151.1, 149.0 (dd, J = 242, 3 Hz), 147.8 (dd, J = 12, 10 Hz), 143.8, 130.1, 129.0, 116.0 (dd, J = 20, 10 Hz), 114.4, 106.2 (dd, J = 24, 7 Hz), 102.6 (dd, J = 27, 2 Hz), 69.5, 68.9, 68.0, 31.8, 29.3, 29.24, 29.20, 29.17, 29.10, 29.0, 26.0, 25.9, 25.8, 22.6, 14.1; LRMS (EI) m/z 540 (M+, 100), 428 (13), 188 (58), 130 (51), 69 (33), 55 (30); HRMS (EI) m/z calcd for $C_{32}H_{42}F_2N_2O_3$ 540.3164, found 540.3173.

Anal. calcd for $C_{32}H_{42}F_2N_2O_3$: C, 71.08; H, 7.83; N, 5.18. Found: C, 70.90; H, 8.00; N, 5.22.

5-(8-(2,6-Difluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL22-8/8-2,6F$_2$). White solid, 70% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 8.29 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 6.96-6.85 (m, 3H), 4.15 (t, J = 6.6 Hz, 2H), 4.10 (t, J = 6.6 Hz, 2H), 4.04 (t, J = 6.6 Hz, 2H), 1.91-1.74 (m, 6H), 1.60-1.26 (m, 18H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.7, 156.4 (dd, J = 248, 5 Hz) 151.1, 143.8, 135.8 (t, J = 14 Hz), 130.1, 129.0, 122.5 (t, J = 10 Hz), 114.4, 112.1 (dd, J = 17, 7 Hz), 74.7 (t, J = 3 Hz), 68.9, 68.1, 31.8, 29.9, 29.4, 29.3, 29.24, 29.21, 29.16, 29.10, 26.1, 25.8, 25.6, 22.7, 14.1; LRMS (EI) m/z 540 (M+, 100), 428 (10), 188 (50), 69 (11); HRMS (EI) m/z calcd for $C_{32}H_{42}F_2N_2O_3$ 540.3163, found 540.3169.

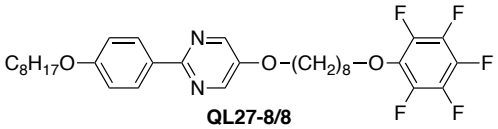
Anal. calcd for $C_{32}H_{42}F_2N_2O_3$ 71.08; H, 7.83; N, 5.18. Found: C, 71.33; H, 7.65; N, 5.21.

5-(8-(3,4-Difluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL22-8/8-3,4F$_2$). White solid, 70% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, J = 8.8 Hz, 2H), 7.05 (ddd, J = 10.1, 9.1, 8.7 Hz, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.75-6.65 (m, 1H), 6.63-6.54 (m, 1H), 4.09 (t, J = 6.4 Hz, 2H), 4.03 (t, J = 6.7 Hz, 2H), 3.90 (t, J = 6.4 Hz, 1H), 1.91-1.70 (m, 8H), 1.55-1.27 (m, 18H), 0.90 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.7, 155.4 (dd, J = 8, 3 Hz), 151.0, 150.5 (dd, J = 245, 14 Hz), 143.8, 144.9 (dd, J = 239, 16 Hz), 130.1, 129.0, 117.1 (dd, J = 18, 2 Hz) 114.4, 109.8 (dd, J = 5, 4 Hz), 104.0 (d, J = 20 Hz), 68.9, 68.7, 68.1, 31.8, 30.9, 29.4, 29.3, 29.2, 29.1, 26.0, 25.9, 25.8, 22.6, 14.1; LRMS (EI) m/z 540 (M+, 100), 428 (14), 188 (55), 130 (18), 69 (15), 55 (14); HRMS (EI) m/z calcd for $C_{32}H_{42}F_2N_2O_3$ 540.3163, found 540.3173.

Anal. calcd for $C_{32}H_{42}F_2N_2O_3$: C, 71.08; H, 7.83; N, 5.18. Found: C, 71.13; H, 7.88; N, 4.84.

5-(8-(3,5-Difluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL22-8/8-3,5F$_2$). White solid, 66% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.28 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 6.42 (d, J = 9.6 Hz, 3H), 4.09 (t, J = 6.4 Hz, 2H), 4.03 (t, J = 6.6 Hz, 2H), 3.93 (t, J = 6.6 Hz, 2H), 1.92-1.72 (m, 6H), 1.55-1.45 (m, 6H), 1.45-1.39 (m, 6H), 1.38-1.27 (m, 6H), 0.90 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (dd, J = 246, 15 Hz), 161.1 (t, J = 14 Hz), 160.7, 157.7, 151.0, 143.8, 130.1, 129.0, 114.4, 98.2 (dd, J = 19, 7 Hz), 96.0 (t, J = 26 Hz), 68.9, 68.6, 68.1, 31.8, 29.4, 29.3, 29.22, 29.19, 29.1, 28.9, 26.0, 25.9, 25.8, 22.6, 14.1; LRMS (EI) m/z 540 (M+, 100), 188 (50), 130 (20), 69 (21), 55 (14); HRMS (EI) m/z calcd for $C_{32}H_{42}F_2N_2O_3$ 540.3163, found 540.3157.

Anal. calcd for $C_{32}H_{42}F_2N_2O_3$: C, 71.08; H, 7.83; N, 5.18. Found: C, 71.44; H, 8.26; N, 5.01.



QL27-8/8

5-(8-(2,3,4,5,6-Pentafluorophenoxy)-1-octyloxy)-2-(4-(1-octyloxy)phenyl)pyrimidine (QL27-8/8). The general procedure described for the synthesis of **QL20-*m*/*n*-*x*F** was repeated with **6** (95 mg, 0.20 mmol), cesium carbonate (96 mg, 0.30 mmol) and 1-bromooctane (84 mg, 0.30 mmol) to give **QL27-8/8** (108 mg, 92% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 8.28 (d, J = 8.6 Hz, 2H), 6.99 (d, J = 9.1 Hz, 2H), 4.17 (t, J = 6.4 Hz, 2H), 4.10 (t, J = 6.4 Hz, 2H), 4.04 (t, J = 6.6 Hz, 2H), 1.94-1.74 (m, 6H), 1.59-1.25 (m, 18H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.7, 151.1, 143.8, 130.1, 129.0, 114.5, 75.8 (t, J = 3 Hz), 68.9, 68.1, 31.8, 29.8, 29.4, 29.28, 29.25, 29.21, 29.14, 29.10, 26.1, 25.8, 25.5, 22.7, 14.1; LRMS (EI) m/z 594 (M+, 100), 482 (38), 188 (97), 149 (17), 97 (16), 85 (12), 83 (14), 81 (12), 71 (18), 69 (32), 57 (35), 55 (32); HRMS (EI) m/z calcd for $C_{32}H_{39}F_5N_2O_3$ 594.2888, found 594.2881.

Anal. calcd for $C_{32}H_{39}F_5N_2O_3$: C, 64.63; H, 6.61; N, 4.71. Found: C, 64.39; H, 6.78; N, 4.78.

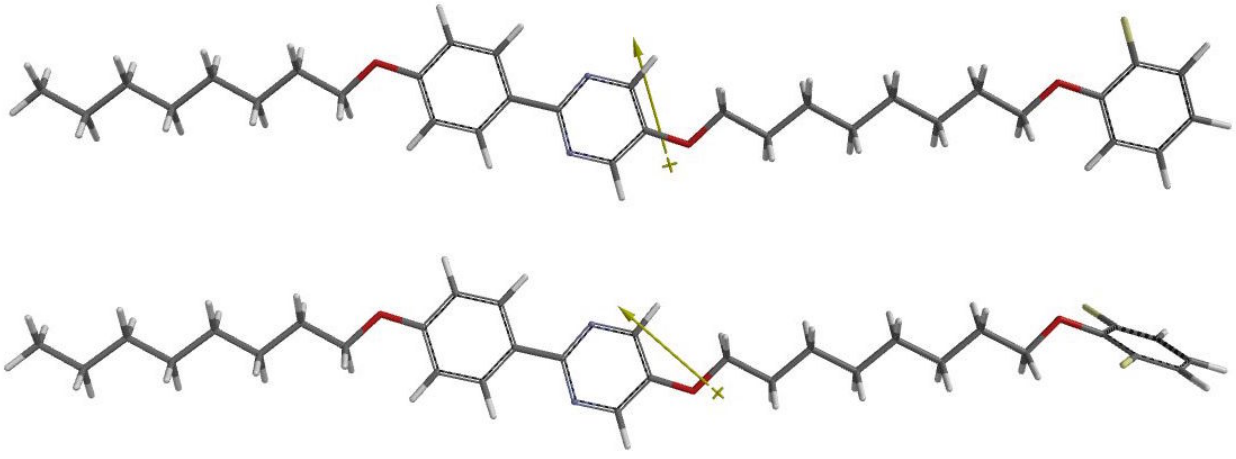


Figure S1. Molecular models of **QL20-8/8-2F** (top) and **QL22-8/8-2,6F$_2$** (bottom) minimized at the B3LYP/6-31G* level (Spartan'14, Wavefunction Inc.) showing the orientation of the molecular dipole moment (2.6 D for **QL20-8/8-2F** and 2.8D for **QL22-8/8-2,6F$_2$**).

Table S1. Potential energies of association ΔE without BSSE correction for unsubstituted and fluoro-substituted *n*-butyloxybenzene dimers in parallel and antiparallel geometries.[a]

	ΔE (kcal mol^{-1})[b]			
X	*Parallel-Syn*	*Parallel-Anti*	*Antiparallel-Syn*	*Antiparallel-Anti*
H	–15.5		–14.1	
2F	–16.4	–17.4	–13.8	–15.9
3F	–15.5	–15.8	–15.3	–15.7
4F	–17.6		–18.4	

[a] Based on energies obtained at the MP2/6-311++G**//MP2/6-31+G** level of theory. [b] Calculated as the difference between the energy of the associated dimer and twice the energy of one molecule obtained at the MP2/6-311++G**//MP2/6-31+G** level.