Benzo-21-Crown-7/Secondary Ammonium Salt [2]Rotaxanes with Fluoro/Chlorocarbon Blocking Groups

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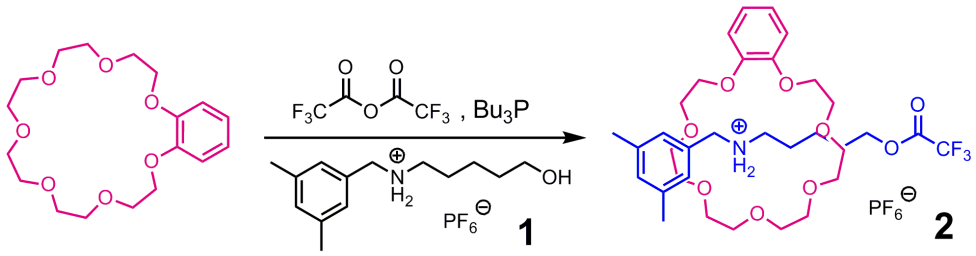
Supporting Information (30 pages)

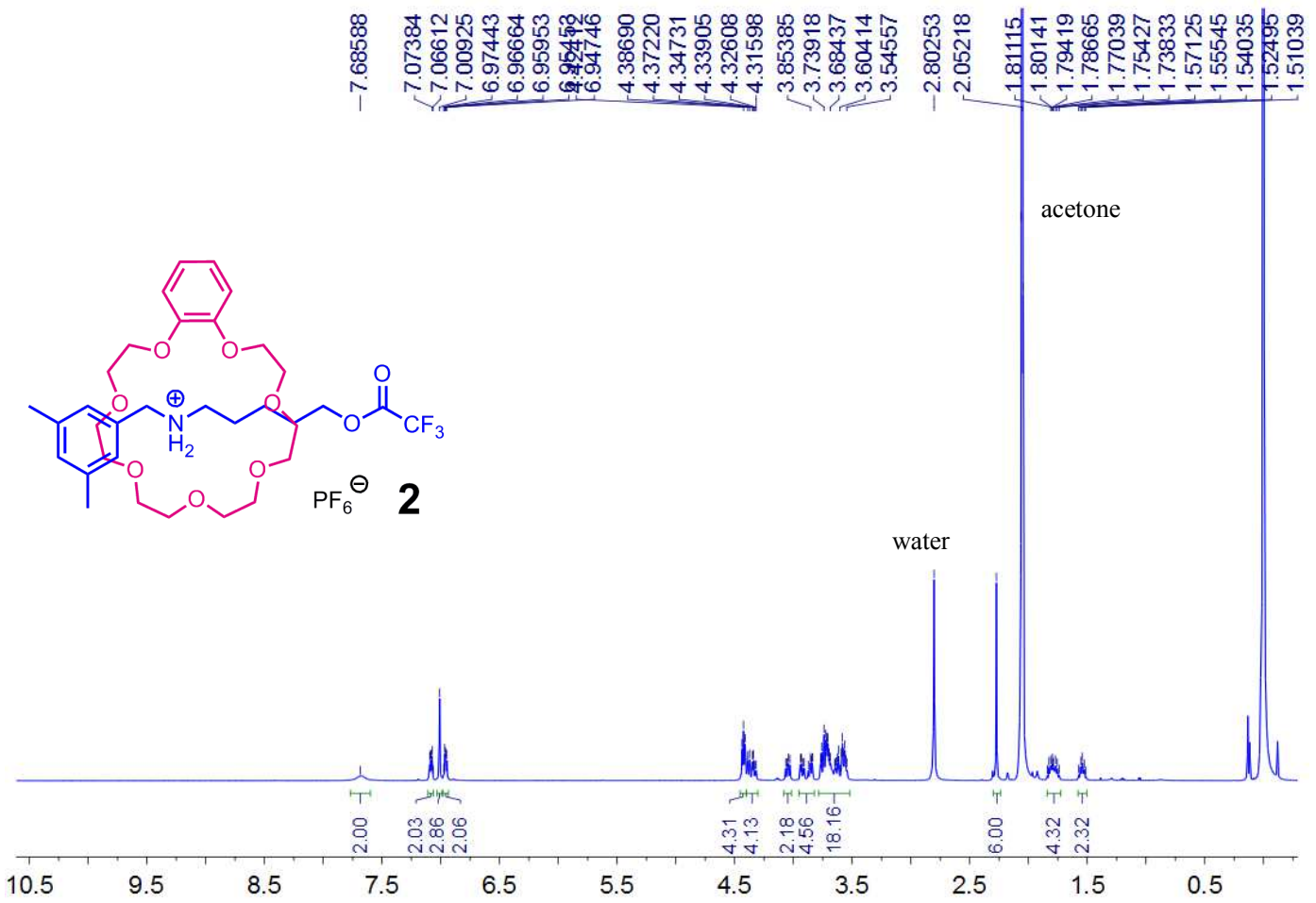
1. Materials and methods

All reagents were commercially available and used as supplied without further purification. Benzo-21-crown-7 (B21C7) and compound **1** were prepared according to the literature procedure.[S1,S2] ^{1}H NMR spectra were collected on a temperature-controlled 400 MHz or 500 MHz spectrometer with the deuterated solvent as the lock and the residual solvent or TMS as the internal reference. Chemical shifts are reported in ppm relative to the signals corresponding to the residual non-deuterated solvent or TMS and coupling constants were recorded in Hertz (Hz). ^{13}C NMR spectra were recorded on a Bruker AVANCE □ 400 or AVANCE DMX-500 spectrometer. ^{19}F NMR spectrum were recorded on a Bruker AVANCE DMX-500 spectrometer. Low-resolution electrospray ionization (LRESI) mass spectra were obtained on a Bruker Esquire 3000 plus mass spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with an ESI interface and an ion trap analyzer. High-resolution electrospray ionization (HRESI) mass spectra were obtained on a Bruker 7-Tesla FT-ICR mass spectrometer equipped with an electrospray source (Billerica, MA, USA) or Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS. The crystals data were collected on an Oxford Diffraction Xcalibur Gemini Ultra diffractometer with an Atlas detector or Bruker Smart Apex II.

2. Synthesis of compound ***2***



To a solution of **1** (114 mg, 0.31 mmol) and B21C7 (100 mg, 0.28 mmol) in dichloromethane (2 mL) was added trifluoroacetic anhydride (59 μL, 0.42 mmol) followed by tributylphosphine (7 μL). After the reaction mixture was stirred overnight, water was added and the mixture was stirred for additional 30 minutes. The mixture was partitioned between H_2O (10 mL) and CH_2Cl_2 (2×10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford a crude product. The crude product was dissolved in a small amount of dichloromethane, which was poured into a large amount of hexane to give crude product **2**. Then, it was recrystallized from ethyl acetate or ethyl acetate/diisopropyl ether to give **2** (230 mg, 60 %) as colorless crystals. M.p. 115.1−116.8 °C. The ^{1}H NMR spectrum of **2** is shown in Figure S1. ^{1}H NMR (400 MHz, acetone-d_6, room temperature) δ (ppm): 7.78 – 7.60 (br, 2H), 7.11 – 7.06 (m, *2*H), 7.01 (s, 3H), 6.98 – 6.93 (m, 2H), 4.45 – 4.40 (m, 4H), 4.40 – 4.30 (m, 4H), 4.08 – 4.02 (m, 2H), 3.95 – 3.82 (m, 4H), 3.78 – 3.52 (m, 18H), 2.27 (s, 6H), 1.84 – 1.72 (m, 4H), 1.57 – 1.51 (m, 2H). The ^{13}C NMR spectrum of **2** is shown in Figure S2. ^{13}C NMR (100 MHz, acetone-d_6, room temperature) δ (ppm): 156.82 (q, J = 41 Hz), 146.99, 138.14, 132.70, 130.29, 127.63, 121.19, 118.87, 114.61(q, J = 283 Hz), 111.82, 71.19, 70.97, 70.76, 70.43, 69.70, 68.24, 67.96, 50.83, 48.89, 27.36, 25.92, 22.89, 20.21. The ^{19}F NMR spectrum of **2** is shown in Figure S3. ^{19}F NMR (470 MHz, acetone-d_6, room temperature) δ (ppm): –72.62 (d, J = 706 Hz), –75.93. LRESIMS is shown in Figure S4: m/z 674.3 $[M - PF_6]^+$ (100%). HRESIMS: m/z calcd for $[M - PF_6]^+$ $C_{34}H_{51}F_3NO_9$, 674.3510; found 674.3493, error −2.5 ppm.



2

Figure S1. ^{1}H NMR spectrum (500 MHz, acetone-d_6, room temperature) of **2**.

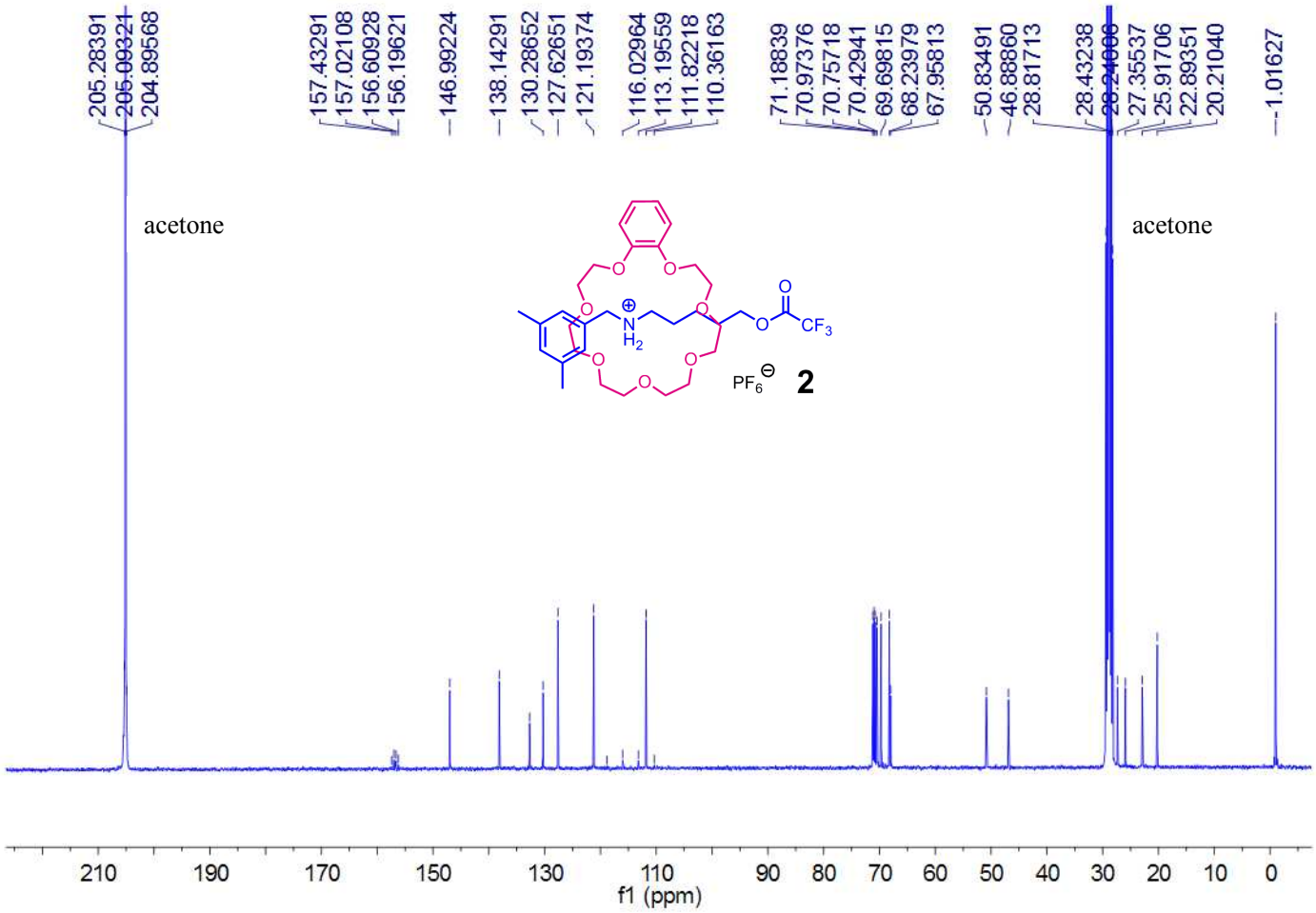


Figure S2. ^{13}C NMR spectrum (100 MHz, acetone-d_6, room temperature) of **2**.

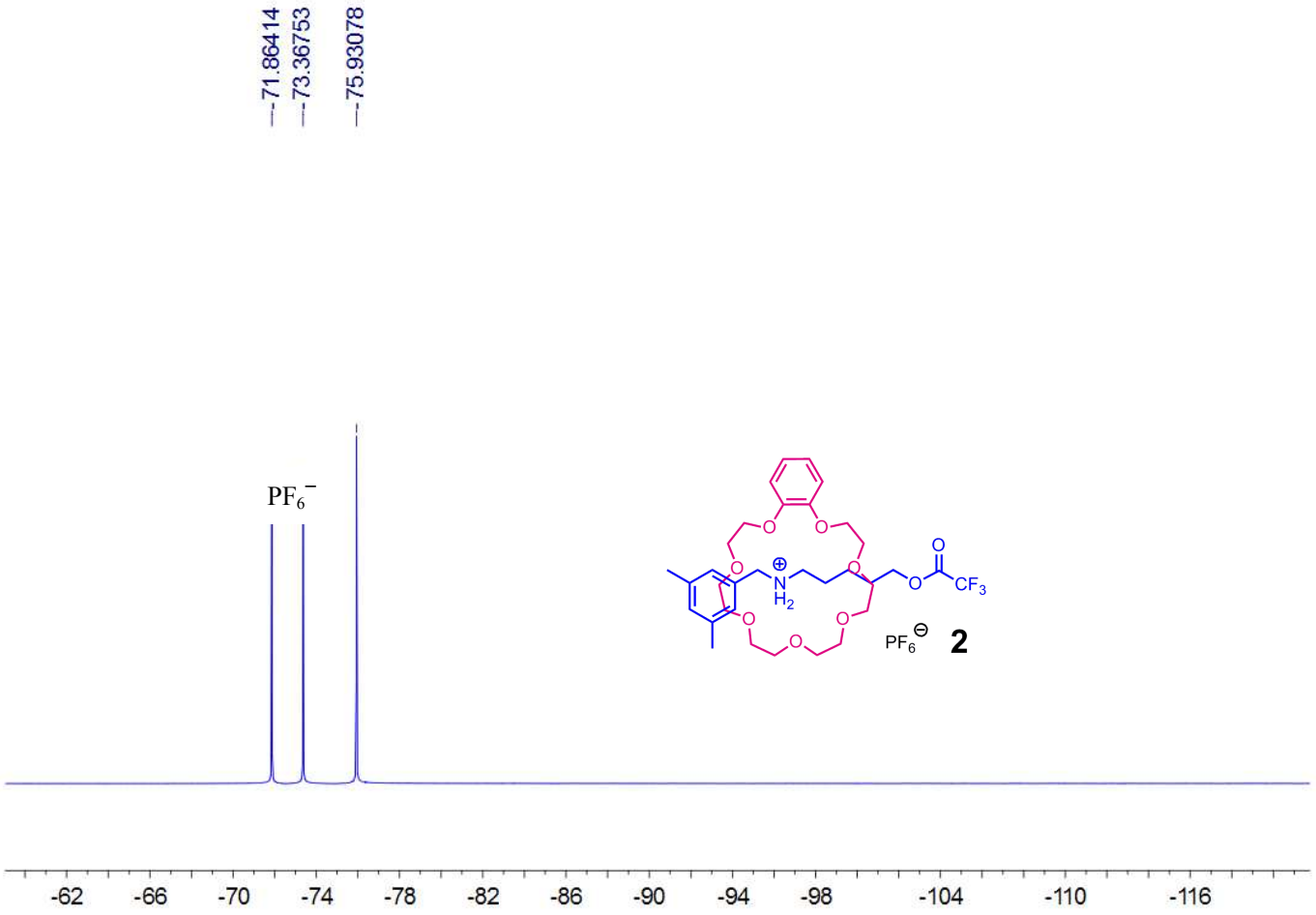


Figure S3. ^{19}F NMR spectrum (470 MHz, acetone-d_6, room temperature) of **2**.

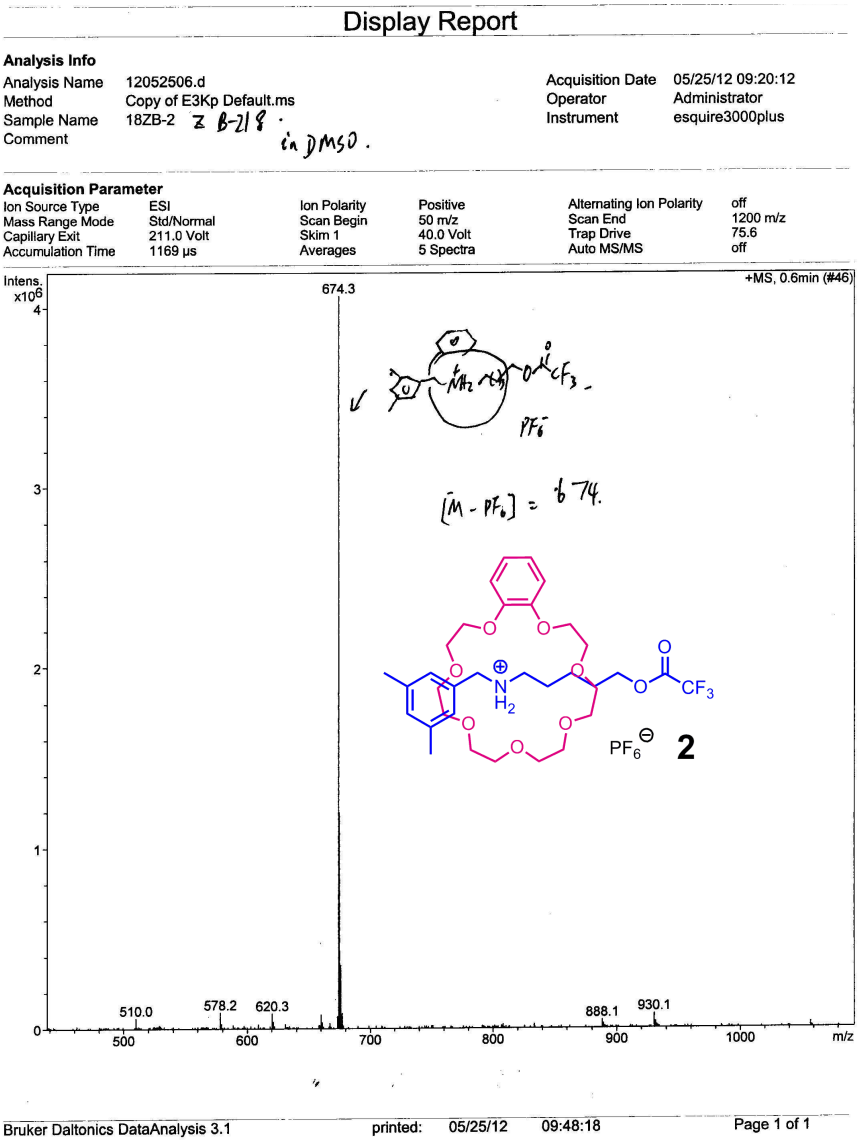
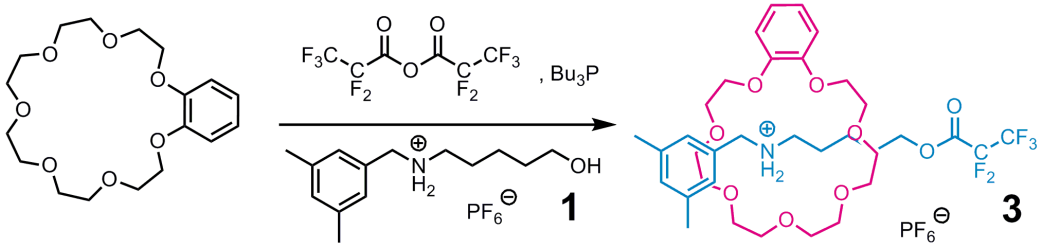


Figure S4. Electrospray ionization mass spectrum of **2**. Assignment of the main peak: *m/z* 674.3 $[M - PF_6]^+$ (100%).

3. Synthesis of compound ***3***



To a solution of **1** (183 mg, 0.50 mmol) and B21C7 (180 mg, 0.51 mmol) in dichloromethane (5 mL) was added pentafluoropropionic anhydride (136 μL, 0.70 mmol) followed by tributylphosphine (25 μL). After the reaction mixture was stirred for 2 days, water was added and the mixture was stirred for additional 30 minutes. The mixture was partitioned between H_2O (10 mL) and CH_2Cl_2 (2×10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford a crude product, which was purified by column chromatography on silica gel (dichloromethane) to afford **3** as an oil. The oil was recrystallized from ethyl acetate/diisopropyl ether at 5 °C to provide the product as colorless crystals (80 mg, 18%). M.p. 109.7−111.4 °C. The proton NMR spectrum of **3** is shown in Figure S5. ^{1}H NMR (400 MHz, acetone-d_6, room temperature) δ (ppm): 7.80 – 7.60 (br, 2H), 7.11 – 7.06 (m, 2H), 7.01 (s, 3H), 6.99 – 6.93 (m, 2H), 4.51 – 4.29 (m, 8H), 4.09 – 3.99 (m, 2H), 3.97 – 3.81 (m, 4H), 3.81 – 3.52 (m, 16H), 2.27 (s, 6H), 1.87 – 1.73 (m, 4H), 1.59 – 1.49 (m, 2H). The ^{13}C NMR spectrum of **3** is shown in Figure S6. ^{13}C NMR (125 MHz, acetone-d_6, room temperature) δ (ppm): 157.76 (t, J = 94 Hz), 141.13, 138.29, 132.83, 130.44, 127.78, 121.33, 111.95, 71.34, 71.11, 70.88, 70.56, 69.82, 68.55, 68.38, 50.96, 46.98, 27.54, 26.05, 22.98, 20.38. The ^{19}F NMR spectrum of **2** is shown in Figure S7. ^{19}F NMR (470 MHz, acetone-d_6, room temperature) δ (ppm): –72.56 (d, J = 706 Hz), –83.82, –122.38. LRESIMS is shown in Figure S8: m/z 724.5 $[M - PF_6]^+$ (100%). HRESIMS : *m/z* calcd for $[M - PF_6]^+$ $C_{34}H_{54}NO_9$, 724.3478; found 724.3460, error 2.6 ppm.

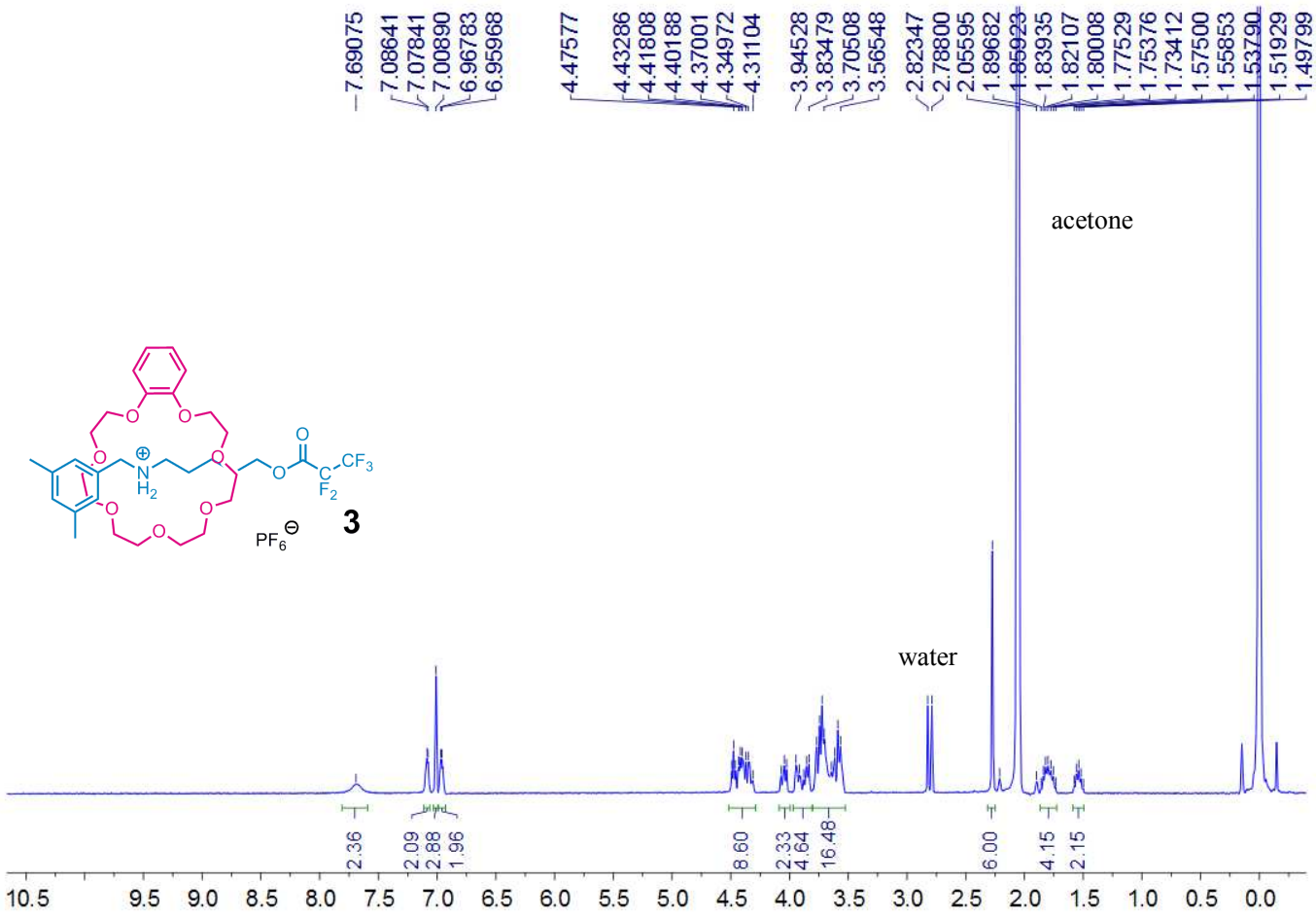


Figure S5. ^{1}H NMR spectrum (400 MHz, acetone-d_6, room temperature) of **3**.

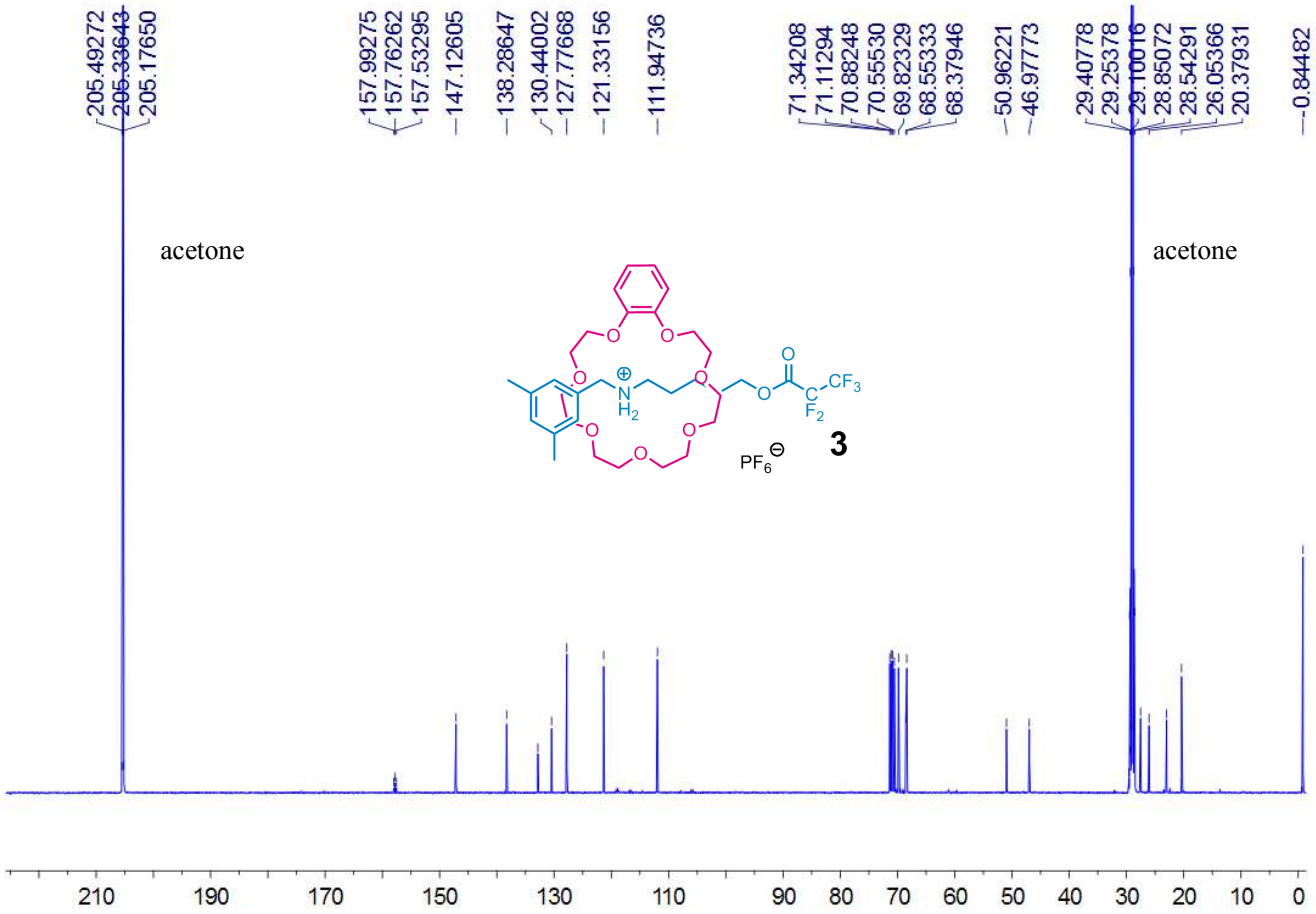


Figure S6. ^{13}C NMR spectrum (125 MHz, acetone-d_6, room temperature) of **3**.

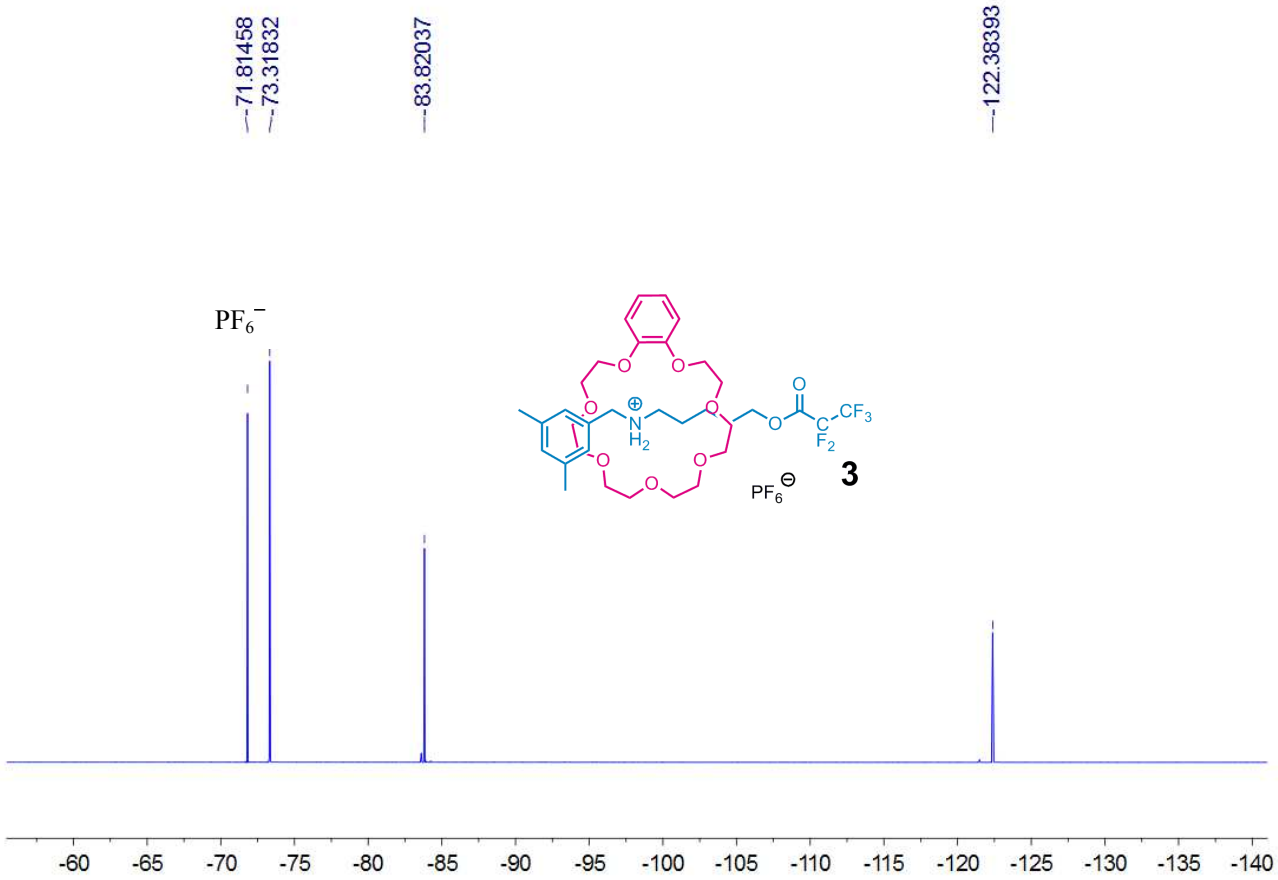


Figure S7. ^{19}F NMR spectrum (470 MHz, acetone-d_6, room temperature) of **3**.

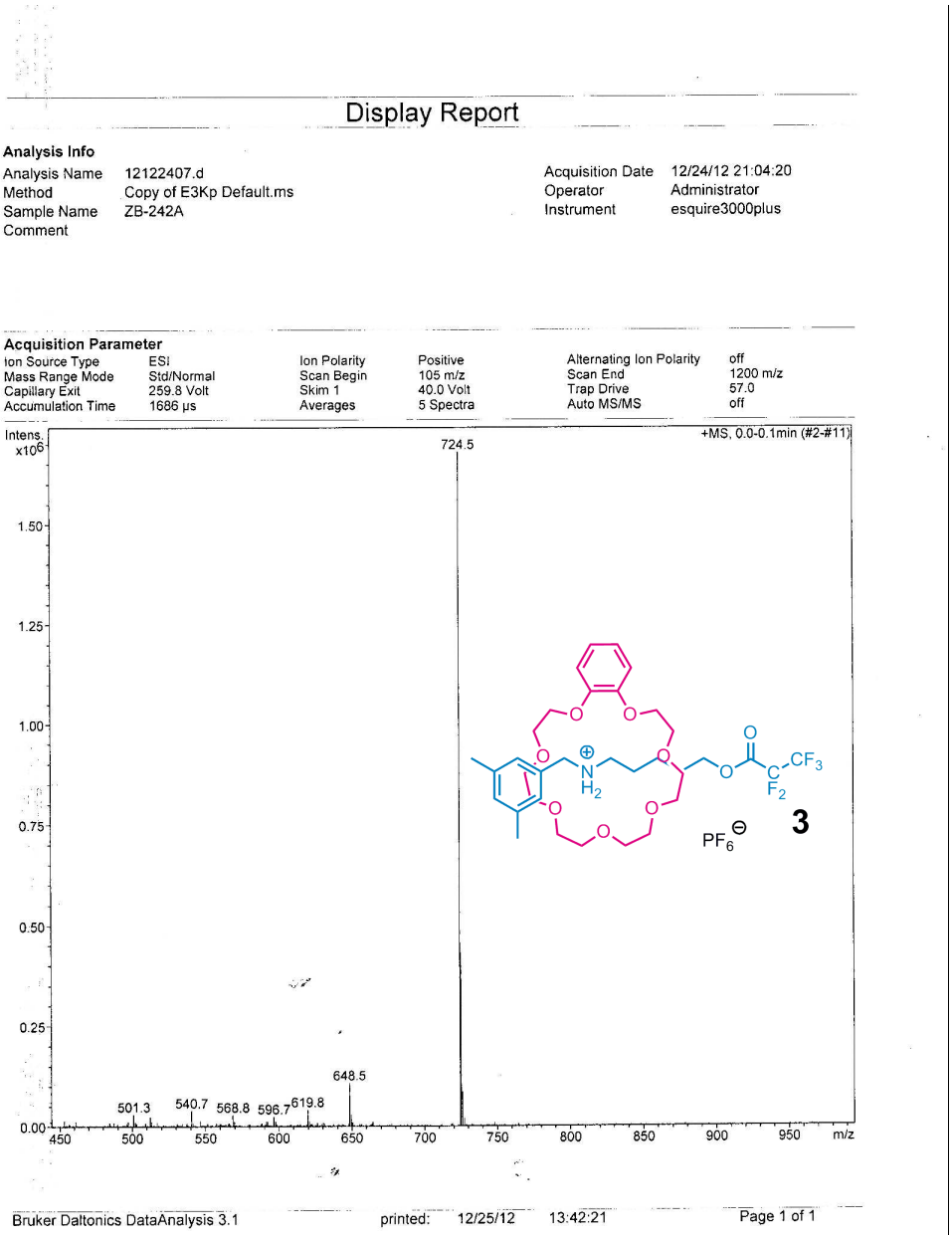
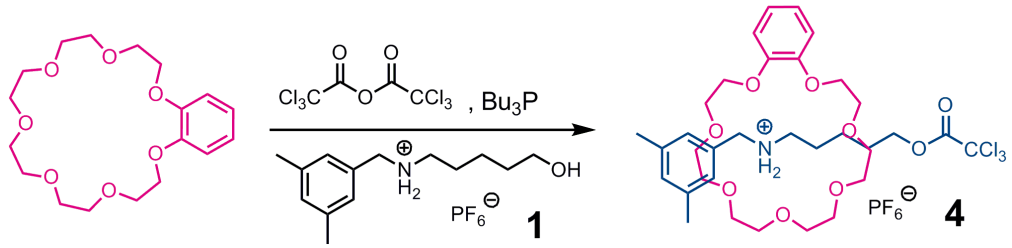


Figure S8. Electrospray ionization mass spectrum of **3**. Assignment of the main peak: *m/z* 724.5 $[M - PF_6]^+$ (100%).

*4. Synthesis of compound **4***



To a solution of **1** (135 mg, 0.37 mmol) and B21C7 (131 mg, 0.37 mmol) in dichloromethane (3 mL) was added trichloroacetic anhydride (92 μL, 0.50 mmol) followed by tributylphosphine (10 μL). After the reaction mixture was stirred for two days, solvent was evaporated to afford a crude product, which was purified by column chromatography on silica gel (dichloromethane) to afford **4** as an oil. The oil was recrystallized from ethyl acetate/diisopropyl ether at −10 °C to provide the product as colorless crystals (110 mg, 34%). M.p. 100.9−102.7 °C. The ^{1}H NMR spectrum of **4** is shown in Figure S9. ^{1}H NMR (400 MHz, acetone-d_6, room temperature) δ (ppm): 7.76 – 7.60 (br, 2H), 7.10 – 7.05 (m, *2*H), 7.01 (s, 3H), 6.99 – 6.93 (m, 2H), 4.46 – 4.30 (m, 8H), 4.08 – 4.02 (m, 2H), 3.95 – 3.82 (m, 4H), 3.79 – 3.53 (m, 18H), 2.27 (s, 6H), 1.87 – 1.72 (m, 4H), 1.62 – 1.52 (m, 2H). The ^{13}C NMR spectrum of **4** is shown in Figure S10. ^{13}C NMR (100 MHz, acetone-d_6, room temperature) δ (ppm): 162.51, 147.97, 139.13, 133.69, 131.28, 128.61, 122.20, 112.81, 72.21, 71.97, 71.75, 71.43, 70.71, 70.00, 69.23, 51.82, 47.87, 28.47, 26.84, 23.89, 21.22. LRESIMS is shown in Figure S11: *m*/*z* 722.5 $[M - PF_6]^+$ (100%). HRESIMS: *m*/*z* calcd for $[M - PF_6]^+$ $C_{34}H_{51}Cl_3NO_9$, 722.2624; found 722.2617, error −1 ppm.

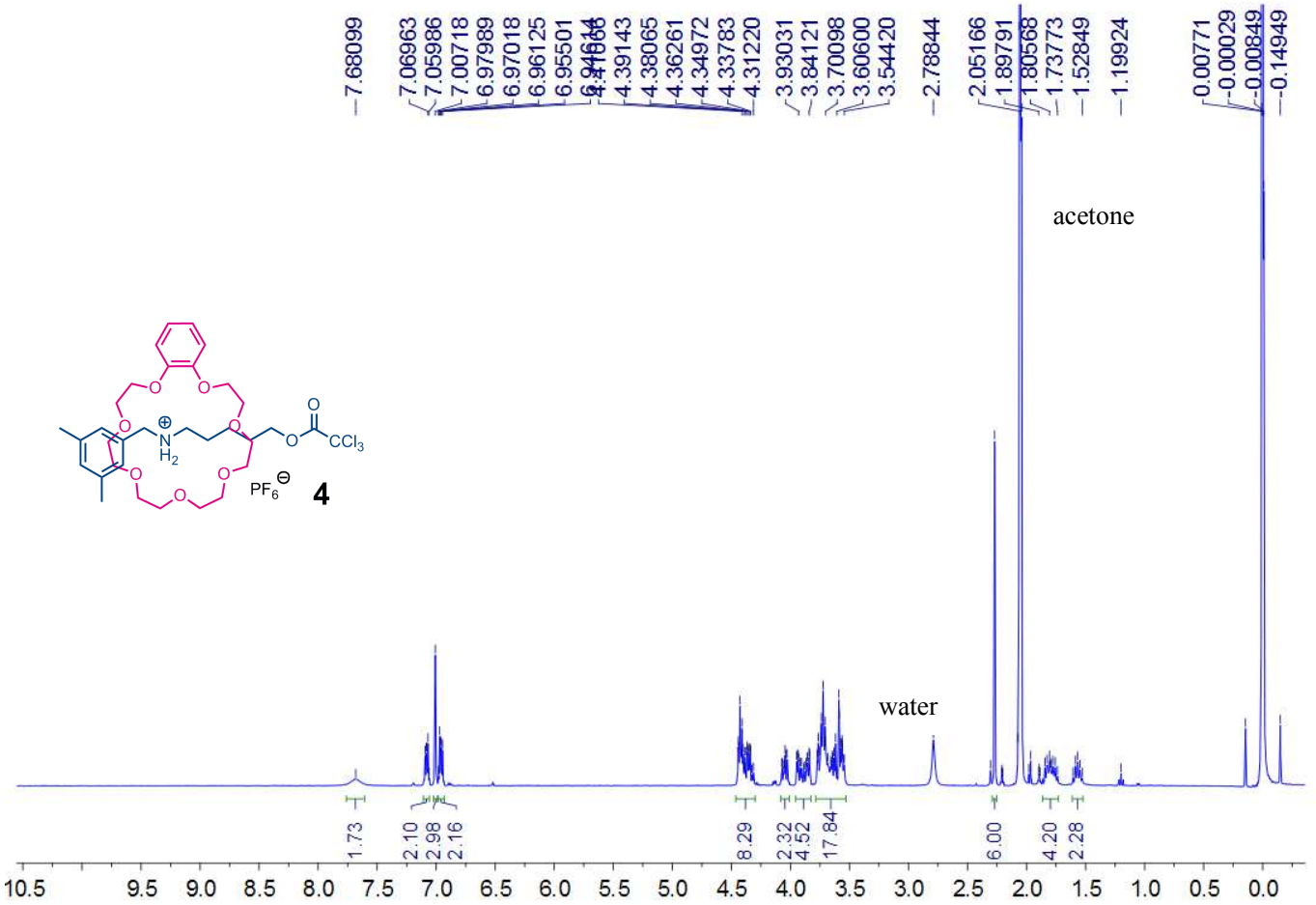


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Figure S9. ^{1}H NMR spectrum (400 MHz, acetone-d_6, room temperature) of **4**.

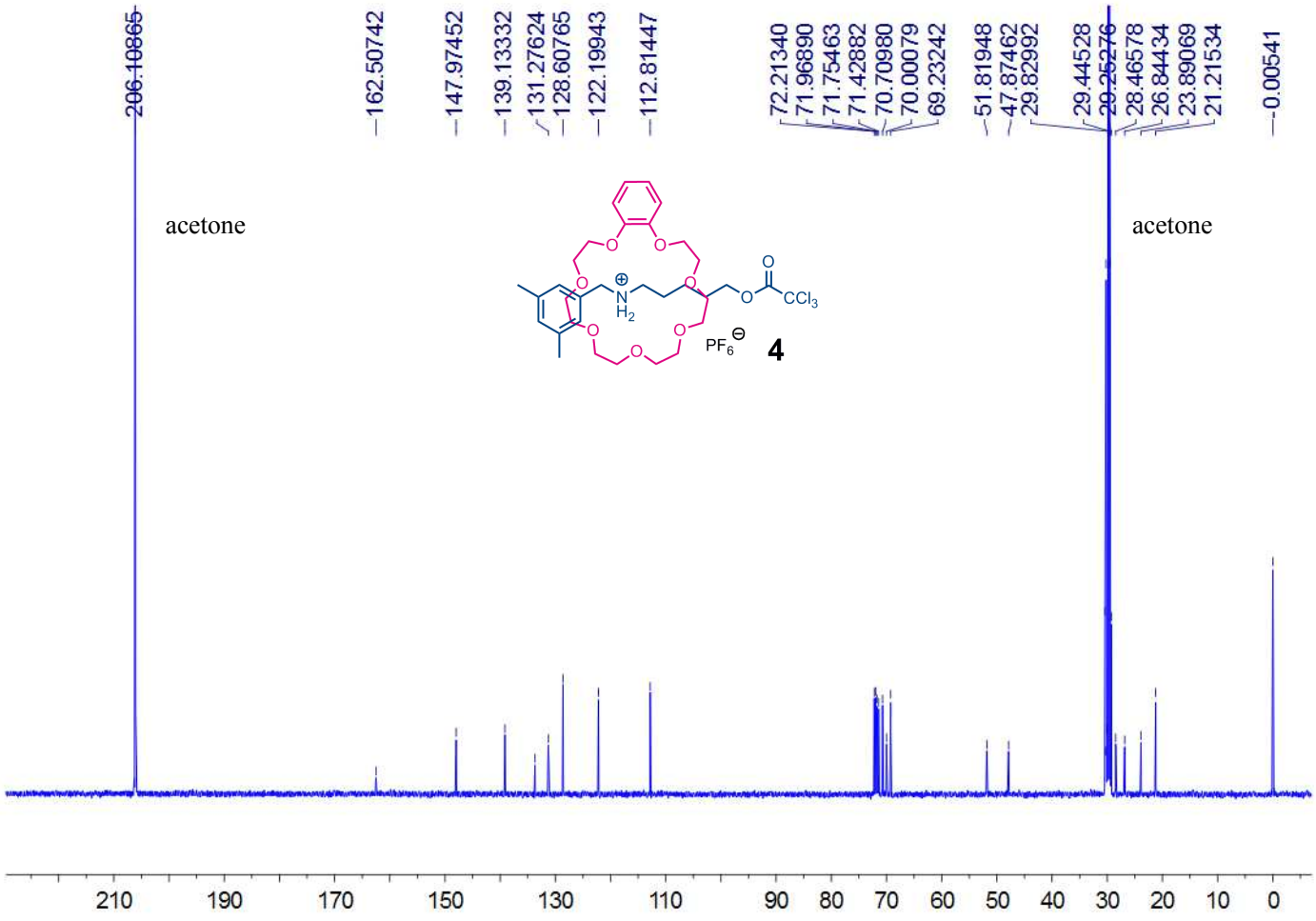

Figure S10. ^{13}C NMR spectrum (100 MHz, acetone-d_6, room temperature) of **4**.

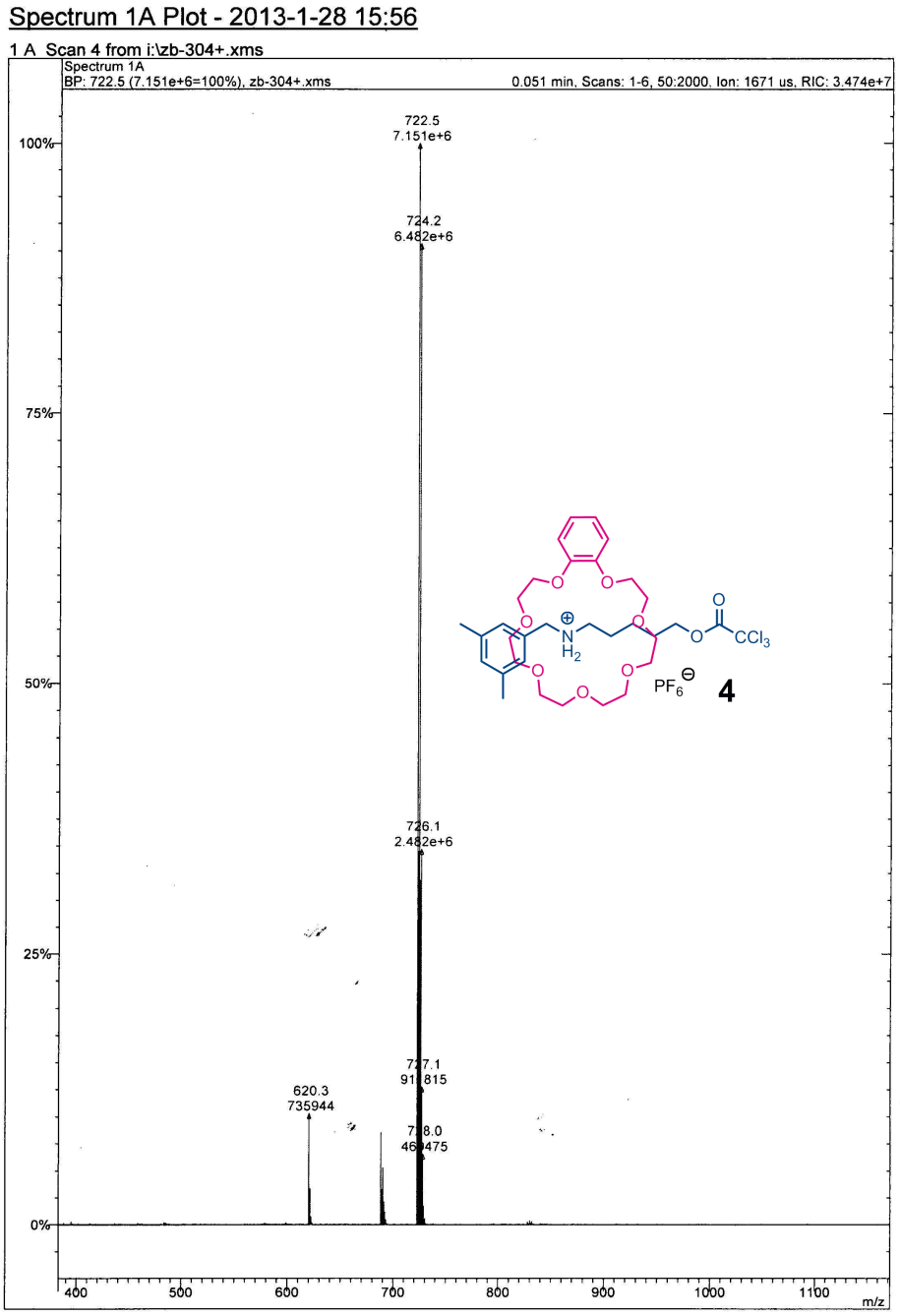

Figure S11. Electrospray ionization mass spectrum of **4**. Assignment of the main peak: *m/z* 722.5 $[M - PF_6]^+$ (100%).

*5. Ball-stick view of the X-ray structure of **P***

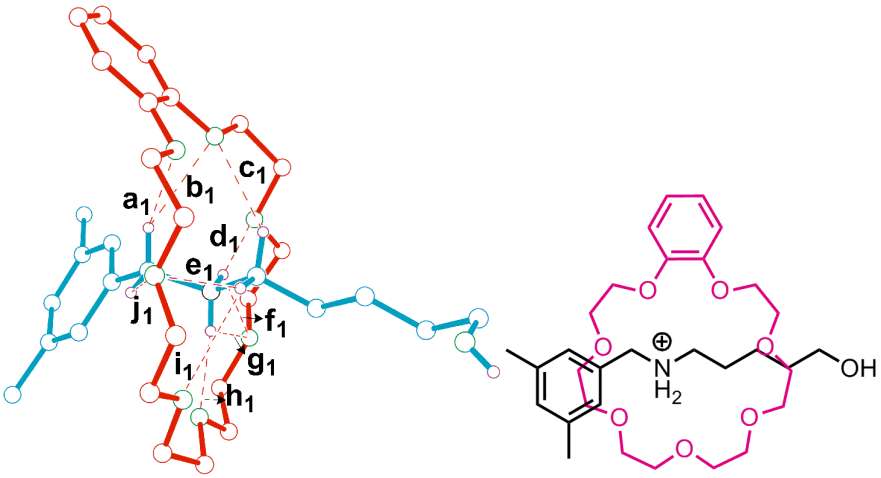

Figure S12. Ball-stick view of the X-ray structure of **P**. Crystals of **P** were obtained by slowly evaporating a dichloromethane/ethyl acetate solution of 1:1 mixture of **1** and B21C7. PF_6 counterions, and hydrogens except the ones involved in hydrogen bonding and the acetyl protons were omitted for clarity. B21C7 parts are red, secondary ammonium salt parts are light blue, hydrogens are purple, oxygens are green, fluorines are dark blue and nitrogens are black. Hydrogen-bond parameters in the threaded structures: H···O distances (Å), C(N)···O distances (Å), C(N)-H···O angles (deg): (a) $\mathbf{a_1}$, 2.54, 3.34, 140; $\mathbf{b_1}$, 2.60, 3.38, 138; $\mathbf{c_1}$, 2.68, 3.46, 138; $\mathbf{d_1}$, 2.04, 2.90, 162; $\mathbf{e_1}$, 2.45, 3.31, 148; $\mathbf{f_1}$, 2.37, 2.88, 116; $\mathbf{g_1}$, 2.56, 2.88, 102; $\mathbf{h_1}$, 2.02, 2.91, 172; $\mathbf{i_1}$, 2.65, 3.27, 122; $\mathbf{j_1}$, 2.66, 3.34, 128.

*6. Partial ^{1}H NMR spectra of **2** heating for over a week*

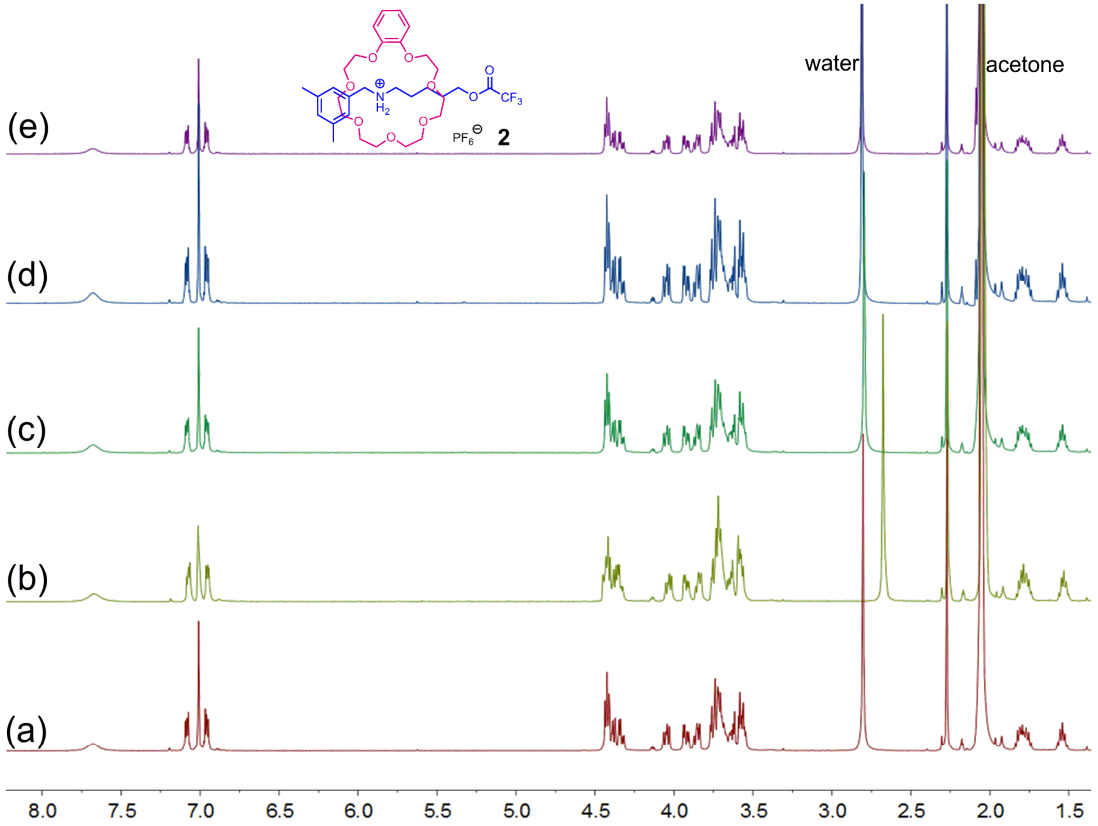

Figure S13. Partial ^{1}H NMR spectra (500 MHz, acetone-d_6) of 5.00 mM **2**: (a) recorded at 298 K; (b) recorded at 313 K; (c) maintained at 333K for 3 h and recorded at 298 K; (d) then maintained at 333K for another 24 h and recorded at 298 K; (e) then maintained at 333 K for a week and recorded at 298 K.

*7. Partial [1]H NMR spectra of analog **5** heating for over a week.*

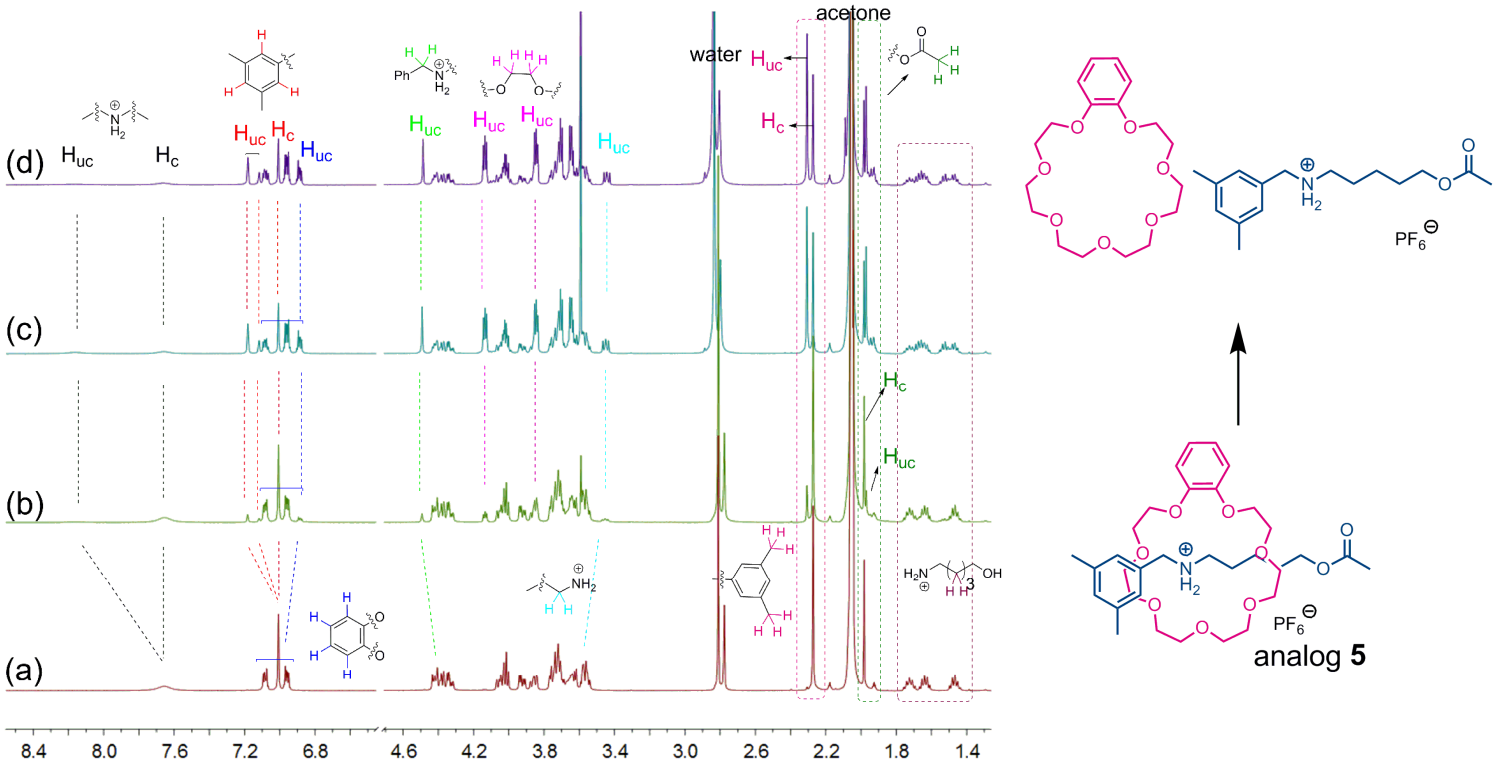

Figure S14. Partial [1]H NMR spectra (400 MHz, acetone-d_6) of 5.00 mM analog **5**: (a) recorded at 298 K; (b) recorded at 313 K; (c) maintained at 333 K for 3 h and recorded at 298 K; (d) then maintained at 333 K for another 24 h and recorded at 298 K. "c" and "uc" denote complexed and uncomplexed species, respectively.

*8. Partial ^{1}H NMR spectra of **2** in DMSO-d_6 at room temperature*

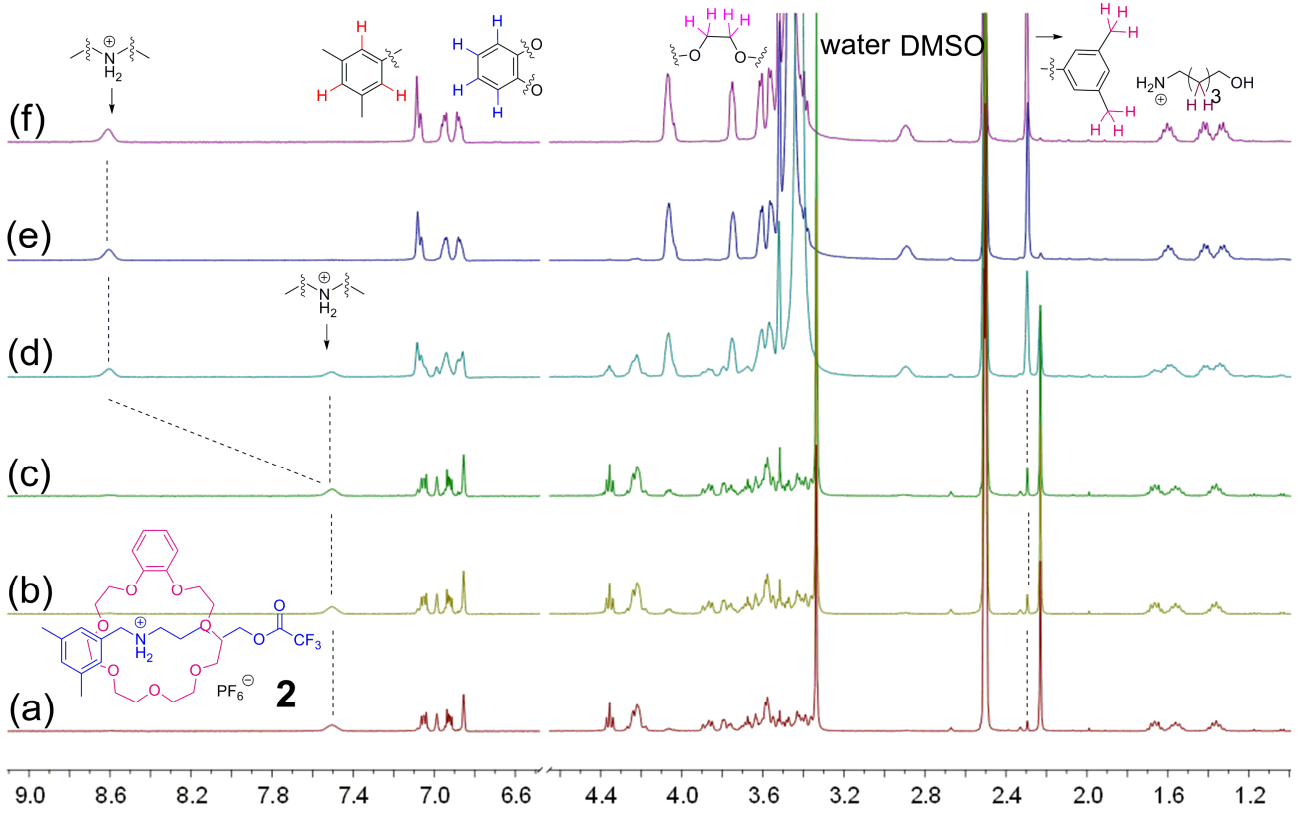

Figure S15. Partial ^{1}H NMR spectra (400 MHz, DMSO-d_6, recorded at 295 K) of 5.00 mM **2**: (a) freshly prepared; (b) maintained at rt for 1 day; (c) maintained at rt for 2 days; (d) maintained at rt for 6 days; (e) maintained at rt for 10 days; (f) after 20 days.

*9. Partial ^{1}H NMR spectra of **3** in acetone-d_6*

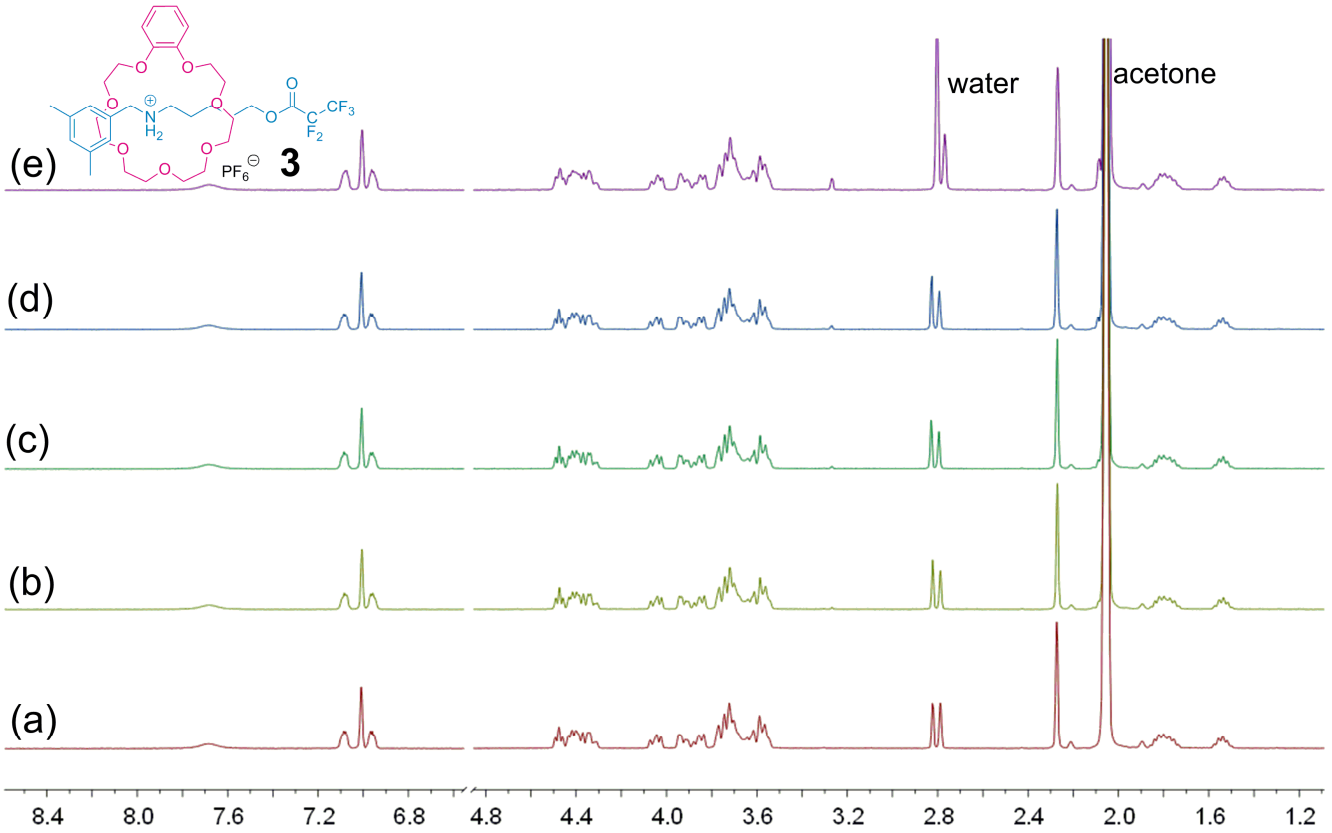

Figure S16. Partial ^{1}H NMR spectra (400 MHz, acetone-d_6, recorded at 295 K) of 5.00 mM **3**: (a) freshly prepared; (b) 18 h; (c) 24 h; (d) 42 h; (e) over 18 days.

*10. Partial ^{1}H NMR spectra of **3** after the addition of TEA.*

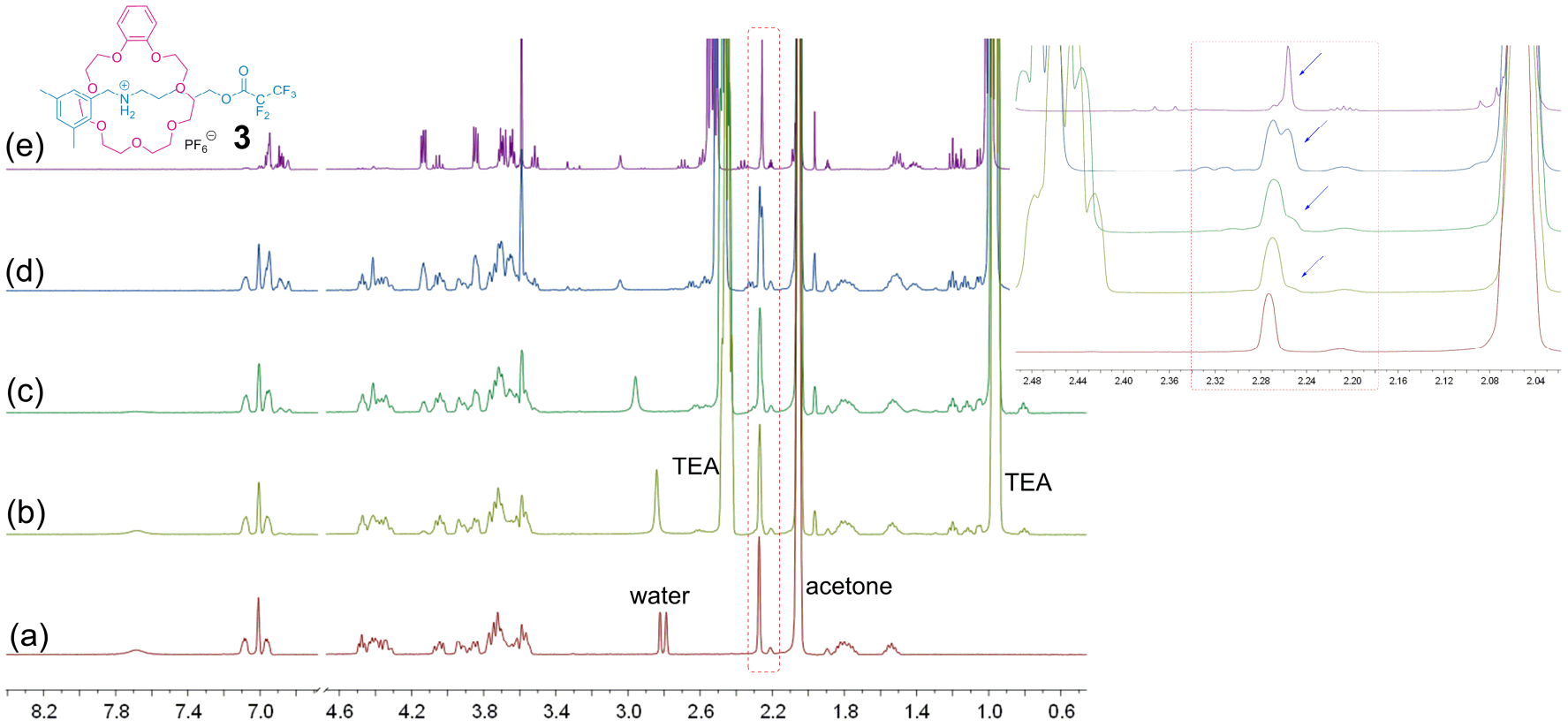

Figure S17. Partial ^{1}H NMR spectra (400 MHz, acetone-d_6, recorded at 295 K) of 5.00 mM **3**: (a) freshly prepared; (b) 100 mM Et_3N was added; (c) after 2 days; (d) after 6 days; (e) after 20 days. The inset represents the spectra between 2.5 and 2.0 ppm.

11. *Partial ^{1}H NMR spectra of **3** in DMSO-d_6 at room temperature*

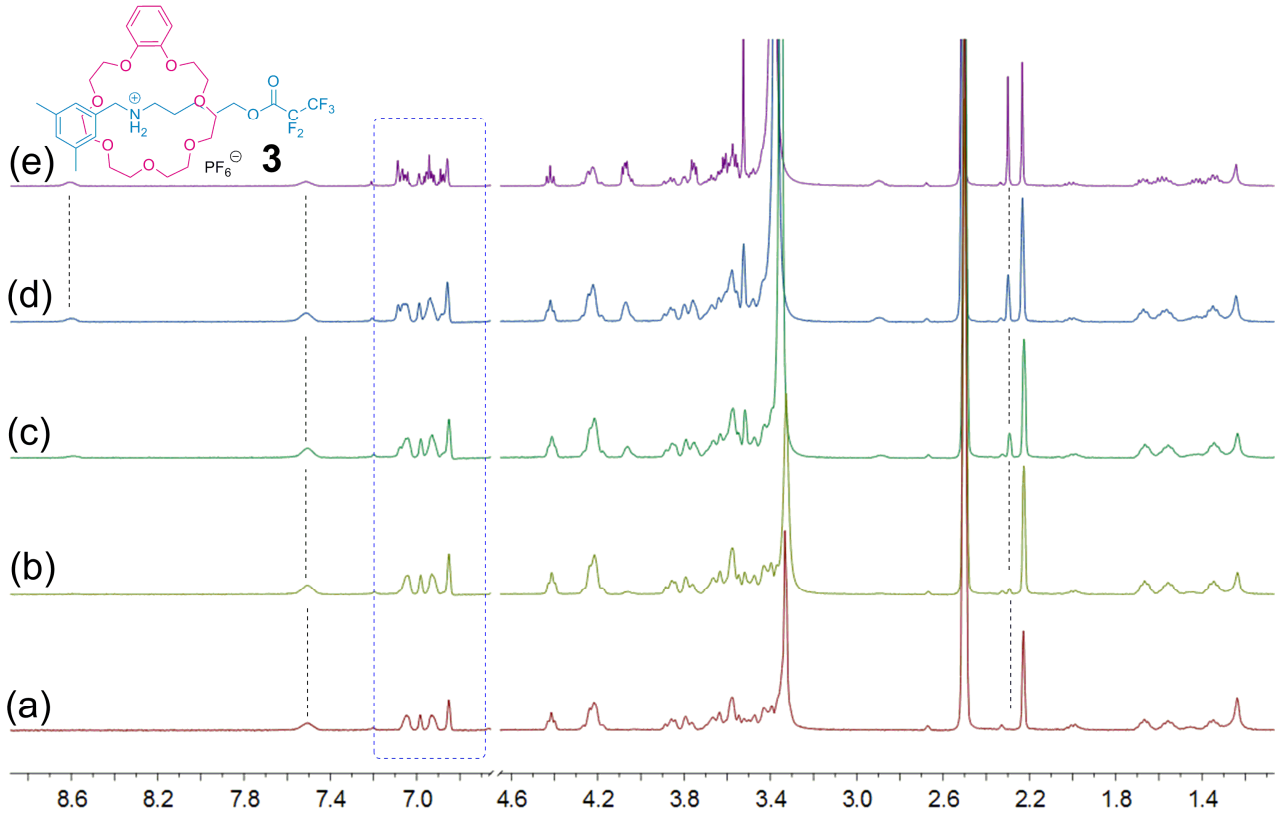

Figure S18. Partial ^{1}H NMR spectra (400 MHz, DMSO-d_6, recorded at 295 K) of 5.00 mM of **3**: (a) freshly prepared; (b) a was maintained at rt for 6 days; (c) b was maintained at rt for 9 days; (d) c was maintained at rt for 12 days; (e) d was maintained at rt for 22 days.

*12. Partial ^{1}H NMR spectra of **3** in DMSO-d_6 at elevated temperature*

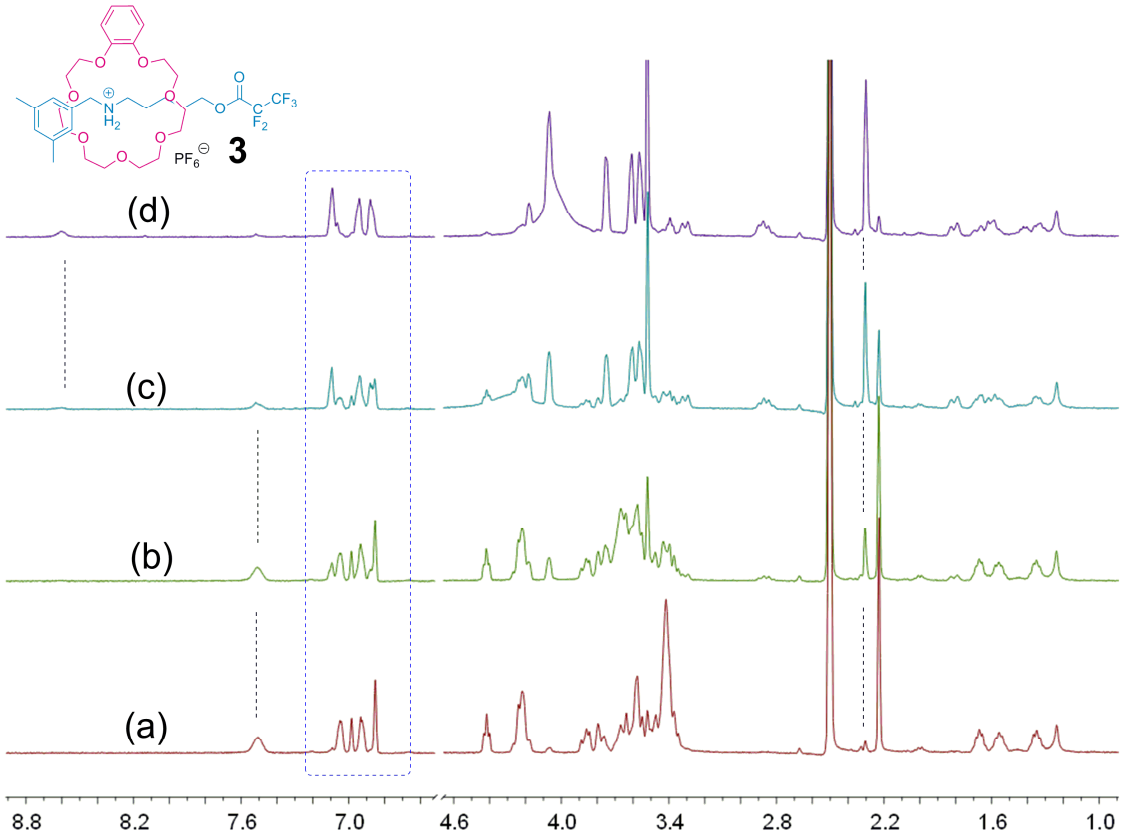

Figure S19. Partial ^{1}H NMR spectra (400 MHz, DMSO-d_6, recorded at 295 K) of 5.00 mM of **3**: (a) freshly prepared; (b) a was maintained at 353 K for 7 h and recorded at 295 K; (c) b was maintained at 353 K for 22 h and recorded at 295 K; (d) c was maintained at rt for 15 days.

*13. Partial ^{1}H NMR spectra of **4** in DMSO-d_6 at elevated temperature*

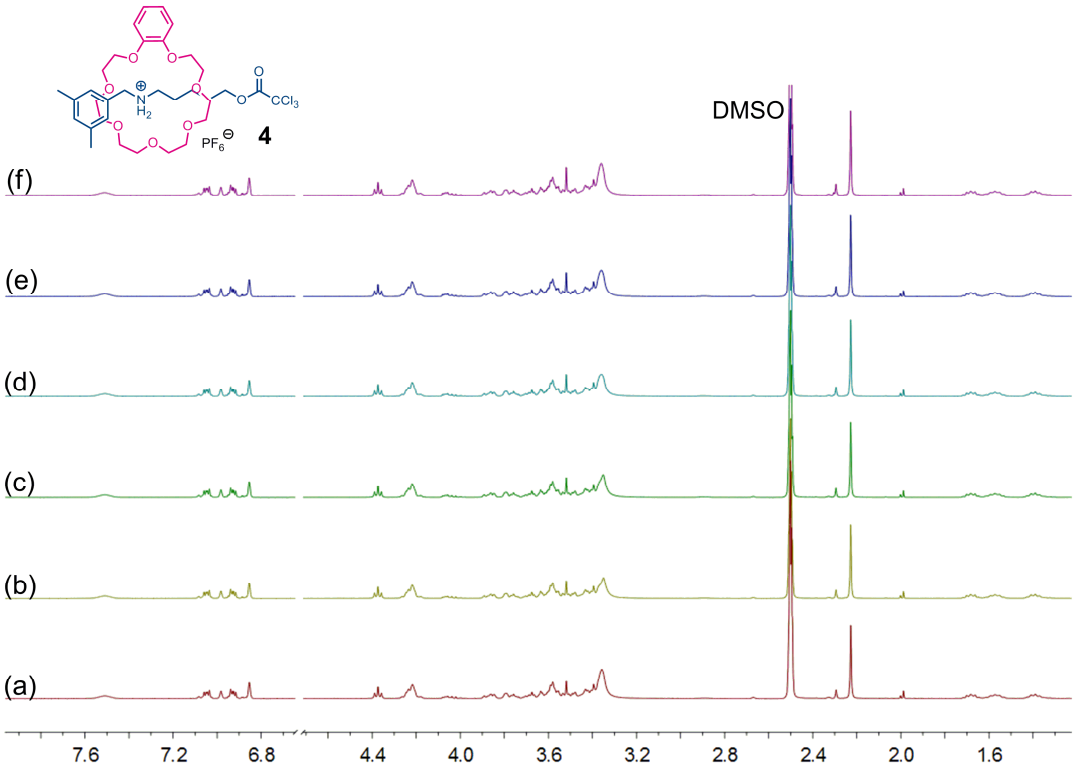

Figure S20. Partial ^{1}H NMR spectra (500 MHz, DMSO-d_6, rt) of 5.00 mM of **4**: (a) freshly prepared; (b) a was maintained at 353 K for 30 min and recorded at 298 K; (c) b was maintained at 353 K for 15 h and recorded at 298 K; (d) c was maintained at 353 K for 24 h and recorded at 298 K; (e) d was maintained at 353 K for 30 h and recorded at 298 K; (f) e was maintained at 353 K for 36 h and recorded at 298 K.

*14. Partial ^{1}H NMR spectra of **4** and TEA in acetone-d_6 at elevated temperature*

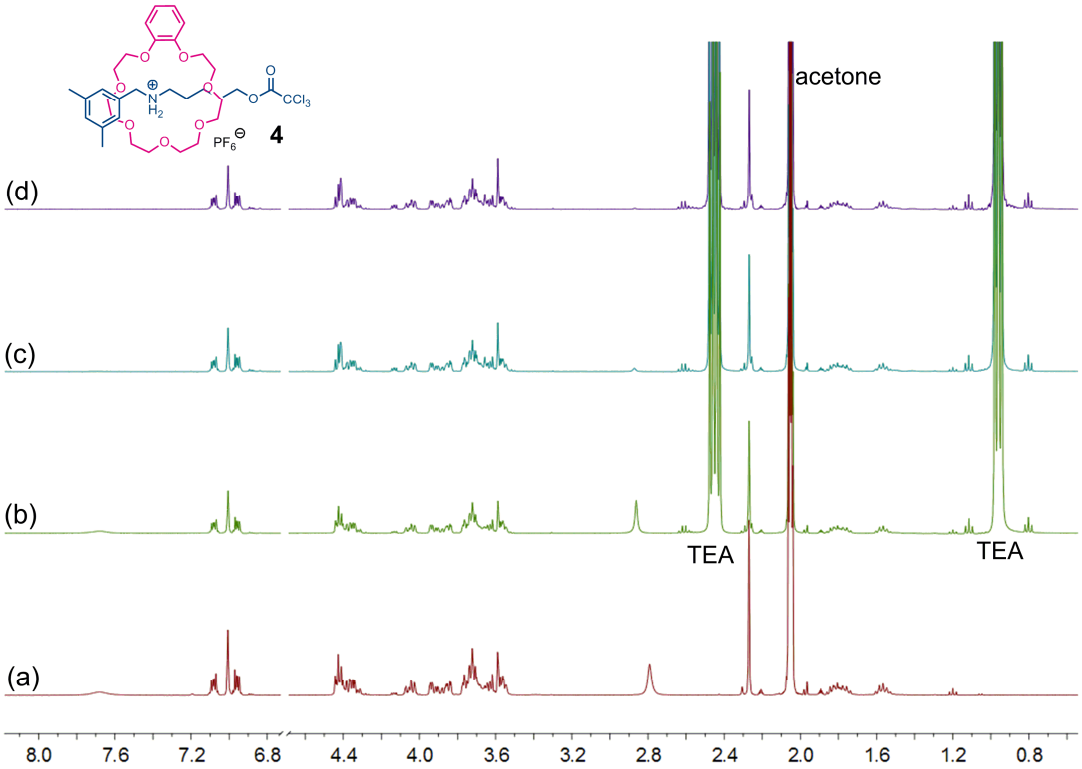

Figure S21. Partial ^{1}H NMR spectra (400 MHz, acetone-d_6, recorded at 295 K) of 5.00 mM of **4**: (a) freshly prepared; (b) 100 mM Et_3N added to a; (c) b was maintained at 333 K for 6 h and recorded at 295 K; (d) c was maintained at 333 K for 12 h and recorded at 295 K. The spectra did not change, indicating the formation of a mechanically interlocked rotaxane.

*15. The solid structures of **2**, **3** and **4***

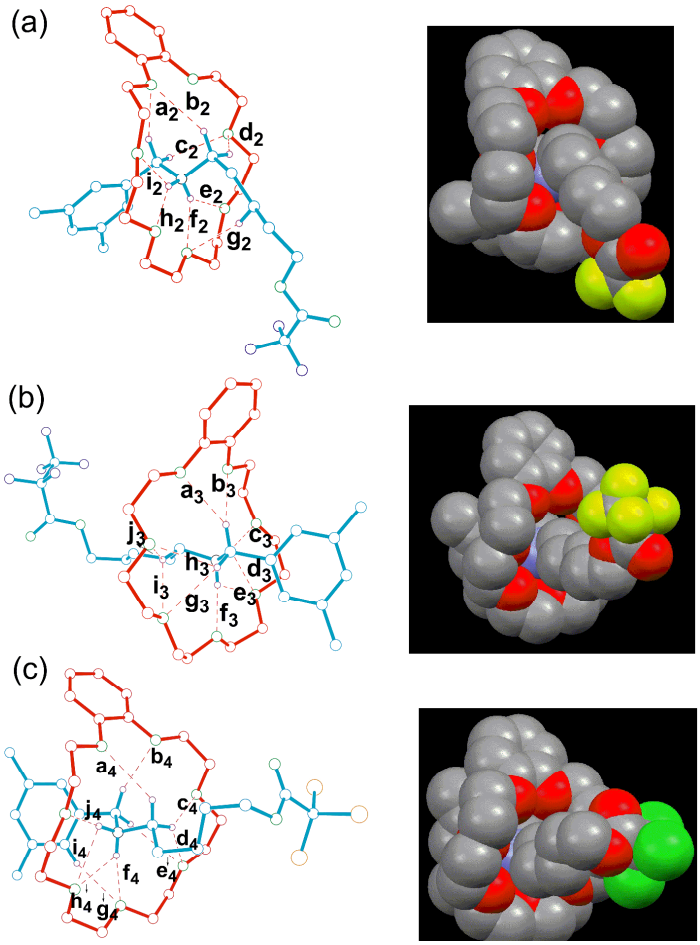

Figure S22. Ball-stick views (left) and spacefill views (right) of the X-ray structures of **2**, **3** and **4**. PF_6 counterions and hydrogens except the ones involved in hydrogen bonding were omitted for clarity. In the left, B21C7 parts are red, secondary ammonium salt parts are light blue, hydrogens are purple, oxygens are green and nitrogens are black. In the right, carbons are grey, oxygens are red, nitrogens are blue, fluorines are yellow and chlorines are green. Hydrogen-bond parameters in the threaded structures: H···O distances (Å), C(N)···O distances (Å), C(N)-H···O angles (deg): (a) $\mathbf{a}_2$, 2.43, 3.33, 154; $\mathbf{b}_2$, 2.55, 3.43, 150; $\mathbf{c}_2$, 2.66, 3.47, 141; $\mathbf{d}_2$, 2.59, 3.37, 138; $\mathbf{e}_2$, 2.37, 3.08, 135; $\mathbf{f}_2$, 2.06, 2.85, 146; $\mathbf{g}_2$, 2.69, 3.64, 164; $\mathbf{h}_2$, 2.07, 2.86, 146; $\mathbf{i}_2$, 2.36, 3.05, 133. (b) $\mathbf{a}_3$, 2.53, 3.41, 149; $\mathbf{b}_3$, 2.71, 3.44, 131; $\mathbf{c}_3$, 1.88, 2.80, 172; $\mathbf{d}_3$, 2.52, 2.97, 110; $\mathbf{e}_3$, 2.55, 2.97, 108 $\mathbf{f}_3$, 1.99, 2.91, 175; $\mathbf{g}_3$, 2.64, 2.43, 130; $\mathbf{h}_3$, 2.64, 3.24, 119; $\mathbf{i}_3$, 2.49, 3.25, 134; $\mathbf{j}_3$, 2.59, 3.31, 130. (c) $\mathbf{a}_4$, 2.70, 3.45, 135; $\mathbf{b}_4$, 2.40, 3.32, 160; $\mathbf{c}_4$, 2.49, 3.27, 138; $\mathbf{d}_4$, 2.44, 3.18, 133; $\mathbf{e}_4$, 2.69, 3.41, 131; $\mathbf{f}_4$, 2.10, 2.99, 167; $\mathbf{g}_4$, 2.69, 3.52, 149; $\mathbf{h}_4$, 2.42, 2.91, 155; $\mathbf{i}_4$, 2.59, 2.91, 102; $\mathbf{j}_4$, 2.04, 2.91, 162.

16. Calculated Structural data of model compounds

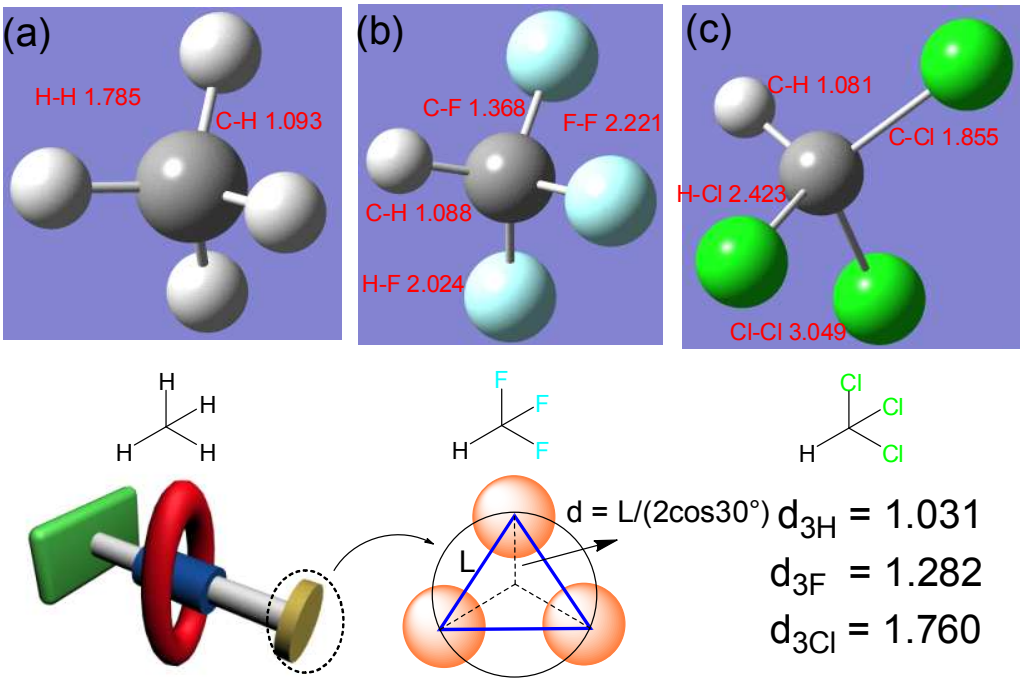

Figure S23. Ball-stick views of the calculated structures (DFT-B3LYP/3-21) of model compounds: (a) CH_4, (b) CHF_3, (c) $CHCl_3$. The rough calculations show the increasing bulkiness of the terminal stoppers.

17. X-ray analysis data

*X-ray analysis data of **P***

Crystallographic data: block, colorless, $C_{32}H_{52}F_6NO_8P$, *FW* 723.72, monoclinic, space group *P* 2_1/c, *a* = 16.4538(11), *b* = 16.4429(8), *c* = 15.0752(8) Å, α = 90.00 (5)°, β = 112.737(7)°, γ = 90.00°, *V* = 3761.6(4) Å^3, *Z* = 4, *D*c = 1.278 g cm^{-3}, *T* = 293(2) K, μ = 0.149 mm^{-1}, 6856 measured reflections, 6856 independent reflections, 436 parameters, 0 restraints, *F*(000) = 1536, R_1 = 0.1371, wR_2 = 0.2807 (all data), R_1 = 0.0804, wR_2 = 0.2330 [I > 2σ(I)], max. residual density 0.718 e•Å^{-3}, and goodness-of-fit (F^2) = 1.054.

*X-ray analysis data of **2***

Crystallographic data: block, colorless, $C_{34}H_{51}F_9NO_9P$, *FW* 819.73, monoclinic, space group *P* 2_1/c, *a* = 13.6071(6), *b* = 15.3919(7), *c* = 23.1024(11) Å, α = 90.00 (5)°, β = 123.978(3)°, γ = 90.00°, *V* = 4012.4(3) Å^3, *Z* = 4, *D*c = 1.357 g cm^{-3}, *T* = 293(2) K, μ = 0.160 mm^{-1}, 7339 measured reflections, 4328 independent reflections, 489 parameters, 582 restraints, *F*(000) = 1720, R_1 = 0.1696, wR_2 = 0.4269 (all data), R_1 = 0.1242, wR_2 = 0.3798 [I > 2σ(I)], max. residual density 1.025 e•Å^{-3}, and goodness-of-fit (F^2) = 1.690.

*X-ray analysis data of **3***

Crystallographic data: block, colorless, $C_{35}H_{51}F_{11}NO_9P$, *FW* 869.74, triclinic, space group *P* -1, *a* = 12.2398(6), *b* = 12.5467(7), *c* = 15.3468(10) Å, α = 66.650(6) (5)°, β = 79.220(5)°, γ = 89.399(4)°, *V* = 2120.3(2) Å^3, *Z* = 2, *D*c = 1.362 g cm^{-3}, *T* = 170(2) K, μ = 0.163 mm^{-1}, 7736 measured reflections, 4563 independent reflections, 516 parameters, 0 restraints, *F*(000) = 908, R_1 = 0.1239, wR_2 = 0.2293 (all data), R_1 = 0.0732, wR_2 = 0.1851 [I > 2σ(I)], max. residual density 0.623 e•Å^{-3}, and goodness-of-fit (F^2) = 1.028.

*X-ray analysis data of **4***

Crystallographic data: block, colorless, $C_{34}H_{51}Cl_3F_6NO_9P$, *FW* 867.22, triclinic, space

group P –1, a = 10.974(2), b = 13.309(3), c = 15.389(3) Å, α = 98.00(3)°, β = 109.51(3)°, γ = 97.42(3)°, V = 2060.5(9) Å^3, Z = 2, Dc = 1.401 g cm^{-3}, T = 295(2) K, μ = 0.339 mm^{-1}, 7229 measured reflections, 6222 independent reflections, 500 parameters, 48 restraints, F(000) = 908, R_1 = 0.0662, wR_2 = 0.1553 (all data), R_1 = 0.0575, wR_2 = 0.1491 [I > 2σ(I)], max. residual density 1.031 e•Å^{-3}, and goodness-of-fit (F^2) = 1.055.

References:

S1. Zhang, C.; Li, S.; Zhang, J.; Zhu, K.; Li, N.; Huang, F. *Org. Lett.* **2007**, *9*, 5553–5556.

S2. Zheng, B.; Zhang, M.; Yan, X.; Huang, F. *Org. Biomol. Chem.* **2013**, *11*, 3880–3885.