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Supporting Information

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The First F···H-N Hydrogen Bonding-Driven Foldamers: New Efficient Receptors for Dialkylammoniums

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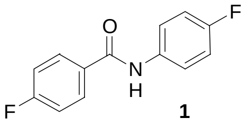
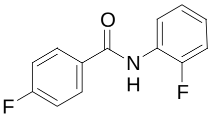
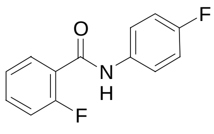
General methods. All reactions were carried out under a dry nitrogen atmosphere. Melting points are uncorrected. All solvents were dried before use following standard procedures. Unless otherwise indicated, all starting materials were obtained from commercial suppliers and were used without further purification. Analytical thin-layer chromatography (TLC) was performed on 0.2 mm silica 60 coated on glass plates with F_{254} indicator. The ^{1}H NMR spectra were recorded on 500, or 300 MHz spectrometers in the indicated solvents. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standards (chloroform: δ 7.27 ppm; DMSO: δ 2.49 ppm). The ^{19}F NMR spectra were recorded on 282 MHz spectrometer in the indicated solvents. Chemical shifts are expressed in parts per million (δ) using residual $CFCl_3$ as internal standards. Mass spectra (EI, ESI, MALDI-TOF) were obtained on a Varian SATURN 2000 or FTMS-7 spectrometer. X-ray analysis data were collected on an SMART APEX diffractometer. Circular dichroism spectra were recorded on a J820 CD spectrometer. Elemental analysis was carried out at the SIOC analytical center.


1

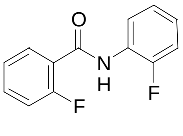
Compound 1. To a stirred solution of 4-fluoroaniline (0.11 g, 1.00 mmol) and triethylamine (0.5 mL) in chloroform was added a solution of 4-fluorobenzoyl chloride (0.16 g, 1.00 mmol) in chloroform (5 mL). The solution was added at room temperature for 1 h. After workup, the crude product was purified by recrystallization from ethanol. The desired compound was obtained as a white powder (0.19 g, 81%). Mp. 179-181 °C. ^{1}H NMR ($CDCl_3$): δ 7.90–7.86 (m, 2 H), 7.78 (br, 1 H), 7.61–7.59 (m, 2 H), 7.21–7.04 (m, 4 H). ^{19}F NMR ($CDCl_3$): δ -107.6 – -117.6 (m, 1 F), -117.8–-117.8 (m, 1 F). ESI-MS: *m/z* 234 [M + 1]$^+$. Anal. Calcd for $C_{13}H_9F_2NO$: C 66.95, H 3.89, N 6.01. IR (cm^{-1}): 3360, 1653, 1611, 1529, 1407, 1097, 834, 761. Found: C 66.92, H 3.87, N 5.82.


2

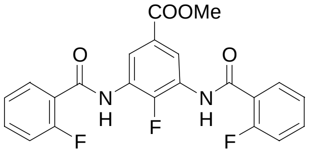
Compound 2. Yield 87%. White powder. Mp. 118-119 °C. ^{1}H NMR ($CDCl_3$): δ 8.47 -8.42 (m, 1 H), 8.00 (br, 1 H), 7.94-7.89 (m, 2 H), 7.23-7.09 (m, 5 H). ^{19}F NMR ($CDCl_3$): δ -107.3– -107.2 (m, 1 F), -131.8 – -131.8 (m, 1 F). EI-MS: *m/z* 234 [M + 1]$^+$.


3

Compound 3. Yield 85%. White powder. ^{1}H NMR ($CDCl_3$): δ 8.47 (d, *J* = 15.3 Hz, 1 H), 8.21–8.15 (m, 1 H), 7.67–7.62 (m, 2 H), 7.58–7.51 (m, 1 H), 7.37–7.32 (m, 1 H), 7.24–7.16 (m, 1 H), 7.12–7.05 (m, 2 H). ^{19}F NMR ($CDCl_3$): δ -113.6 – -113.5 (m, 1 F), -117.8 – -117.7 (m, 1 F). ESI-MS: *m/z* 234 [M + H]$^+$. Anal. Calcd for $C_{13}H_9F_2NO$: C 66.95, H 3.89, N 6.01. Found: C 66.72, H 3.43, N 5.95.

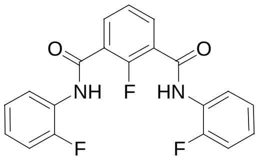

4

Compound 4. Yield 83%. White powder. ^{1}H NMR (CDCl$_3$): δ 8.83 (d, *J* = 17.1 Hz, 1 H), 8.53-8.47 (m, 1 H), 8.22-8.16 (m, 1 H), 7.59-7.51 (m, 1 H), 7.36-7.31 (m, 1 H), 7.24-7.09 (m, 4 H). ^{19}F NMR (CDCl$_3$): δ -13.43 – -113.26 (m, 1 F), -131.26 – -131.17 (m, 1 F). IR (cm^{-1}): 3408, 1612, 1544, 1481, 1458, 1333, 1286, 1261, 1211, 1087, 821, 784, 753, 602. EI-MS: *m/z* 233 [M]$^+$.



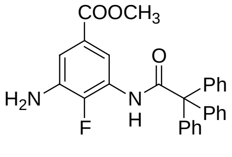
5

Compound 5. To a stirred solution of methyl 4-fluoro-3,5-diaminobenzoate (0.35 g, 1.90 mmol) and triethylamine (0.90 mL. 6.50 mmol) in dichloromethane (20 mL) was added a solution of 2-fluorobenzoyl chloride (0.62 g, 4.00 mmol) in dichloromethane (10 mL) at 0 °C. The mixture was stirred at room temperature for 1 h and then washed with hydrochloric acid (0.5 N, 5 mL × 5), water (10 mL), brine (10 mL), dried over sodium sulfate. Upon removal of the solvent, the crude product was purified by column chromatography (chloroform/methanol 50:1) to give compound 5 as a white solid (0.71 g, 87%). Mp. 199-200 °C. ^{1}H NMR (CDCl$_3$): δ 8.92 (d, *J* = 7.8 Hz, 2 H), 8.84 (d, *J* = 17.1 Hz, 2 H), 8.26 – 8.21 (m, 2 H), 7.61 – 7.55 (m, 2 H), 7.39 – 7.34 (m, 2 H), 7.24 – 7.20 (m, 2 H), 3.95 (s, 3 H). ^{19}F NMR (CDCl$_3$): δ -113.36 – -113.21 (m, 2 F) , -139.42 (s, 1 F). IR (cm^{-1}): 3456, 3322, 1722, 1689, 1658, 1612, 1525, 1481, 1445, 1324, 769, 751. EI-MS: *m/z* 428 [M]$^+$. Anal. Calcd for $C_{22}H_{15}F_3N_2O_4$: C 61.69, H 3.53, N 6.54. Found: C 61.58, H 3.63, N 6.47.



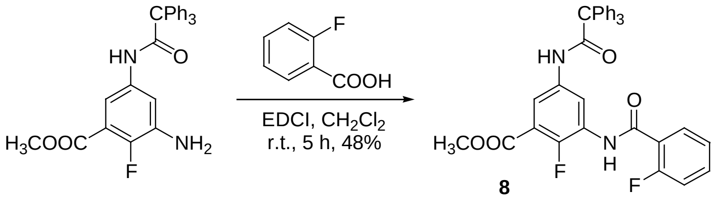
6

Compound 6. This compound was prepared as a white solid (0.31 g, 83%) from the reaction of 2-fluoroaniline (0.23 g, 2.00 mmol) and 2-fluoro-isophthalic dichloride (0.20 g, 1.00 mmol) in dichloromethane (20 mL) in the presence of triethyl amine (0.5 mL, 3.5 mmol). Mp. 168-171 °C. ^{1}H NMR (CDCl$_3$): δ 8.57 (d, *J* = 13.2 Hz, 2 H), 8.51 (t, *J* = 7.8 Hz, 2 H), 8.32 (t, *J* = 7.5 Hz, 2 H), 7.52 (t, *J* = 7.5 Hz, 1 H), 7.25-7.13 (m, 6 H). ^{19}F NMR (CDCl$_3$): δ -117.1 (s, 1 F), -130.9 – -130.8 (m, 2 F). IR (cm^{-1}): 3429, 2924, 2853, 1685, 1664, 1618, 1542, 1458, 1326, 757. MALDI-MS: *m/z* 371 [M + H]$^+$. Anal. Calcd for $C_{20}H_{13}F_3N_2O_2$: C 64.87, H 3.54, N 7.56. Found: C 64.87, H 3.50, N 7.64.



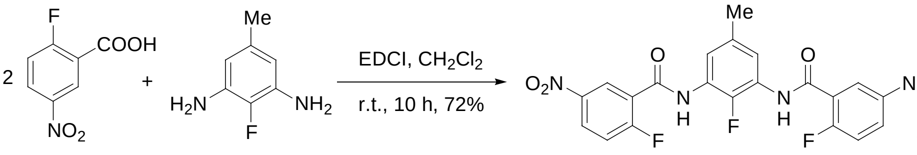
7

Compound 7. To a stirred solution of methyl 4-fluoro-3,5-diaminobenzoate (0.40 g, 2.17 mmol) and triethylamine (0.40 mL, 2.90 mmol) in dichloromethane (15 mL) was added a solution of triphenylacetic chloride (0.66 g, 2.17 mmol) in dichloromethane (20 mL) at room temperature. The mixture was stirred at room temperature for another 30 min. After workup, the crude product was purified by column chromatography (dichloromethane/methanol 30:1) to give compound 7 as a yellow solid (0.50 g, 50%). Mp. 190-192 °C. ^{1}H NMR (CDCl$_3$): δ 8.43 (d, d, J_1 = 2.4 Hz, J_2 = 4.5 Hz, 1 H), 7.72 (d, *J* = 2.4 Hz, 2 H), 7.38 – 7.24 (m, 16 H), 3.88 (s, 3 H), 3.76 (s, 2 H). ^{19}F NMR (CDCl$_3$): δ -146.6 – -146.4 (m, 1 F). ESI-MS: *m/z* 455 [M + H]$^+$. Anal. Calcd for $C_{28}H_{23}FN_2O_3$: C 73.99, H 5.10, N 6.16. Found: 73.68, H 4.98, N 5.99.



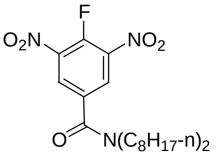
8

Compound 8. White solid. Mp. 234-236 °C. ^{1}H NMR ($CDCl_3$): δ 8.88 (d, d, J_1 = 3.6 Hz, J_2 = 13.5 Hz, 1 H), 8.47 (d, d, J_1 = 3.0 Hz, J_2 = 3.0 Hz, 1 H), 8.10 – 8.03 (m, 2 H), 7.53 – 7.46 (m, 1 H), 7.41 (s, 1 H), 7.32 – 7.18 (m, 16 H), 7.15 – 7.18 (m, 1 H). ^{19}F NMR ($CDCl_3$): δ -113.1 – -113.0 (m, 1 F), -133.4 – -133.3 (m, 1 F). EI-MS: *m/z* 576 $[M]^+$. Anal. Calcd for $C_{35}H_{26}F_2N_2O_4$: C 72.91, H 4.55, N 4.86. Found: C 72.67, H 4.90, N 4.73.



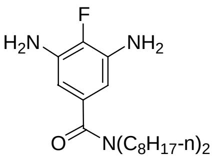
9

Compound 9. Pale yellow solid. Mp. > 250 °C. ^{1}H NMR (DMSO-*d*$_6$): δ 10.53 (br, 2 H), 8.54-8.45 (m, 4 H), 7.66-7.52 (m, 4 H), 2.33 (s, 3 H). ^{19}F NMR ($CDCl_3$): δ -104.2 (br, 2 F), -136.3 (br, 1 F). ESI-MS: *m/z* 475 $[M + H]^+$.



13

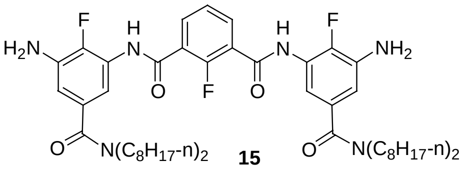
Compound 13. A solution of **12** (2.78 g, 12.0 mmol), oxalyl dichloride (2 mL, 24.8 mmol), and DMF (0.1 mL) in THF was stirred at room temperature for 0.5 h and then concentrated in vacuo. The resulting oily residue was dissolved in THF (40 mL) and the solution was cooled to –10 °C. Then, a solution of dioctyl amine (0.29 g, 12.0 mmol) and triethyl amine (4 mL) in THF (50 mL) was added dropwise with stirring. Stirring was continued for another 1 h and the solvent was removed under reduced pressure. The resulting residue was triturated in chloroform (50 mL). The organic solution was washed with aqueous potassium carbonate (1 N, 15 mL), water (15 mL), brine (15 mL), and then dried over sodium sulfate. Upon removal of the solvent in vacuo, the crude product was chromatographed with chloroform-methanol (40:1), to afford **13** as a yellow oil (3.21 g, 59%). ^{1}H NMR ($CDCl_3$): δ 8.35 (d, *J* = 6.0 Hz, 2 H), 3.48 (t, *J* = 5.4 Hz, 2 H), 3.20 (t, *J* = 5.4 Hz, 2 H), 0.89 (t, *J* = 2.1 Hz, 6 H). ^{19}F NMR ($CDCl_3$): δ -13.7 (t, *J* = 6.0 Hz, 2 H). This compound is unstable and was used for next step immediately after chromatography.



14

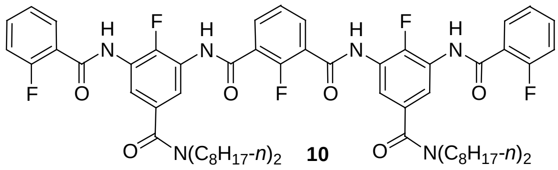
Compound 14. A suspension of **13** (3.00 g) and Pd-C (0.15 g) in methanol (50 mL) and THF (30 mL) was stirred under hydrogen gas (1 atm.) at room temperature for 48 h. The solid was filtered and the filtrate was concentrated under reduced pressure. The crude product was subjected to flash chromatography (chloroform-methanol 20:1) to give **14** as a pale yellow solid (2.46 g, 92%). Mp. 123-125 °C. ^{1}H NMR ($CDCl_3$): δ = 6.17 (d, *J* = 7.8 Hz, 2 H), 3.72 (s, 4 H), 3.44 (t, *J* = 5.4 Hz, 2 H), 3.22 (t, *J* = 5.4 Hz, 2 H), 1.31 (m, 16 H), 0.90 (t, *J* = 5.4 Hz, 6 H). ^{19}F NMR ($CDCl_3$): δ -157.6

(t, *J* = 9.0 Hz). MALDI-MS: *m/z* 394.3 $[M + H]^+$. Anal. Calcd for $C_{23}H_{40}FN_3O$: C 70.19, H 10.24, N 10.68. Found: C 70.53, H 10.03, N 10.32.



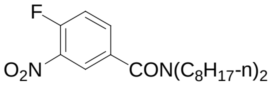
15

Compound 15. To a solution of 2-fluoro-isophthalic acid (0.61 g, 3.30 mmol) in THF (20 mL) was added oxalyl dichloride (1.5 mL, 18.6 mmol) and DMF (0.1 mL), respectively. The solution was stirred at room temperature for 0.5 h and then concentrated in vacuo. The resulting pale yellow solid was dissolved in dichloromethane (60 mL) and to the solution was added a solution of 11 (2.61 g, 6.60 mmol) and triethyl amine (2.00 g, 20.0 mmol) in dichloromethane (20 mL). After stirring for 0.5 h at room temperature, the solution was concentrated under reduced pressure. The resulting residue was triturated with chloroform (50 mL). After workup, the crude product was purified by column chromatography (dichloromethane/methanol 30:1), to afford the required compound as a white solid (0.40 g, 33% based on the consumed **14** and unreacted **14** (1.58 g). Mp. 167-168 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64 (d, *J* = 11.7 Hz, 2 H), 8.27 (t, *J* = 7.5 Hz, 2 H), 7.84 (d, *J* = 4.8 Hz, 2 H), 7.50 (t, *J* = 7.8 Hz, 1 H), 6.64 (d, *J* = 8.1Hz, 2 H), 3.89 (s, 4 H), 3.45 (t, *J* = 6.9 Hz, 4 H), 3.28 (t, *J* = 6.9 Hz, 4 H), 1.35 – 1.31 (m, 32 H), 0.90 – 0.88 (m, 12 H). ^{19}F NMR: -113.1 – -113.0 (m, 2 F), -144.2 (d, *J* = 7.8 Hz, 1 F). MALDI-MS: *m/z* 935 $[M + H]^+$. Anal. Calcd for $C_{54}H_{81}F_3N_6O_4$: C 69.35, H 8.73, N 8.99. Found: C 69.17, H 8.70, N 8.84.



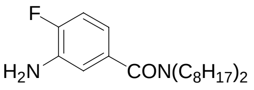
10

Compound 10. To a solution of **15** (0.20 g, 0.22 mmol) and triethyl amine (0.1 mL, 0.07 mmol) in chloroform (10 mL) was added a solution of 2-fluorobenzoyl chloride (80 mg, 0.50 mmol) in chloroform (1 mL). The solution was stirred at room temperature for 1 h. After workup, the crude product was purified by column chromatography (dichloromethane-methanol 25:1). Compound **7** was obtained as a white solid (0.12 g, 47%).



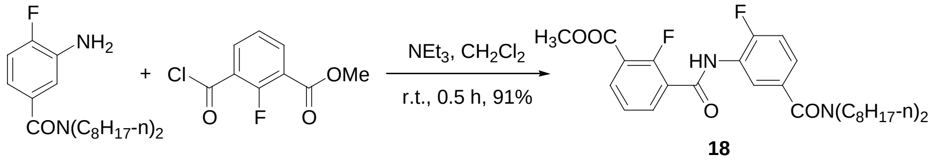
16

Compound 16. This compound was prepared from the reaction of 4-fluoro-3-nitrobenzoyl chloride and dioctylamine in THF in the presence of triethylamine at 0 °C. Yield 45%. Yellow oil. ^{1}H NMR ($CDCl_3$): δ 8.09 (d, d, J_1 = 2.1 Hz, J_2 = 5.1 Hz, 1 H), 7.68 – 7.63 (m, 1 H), 7.37 – 7.26 (m, 1 H), 3.46 (br, 2 H), 3.17 (br, 2 H), 1.64 – 1.19 (m, 24 H), 0.86 (br, 6 H). ^{19}F NMR ($CDCl_3$): δ -116.2 (m, 1 F). ESI-Ms: *m/z* 409 $[M + H]^+$. Anal. Calcd for $C_{23}H_{37}FN_2O_3$: C 67.62, H 9.13, N 6.86. Found: C 67.80, H 9.59, N 7.07.



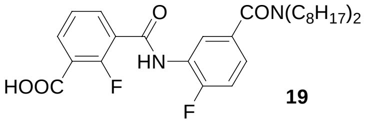
17

Compound 17. A suspension of 16 (1.30 g, 3.18 mmol) and Pd-C (10%, 150 mg) in methanol (30 mL) and THF (30 mL) was stirred under 1 atmosphere of hydrogen gas at room temperature for 24 h. After workup, the crude product was purified by flash chromatography (chloroform/methanol 30:1) to give **17** (1.18 g, 98%) as a liquid. ^{1}H NMR ($CDCl_3$): δ 9.96 – 6.89 (m, 1 H), 6.77 – 6.72 (m, 1 H), 3.86 (br, 2 H), 1.64 – 1.19 (m, 24 H), 3.41 (br, 2 H), 3.16 (br, 2 H), 1.59 – 1.18 (m, 24 H), 0.85 (br, 6 H). ^{19}F NMR ($CDCl_3$): δ -134.7 – -134.7 (m, 1 F). ESI-MS: *m/z* 379 $[M + H]^+$. Anal. Calcd for $C_{23}H_{39}FN_2O$: C 72.97, H 10.38, N 7.40. Found: C 72.75, H 10.38, N 7.40.



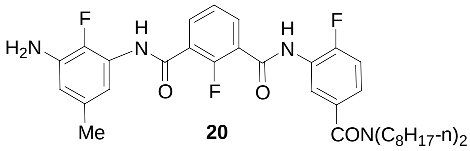
18

Compound 18. Colorless liquid. ^{1}H NMR ($CDCl_3$): δ 8.83 (d, d, J_1 = 3.0 Hz, J_2 = 12.9 Hz, 1 H), 8.56 (d, *J* = 7.8 Hz, 1 H), 8.37 – 8.31 (m, 1 H), 7.60 (m, 2 H), 8.16 – 8.10 (m, 1 H), 7.42 – 7.37 (m, 1 H), 3.98 (s, 3 H), 3.46 (t, *J* = 6.6 Hz, 2 H), 3.23 (t, *J* = 6.6 Hz, 2 H), 1.65 – 1.18 (m, 24 H), 0.88 – 0.83 (m, 6 H). ^{19}F NMR ($CDCl_3$): δ -112.8 – -112.7 (m, 1 F), -129.3 – -129.2 (m, 1 F). ^{13}C NMR ($CDCl_3$): δ 169.8, 160.1, 136.3, 135.8, 133.6, 133.6, 125.5, 124.4, 124.3, 123.3, 123.2, 121.8, 120.1, 114.9, 114.6, 52.3, 31.4, 29.3, 29.0, 28.9, 28.8, 28.7, 28.7, 26.7, 26.2, 22.2, 13.7. LRMS-ESI-MS: *m/z* 559 $[M + H]^+$. HRMS-ESI-MS: *m/z* 559.3342. Calcd for $C_{32}H_{45}F_2N_2O_4$: 559.3355.



19

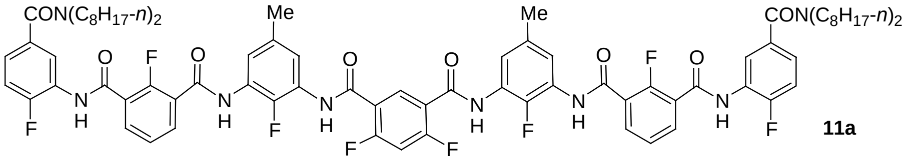
Compound 19. This compound was hydrolyzed quantitatively from **18** with LiOH as base. Mp. 177-179 °C. ^{1}H NMR (DMSO): δ 13.47 (br, 1 H), 10.42 (s, 1 H), 8.02 (t, *J* = 6.6 Hz, 1 H), 7.92 – 7.83 (m, 2 H), 7.42 – 7.31 (m, 1 H), 3.33 (br, 1 H), 3.15 (br, 2 H), 1.52 – 1.11 (m, 24 H), 0.80 (br, 6 H). ^{19}F NMR (DMSO): δ -113.4 (s, 1 F), -122.5 (s, 1 F). ^{13}C NMR (DMSO): δ 171.4, 167.1, 167.0, 165.0, 163.2, 162.1, 158.6, 158.0, 154.7, 136.5, 136.4, 135.9, 135.9, 128.0, 128.0, 127.8, 126.7, 126.7, 125.2, 122.5, 122.4, 118.4, 118.1, 11.2, 50.8, 46.7, 46.7, 46.6, 33.9, 33.6, 33.5, 31.1, 30.8, 30.6, 30.4, 30.7, 30.3, 30.3, 29.4, 28.8, 28.7, 28.9, 28.6, 28.3, 28.3, 24.4, 24.3, 23.4, 16.8, 16.3, 13.4. LRMS-ESI-MS: *m/z* 545 $[M + H]^+$. HRMS-ESI-MS: *m/z* 545.3185. Calcd for $C_{31}H_{43}F_2N_2O_4$: 545.3168.



20

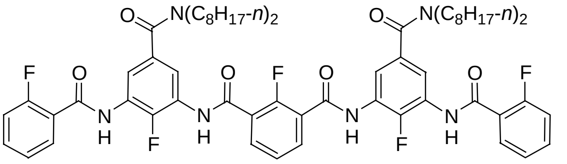
Compound 20. A mixture of **19** (0.50 g, 0.92 mmol), 2-fluoro-5-methylbenzene-1,3-diamine (0.32 g, 0.92 mmol), EDCI (0.20 g, 1.02 mmol) and DMAP (10 mg) in dichloromethane (30 mL) was stirred at room temperature for 12 h. After workup, the resulting residue was subjected to column chromatography (dichloromethane/AcOEt 4:1) to give **20** as a white solid (0.28 g, 45%). Mp. 131-132 °C. ^{1}H NMR ($CDCl_3$): δ 8.99 (d, *J* = 11.1 Hz, 1 H), 8.75 (d, *J* = 10.5, 1H), 8.58 (d, *J* = 6.3, 1 H), 8.30 (s, 2 H), 8.21 – 8.15 (m, 1 H), 7.99 (d, d, J_1 = 2.7 Hz, J_2 = 3.9 Hz, 1 H), 7.61 – 7.53 (m, 3 H), 7.36 (t, *J* = 7.5 Hz, 1 H), 7.67 (d, *J* = 4.2 Hz, 1 H), 7.56 (t, *J* = 6.9 Hz, 1 H), 7.28 – 7.25 (m, 2 H), 6.53 (d, *J* = 7.8 Hz, 1 H), 3.90 (br, 2 H), 3.56 (br, 2 H), 3.36 (br, 2 H), 2.37 (s, 3 H), 1.74 – 1.32 (m, 24 H), 1.02 – 0.98 (m, 6 H). ^{19}F NMR ($CDCl_3$): δ -116.3 (br, 1 F), -128.5 (br, 1 F),

-156.4 (br, 1 F). ^{13}C NMR (CDCl$_3$): δ 172.1, 162.7, 162.5, 162.5, 161.2, 157.9, 156.4, 153.1, 144.2, 141.1, 137.4, 137.2, 137.4, 137.2, 136.1, 136.0, 135.8, 135.8, 135.7, 135.6, 127.9, 127.7, 127.5, 127.4, 127.3, 127.3, 125.6, 125.5, 125.0, 124.8, 124.5, 124.3, 122.6, 117.2, 117.0, 115.6, 115.6, 114.2, 51.2, 47.0, 33.7, 33.7, 31.6, 31.6, 31.3, 31.2, 32.0, 30.9, 30.5, 30.5, 29.4, 29.0, 28.5, 24.5, 24.4, 23.2, 16.0. LRMS-ESI-MS: *m/z* 667 [M + H]$^+$. HRMS-ESI-MS: *m/z* 667.3830. Calcd for $C_{38}H_{50}F_3N_4O_3$: 667.3832.



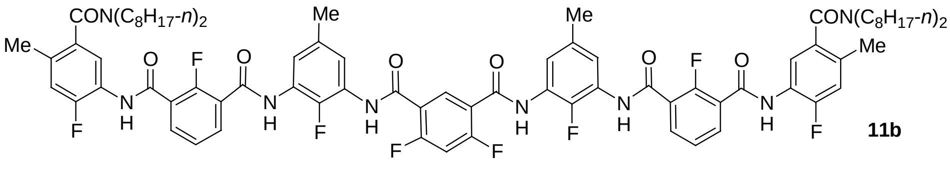
11a

Compound 11a. To a stirred solution of **20** (0.22 g, 0.33 mmol) and triethylamine (0.40 g, 0.40 mmol) in dichloromethane (5 mL) was added a solution of 5-fluoroisophthaloyl dichloride (36 mg, 0.16 mmol) in dichloromethane (1 mL). The mixture was stirred at room temperature for 1 h. After workup, the resulting residue was purified by column chromatography (CH_2Cl_2/AcOEt 3:1) to afford **11a** as a white solid (0.14 g, 55%). Mp. 71-73 °C. ^{1}H NMR (CDCl$_3$): δ 9.03 (d, *J* = 9.6 Hz, 2 H), 8.84 – 8.81 (m, 4 H), 8.24 (d, *J* = 6.3 Hz, 2 H), 8.12 – 7.99 (m, 6 H), 7.86 (d, *J* = 5.4 Hz, 4 H), 7.36 – 7.27 (m, 3 H), 6.99 – 6.96 (m, 4 H), 3.31 (br, 4 H), 3.14 (br, 4 H), 2.32 (s, 6 H), 1.50 – 1.15 (m, 48 H), 0.88 – 0.81 (m, 12 H). ^{19}F NMR (CDCl$_3$): δ -115.7 (br, 2 F), -115.8 (br, 1 F), -127.3 (br, 2 F), -147.6 (br, 2 F). ^{13}C NMR (CDCl$_3$): δ 170.2, 161.1, 160.9, 156.0, 154.7, 151.4, 144.1, 140.9, 135.1, 134.5, 134.5, 133.5, 133.4, 125.8, 125.7, 125.2, 125.1, 123.5, 123.4, 122.5, 122.7, 122.6, 122.5, 121.2, 119.1, 115.2, 115.0, 49.3, 45.1, 31.8, 31.7, 29.7, 29.3, 29.0, 28.6, 27.4, 27.1, 26.5, 22.6, 22.6, 21.5, 14.1. IR (cm^{-1}): ν 3449, 2927, 1686, 1610, 1544, 1444, 1317, 1266, 897, 753. LRMS-MALDI-MS: *m/z* 1503 [M + Na]$^+$. HRMS-MALDI-MS: *m/z* 1503.7366, calcd for $C_{84}H_{99}F_7N_8O_8Na$: 1503.7390.



10

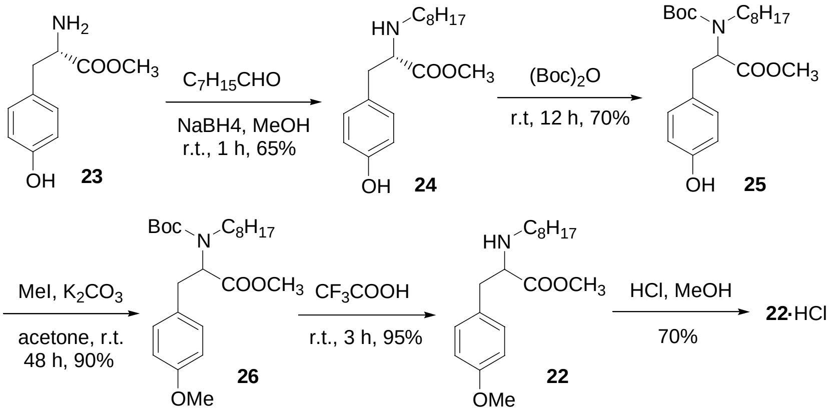
Compound 10. Mp. 78-80 °C. ^{1}H NMR (CDCl$_3$): δ 8.87 – 8.91 (m, 4 H), 8.34 (d, *J* = 6.6 Hz, 2 H), 8.26 – 8.10 (m, 6 H), 7.57 – 7.44 (m, 3 H), 7.33 (d, *J* = 7.8 Hz, 2 H), 7.26 – 7.14 (m, 2 H), 3.45 (t, *J* = 7.5 Hz, 4 H), 3.28 (t, *J* = 7.5 Hz, 3 H) 1.43 – 1.10 (m, 48 H), 0.90 – 0.77 (m, 12 H). ^{19}F NMR (CDCl$_3$): δ -116.9 – -116.1 (m, 2 F), -151.7 – -151.0 (m, 3 F). ^{13}C NMR (CDCl$_3$): δ 169.6, 161.7, 160.8, 160.7, 158.4, 141.6, 134.8, 133.8, 133.7, 133.1, 133.1, 131.1, 126.0, 125.9, 125.5, 125.4, 124.7, 124.6, 122.5, 122.3, 120.2, 120.1, 116.2, 115.9, 115.6, 115.5, 49.0, 44.9, 31.5, 31.4, 31.3, 31.0, 29.8, 29.3, 29.2, 29.0, 28.9, 28.9, 28.8, 28.6, 28.2, 27.0, 26.7, 26.2, 22.3, 22.1, 13.7, 13.6. IR (cm^{-1}): ν 3443, 2926, 2855, 1691, 1612, 1541, 1438, 1318, 1278, 820, 752. ESI-MS: *m/z* 1180 [M + H]$^+$. Anal. Calcd for $C_{68}H_{87}F_5N_6O_6$: C 69.25, H 7.43, N 7.13. Found: C 69.68, H 7.75, N 6.70.



11b

Compound 11b. Mp. 51-52 °C. ^{1}H NMR (CDCl$_3$): δ 8.86 – 8.79 (m, 6 H), 8.19 – 8.12 (m, 4 H), 7.99 – 7.92 (m, 8 H), 7.35 (t, *J* = 1.8 Hz, 1 H), 7.32 (t, *J* = 3.0 Hz, 2 H), 6.79 (d, *J* = 8.4 Hz, 2 H), 3.43 (br, 4 H), 3.02 (br, 4 H), 2.37 (s, 6 H), 2.10 (s, 6 H), 1.46 – 1.11 (m, 48 H), 0.90 – 0.75 (m, 12

H). ^{13}C NMR ($CDCl_3$): δ 170.2, 161.3, 161.2, 161.2, 161.1, 160.9, 160.5, 158.8, 156.8, 156.8, 154.6, 152.2, 152.0, 152.0, 152.0, 151.9, 143.3, 141.4, 139.3, 135.6, 135.5, 135.1, 134.6, 134.6, 133.0, 132.9, 132.3, 132.2, 132.2, 125.5, 125.5, 125.4, 125.3, 125.3, 125.2, 125.1, 123.3, 123.2, 122.8, 122.7, 122.5, 122.4, 121.2, 121.2, 121.1, 119.1, 119.0, 116.9, 116.7, 114.1, 48.8, 44.8, 31.9, 31.8, 31.7, 29.7, 29.7, 29.4, 29.4, 29.3, 29.0, 27.5, 27.2, 26.6, 22.7, 22.7, 22.5, 21.6, 18.5, 14.1, 14.0. ^{19}F NMR ($CDCl_3$): δ -115.7 (br, 2 F), -115.8 (br, 1 F), -127.3 (br, 2 F), -147.6 (br, 2 F). MALDI-MS: *m/z* 1509 $[M + H]^+$. HRMS-MALDI-MS: 1509.7860. Calcd for $C_{86}H_{104}F_7N_8O_8$: 1509.7905.



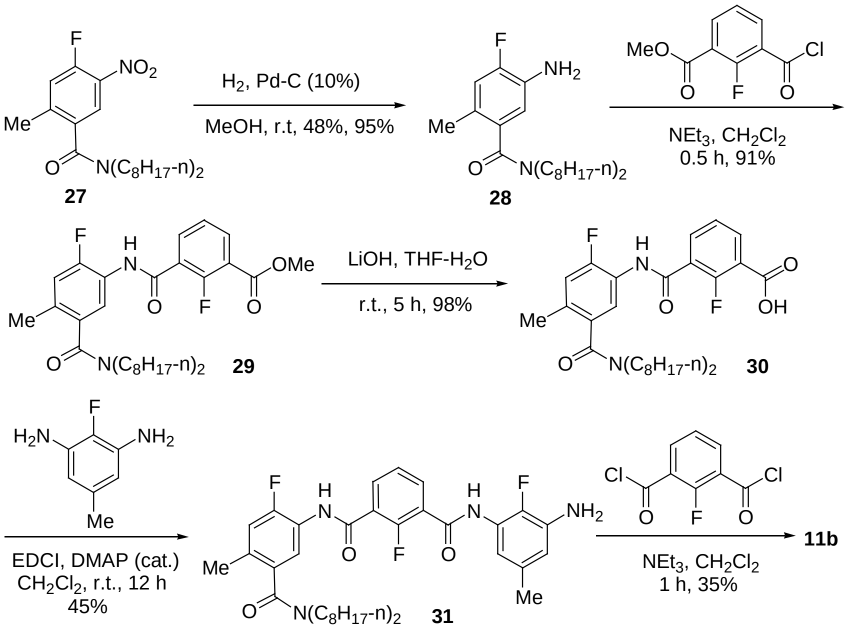
Compound 24. To a solution of **23**·HCl (2.20 g, 10.0 mmol) and n-octaldehyde (1.30 g, 10.0 mmol) in methanol (20 mL) was added potassium hydroxide (0.60 g, 10.5 mmol). The mixture was stirred at °Cfor 10 min and sodium borohydride (0.40 g, 10.5 mmol) was added. After stirring at room temperature for 1 h, the solvent was evaporated and the resulting residue was triturated with dichloromethane (30 mL). The organic phase was washed with sodium carbonate solution (0.5 N, 8 mL), water, brine and dried over magnesium sulfate. Upon removal of the solvent, the crude material was purified by column chromatography (dichloromethane/EtOAc 10:1) to afford **23** a white solid (2.10 g, 65%). ^{1}H NMR ($CDCl_3$): 6.93 (d, *J* = 8.1 Hz, 2 H), 6.62 (d, *J* = 8.1 Hz, 2 H), 3.59 (s, 3 H), 3.46 (t, *J* = 6.6 Hz, 3 H), 3.89 – 2.79 (m, 2 H), 2.54 – 2.36 (m, 2 H), 1.39 – 1.16 (m, 12 H), 0.82 (t, *J* = 6.6 Hz, 3 H). ESI-MS: *m/z* 308 $[M + H]^+$. Anal. Calcd for $C_{18}H_{29}NO_3$: C 70.32, H 9.51, N 4.56. Found: C 70.21, H 9.52, N 4.20.

Compound 25. A solution of **24** (1.54 g, 5.00 mmol) and $(Boc)_2O$ (0.79 g, 5.00 mmol) in dichloromethane (30 mL) was stirred at room temperature for 12 h. After workup, the resulting residue was subjected to column chromatography (dichloromethane/EtOAc 10:1) to yield 25 as a liquid (1.40 g, 70%). ^{1}H NMR ($CDCl_3$): δ 6.95 (d, *J* = 8.1 Hz, 2 H), 6.75 (d, *J* = 8.1 Hz, 2 H), 3.78 – 3.27 (m, 4 H), 3.19 – 2.98 (m, 4 H), 1.38 (s, 9 H), 1.16 – 1.11 (m, 12 H), 0.80 (t, *J* = 6.6 Hz, 3 H). ESI-MS: *m/z* 408 $[M + H]^+$. Anal. Calcd for $C_{23}H_{37}NO_5$: C 67.78, H 9.15, N 3.44. Found: C 67.75, H 8.82, N 3.32.

Compound 26. A suspension of 25 (1.00 g, 2.50 mmol), methyl iodide (1.644g, 10 mmol) and potassium carbonate (0.41 g, 3.00 mmol) in acetone (50 mL) was stirred at room temperature for 48 h. The solvent was evaporated and the resulting residue triturated with dichloromethane (50 mL). The organic phase was then washed with water, brine and dried over sodium sulfate. Upon removal of the solvent, the crude product was purified by column chromatography (dichloromethane/EtOAc 10:1) to give 26 as colorless oil (0.95 g, 90%). ^{1}H NMR ($CDCl_3$): δ 7.02 (d, *J* = 8.1 Hz, 2 H), 6.77 (d, *J* = 8.1 Hz, 2 H), 3.83 – 2.97 (m, 4 H), 3.66 (s, 3 H), 3.22 – 2.97 (m, 4 H), 1.37 (s, 9 H), 1.29 – 1.13 (m, 12 H), 0.81 (t, *J* = 6.6 Hz, 3 H). ESI-MS: *m/z* 422 $[M + H]^+$. Anal. Calcd for $C_{24}H_{39}FNO_5$: C 68.38, H 9.32, N 3.32. Found: C 68.40, H 9.16, N 3.41.

Compound 22. A solution of 26 (0.84 g, 2.00 mmol) in trifluoroacetic acid (12 mL) was stirred at room temperature for 3 h and then concentrated under reduced pressure. The resulting residue was triturated with dichloromethane (50 mL) and the solution washed with saturated sodium carbonate solution (10 mL × 2), water, brine and dried over magnesium sulfate. After the solvent was removed under reduced pressure, the crude product was subjected to flash chromatography (dichloromethane/EtOAc 8:1) to give 22 as colorless oil (0.61 g, 95%). ^{1}H NMR (CDCl$_3$): δ 7.11 (d, *J* = 8.1 Hz, 2 H), 6.85 (d, *J* = 8.1 Hz, 2 H), 3.79 (s, 3 H), 3.64 (s, 3 H), 3.50 (t, *J* = 6.6 Hz, 3 H), 2.91 – 2.88 (m, 2 H), 2.60 – 2.40 (m, 2 H), 1.43 – 1.24 (m, 12 H), 0.89 (t, *J* = 6.6 Hz, 3 H). ESI-MS: *m/z* 322 [M + H]$^+$. Anal. Calcd for $C_{19}H_{31}NO_3$: C 70.99, H 9.72, N 4.36. Found: C 70.71, H 9.62, N 4.17.

Compound 22·Cl. To a solution of 22 (0.50 g, 1.55 mmol) in methanol (5 mL) was added hydrochloric acid (0.2 N, 15 mL). After stirring for 2 h, the solvent was evaporated. The resulting solid was recrystallized from dichloromethane and hexane (1:2) to give **22·Cl** as white solid (0.40 g, 70%). ^{1}H NMR (CDCl$_3$): δ 7.12 (d, *J* = 8.1 Hz, 2 H), 6.76 (d, *J* = 8.1 Hz, 2 H), 3.70 (s, 3 H), 3.63 (s, 3 H), 3.37 (t, *J* = 6.6 Hz, 3 H), 2.95 – 2.87 (m, 2 H), 1.91 – 1.87 (m, 2 H), 1.18 – 1.15 (m, 12 H), 0.82 (t, *J* = 6.6 Hz, 3 H). ESI-MS: *m/z* 322 [M - Cl]$^+$. Anal. Calcd for $C_{19}H_{32}ClNO_3$: C 63.76, H 9.01, N 3.91. Found: C 63.79, H 8.43, N 3.93.



Compound 27. This compound was prepared as yellow oil in 85% yield from the reaction of 4-fluoro-2-methyl-5-nitrobenzoyl chloride and dioctylamine in dichloromethane in the presence of triethylamine. ^{1}H NMR (CDCl$_3$): δ 7.90 (d, *J* = 6.0 Hz, 1 H), 7.16 (d, *J* = 10.8 Hz, 1 H), 3.47 (br, 2 H), 3.05 (t, *J* = 7.2 Hz, 2 H), 2.36 (s, 3 H), 1.67 – 1.11 (m, 24 H), 0.89 – 0.81 (m, 6 H). ^{19}F NMR (CDCl$_3$): δ -117.7 (d, d, J_1 = 9.0 Hz, J_2 = 4.8 Hz, 1 F). ESI-MS: *m/z* [M + 1]$^+$. Anal. Calcd for $C_{24}H_{39}FN_2O_3$: C 68.21, H 9.30, N 6.63. Found: C 68.14, H 9.26, N 6.61.

Compound 28. The compound was prepared as pale oil in 95% yield from **27** according to the method described above for **17**. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.81 (d, *J* = 11.7 Hz, 1 H), 6.57 (d, *J* = 9.0 Hz, 1 H), 3.70 (br, 2 H), 3.55 (br, 2 H), 3.07 (t, J = 7.5 Hz, 2 H), 2.14 (s, 3 H), 1.62-0.96 (m, 24 H), 0.88-0.73 (m, 6 H). ^{19}F NMR: -135.46 (t, *J* = 11.1 Hz). ESI-MS: *m/z* 393 [M + H]$^+$. Anal. Calcd for $C_{24}H_{41}FN_2O_1$: C 73.42, H 10.53, N 7.14. Found: C 73.61, H 10.43, N 7.13.

Compound 29. A solution of 2-fluoro-3-methoxycarbonylbenzoyl chloride (0.22 g, 1.00 mmol), **17** (0.39 g, 1.00 mmol) and triethyl amine (0.5 mL) in dichloromethane (20 mL) was stirred at room temperature for 0.5 h. After workup, the resulting residue was purified by column chromatography (dichloromethane-methanol 40:1), to afford **18** as a yellow oil (0.52 g, 91%). ^{1}H NMR ($CDCl_3$): δ 8.74 (d, d, *J* = 2.1 Hz, *J* = 13.3 Hz, 1H), 8.35 – 8.29 (m, 1 H), 8.13 – 8.08 (m, 1 H), 7.40 (t, *J* = 7.8 Hz, 1 H), 7.02 (d, *J* = 12.0 Hz, 1 H), 3.91 (s, 3 H), 3.47 (br, 2 H), 3.09 (br, 2 H), 2.27 (s, 3 H), 1.66 – 1.16 (m, 24 H), 0.88 – 0.78 (m, 6 H). ^{19}F NMR ($CDCl_3$): δ -112.9 – -112.8 (m, 1 F), -130.7 – -130.7 (m, 1 F). ESI-MS: *m/z* 573 $[M + H]^+$. Anal. Calcd for $C_{33}H_{46}FN_2O_4$: C 69.20, H 8.10, N 4.89. Found: C 69.16, H 8.15, N 4.93.

Compound 30. A solution of **29** (0.46 g, 0.80 mmol) and lithium hydroxide (48 mg, 2.0 mmol) in THF (15 mL) and water (5 mL) was stirred at room temperature for 5 h and neutralized with hydrochloride acid (1 N) to pH = 6. Upon concentration under reduced pressure, the solid was filtered, washed with water thoroughly and dried in vacuo to give **30** as a pale yellow solid (0.56 g, 98%), which was recrystallized from ethanol for analysis. Mp. 181-183 °C. ^{1}H NMR (DMSO-d_6): δ 292 (s, 1 H), 8.01 – 7.96 (m, 1 H), 7.66 (d, *J* = 7.2 Hz, 1 H), 7.41 (t, *J* = 7.5 Hz, 1 H), 7.23 (d, *J* = 12.0 Hz, 1 H), 3.34 (br, 2 H), 3.02 (br, 2 H), 2.16 (m, 3 H), 1.56 – 1.05 (m, 24 H), 0.85 (t, *J* = 7.2 Hz, 3 H), 0.79 (t, *J* = 6.9 Hz, 3 H). ^{19}F NMR (DMSO-d_6): δ = -113.42 (t, *J* = 6.0 Hz, 1 F), -124.07 (t, *J* = 10.5 Hz, 1 F). Anal. Calcd for $C_{32}H_{44}F_2N_2O_4 \cdot H_2O$: C 66.64, H 8.04, N 4.86. Found: C 66.53, H 8.30, N 4.69.

Compound 31. Mp. 139-140 °C. ^{1}H NMR ($CDCl_3$): δ 8.62 (d, *J* = 9.9 Hz, 1 H), 8.50 (d, *J* = 10.8 Hz, 1 H), 8.27 – 8.18 (m, 3 H), 7.58 (d, *J* = 6.0 Hz, 1 H), 7.45 (t, *J* = 7.8 Hz, 1 H), 7.02 (d, *J* = 11.4 Hz, 2 H), 6.41 – 6.39 (m, 1 H), 3.90 (br, 2 H), 3.72 (br, 2 H), 3.46 (br, 2 H), 2.25 (s, 6 H), 1.69 – 0.86 (m, 24 H), 0.82 – 0.78 (m, 6 H). ^{19}F NMR ($CDCl_3$): δ -116.7 – -116.6 (m, 1 F), -130.7 – -130.5 (m, 1 F), -156.8 (s, 1 F). ESI-MS: *m/z* 681 $[M+1]^+$. Anal. Calcd for $C_{39}H_{51}F_3N_4O_3$: C 68.80, H 7.55, N 8.23. Found: C 68.66, H 8.03, N 7.81.

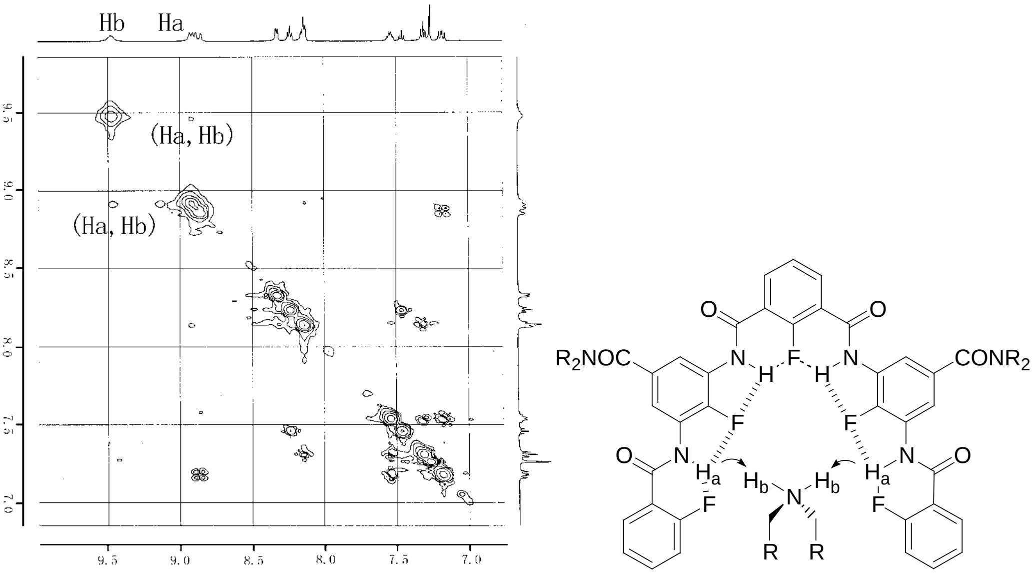


Figure S1. Partial NOESEY spectrum (500 MHz) of **10** and **21**·HCl (1:1 4.0 mM) in chloroform-*d*, mixing time: 0.5 s) at 23 ºC.

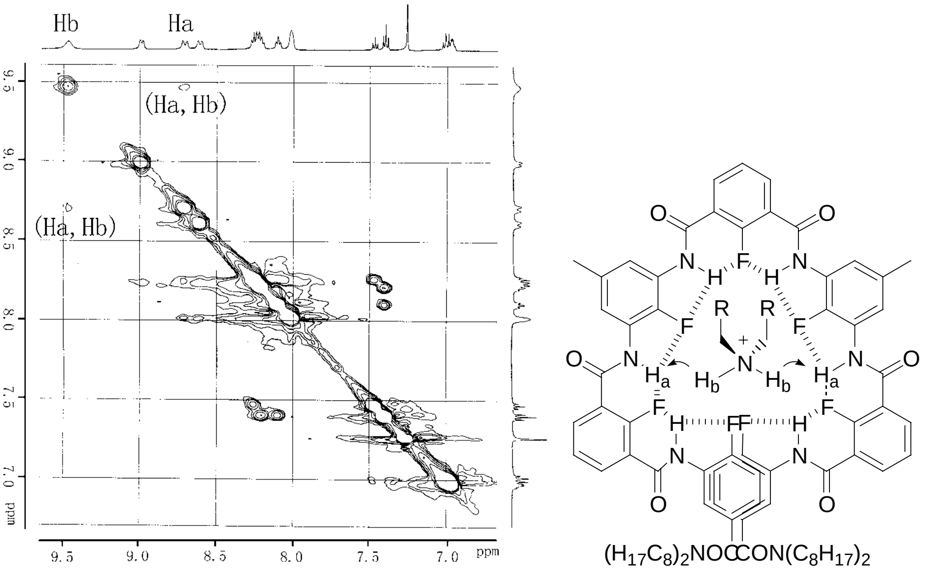


Figure S2. Partial NOESEY spectrum (500 MHz) of **11a** and **21**·HCl (1:1 5.0 mM) in chloroform-*d*, mixing time: 0.5 s) at 23 ºC.

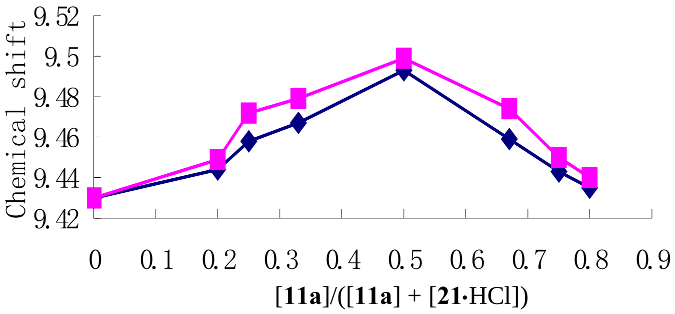


Figure S3. Job's plot of complexes of **10** (■) and **11a** (♦) with **21**·HCl (total concentration: 1.4 mM) with the NC*H*2 signal of **21**·HCl as probe (300 Hz, in chloroform-d at 25 °C).

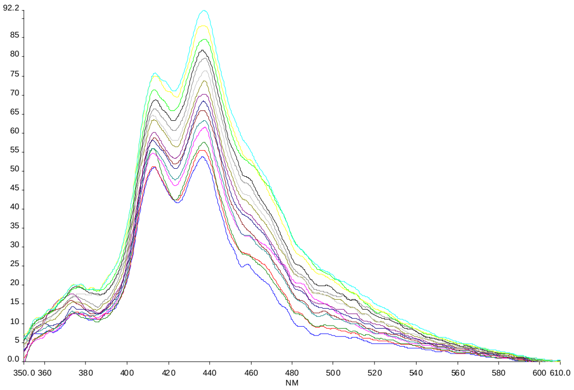


Figure S4. Fluorescent spectra of **10** (5×10^{-6} M, excitation wavelength = 330 nm) in chloroform at 25 °C, decreased gradually with the addition of **21**·HCl (0 to 1.6×10^{-5} M).

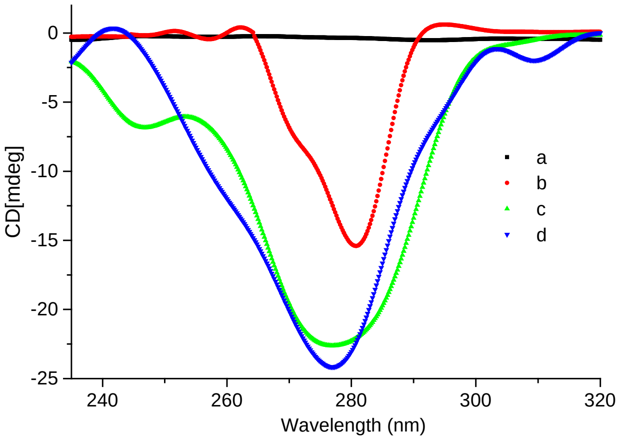


Figure S5. Induced CD spectra of complexes of **22**·HCl (1.0 mM) with **11a** (0.2 mM) in MeOH-$CHCl_3$ (1:3 v/v), b) MeOH-$CHCl_3$ (1:20 v/v), c) MeOH-$CHCl_3$ (1:100 v/v), and d) $CHCl_3$ at 25 °C.