Reversible capture and release of a ligand mediated by a long-range relayed polarity switch in a urea oligomer

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Supplementary Methods

General Information

Where specified, procedures were performed under an atmosphere of nitrogen. Air and moisture-sensitive liquids/solutions were transferred to reaction vessels by syringe under an atmosphere of nitrogen. Solvents and reagents were purchased from commercial suppliers and were used without further purification unless otherwise specified. Agitation was achieved using Teflon coated stirrer bars by magnetic induction. All thin layer chromatography (TLC) experiments were conducted on pre-coated plastic plates (Macherey-Nagel polygram SIL G/UV254) and visualized using ultraviolet light (254 nm) or staining. Flash chromatography was performed on an automated Biotage Isolera™ Spektra Four using gradient elution on pre-packed silica gel Sfär Duo columns. Solvent systems for TLC and flash chromatography are reported in solvent:solvent volume ratios. All variable-temperature NMR experiments were conducted using a Bruker AVANCE III HD 500 MHz NMR Spectrometer with 5 mm DCH ¹³C–¹H/D Cryo Probe (500 MHz). All room temperature NMR experiments were conducted using a Bruker Nano 400 Spectrometer (400 MHz) or a Bruker AVANCE III HD 500 MHz NMR Spectrometer with 5 mm DCH ¹³C–¹H/D Cryo Probe (500 MHz), with chemical shifts reported (δ in ppm) relative to the specified deuterated solvent. All ³¹P NMR spectra are referenced relative to an external standard (Ph₃PO) as detailed within. All NMR characterization experiments were performed at 25 °C and 1 atm unless otherwise specified. Multiplicity is reported as follows – s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. All spin-spin coupling constants (J) are reported in hertz (Hz) to the nearest 0.1 Hz. High-resolution mass spectrometry experiments (HR-MS) were performed on a Bruker micrOTOF Spectrometer using electrospray ionization, positive ion mode or a Bruker Ultraflex using MALDI with only molecular ion ([M+H]⁺ or [M+Na]⁺) peaks being reported.
**Synthetic Schemes**

**Scheme S1.** Synthesis of capture-and-release oligoureia 1 and control oligoureia 2. Reagents and conditions: (a) 4-\(n\)-butyloxyphenyl isocyanate (3.3 equiv), DCM, 0 °C to RT, 30 mins; (b) NaOH (8.0 equiv), EtOH/THF/H2O, RT, 2 h; (c) 3,5-bis(trifluoromethyl)phenyl isocyanate (0.5 equiv, added over 80 mins, −10 °C to 0 °C), 0 °C to RT, 2.5 h; (d) benzaldehyde (1.0 equiv), MeOH/THF, RT, 20.5 h; (e) NaBH4, MeOH/THF, 0 °C to RT, 3.5 h; (f) 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.0 equiv), DCM, 0 °C to RT, 1.5 h; (g) dimethylcarbamoyl chloride (1.2 equiv), TEA (1.5 equiv), DCE, 45 °C, 22 h. For all compounds, Ar = 4-\(n\)-BuO-Ph and Ar\(^{'}\) = 3,5-bis(CF\(_3\))-Ph.

**Scheme S2.** Synthesis of control compounds 3-5. Reagents and conditions: (a) 3,5-bis(trifluoromethyl)phenyl isocyanate (1.0 equiv), 0 °C to RT, 1 h; (b) 4-methoxyphenyl isocyanate (0.5 equiv), DCM, RT, 3 h; (c) 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.0 equiv), DCM, 0 °C to RT, 0.5 h; (d) dimethylcarbamoyl chloride (0.5 equiv), TEA (1.3 equiv), DCE, 45 °C, 30 h; (e) 4-\(n\)-butyloxyphenyl isocyanate (1.0 equiv), DCM, RT, 50 mins. For all compounds, Ar = 3,5-bis(CF\(_3\))-Ph, Ar\(^{'}\) = 4-MeO-Ph and Ar\(^{''}\) = 4-\(n\)-BuO-Ph.
**Scheme S3.** Synthesis of control thiourea 6. Reagents and conditions: (a) benzaldehyde (2.0 equiv), MeOH, RT, 17 h; (b) NaBH₄, MeOH, 0 °C to RT, 3 h; (c) dimethylcarbamoyl chloride (0.5 equiv), TEA (1.3 equiv), DCE, 45 °C, 24 h; (d) 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.0 equiv), DCM, 0 °C to RT, 2.5 h. For all compounds, Ar = 4-n-BuO-Ph and Ar⁺ = 3,5-bis(CF₃)-Ph.

**Scheme S4.** Synthesis of capture-and-release oligourea 7. Reagents and conditions: (a) Ethyl trifluoroacetate (2.0 equiv), MeOH, −78 °C to RT, 19 h; (b) 4-n-butyloxyphenyl isocyanate (4.4 equiv), DCM, 0 °C to RT, 20 mins; (c) NaOH (8.0 equiv), EtOH/THF/H₂O/DMF, RT, 2 h; (d) 3,5-bis(trifluoromethyl)phenyl isocyanate (1.0 equiv, added over 70 mins, −10 °C to 0 °C), 0 °C to RT, 1 h; (e) N-benzyl-N-Boc-2-aminoacetaldehyde (1.0 equiv), MeOH/THF, RT, 19 h; (f) NaBH₄, MeOH/THF, 0 °C to RT, 3 h; (g) 4-n-butyloxyphenyl isocyanate (1.0 equiv), DCM, RT, 1.5 h; (h) TFA, DCM, RT, 27.5 h (i) 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.0 equiv), DCM, RT, 2 h. For all compounds, Ar = 4-n-BuO-Ph and Ar⁺ = 3,5-bis(CF₃)-Ph.
Scheme S5. Synthesis of pyridinium borate salt S8 and phosphazenium borate salt S9. Reagents and conditions: (a) NaBArF₄ (1.0 equiv), MeCN, RT, 2 h; (b) S8 (1.0 equiv), DCM, RT, 1 min.

Scheme S6. Synthesis of oligoureia S10 containing alkyl ureas as the communication channel. Reagents and conditions: (a) benzaldehyde (1.0 equiv), MeOH, RT, 21 h; (b) NaBH₄, MeOH, 0 °C to RT, 96 h; (c) 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.0 equiv), DCM, RT, 1 h; Ar = 3,5-bis(CF₃)-Ph.

Experimental Procedures

4,7,10-Tris(4-n-butyloxyanilinylcarbonyl)-1,4,7,10,13-pentaazatridecane, 1-1

Step 1 (tris-urea formation): To a solution of 1,13-(bis(trifluoroacetyl))tetraethylenepentamine¹ (1.006 g, 2.64 mmol, 1.0 equiv) in lab grade CH₂Cl₂ (21.4 mL) at 0 °C under air was added over 5 min a solution of 4-butoxyphenyl isocyanate (1.665 g, 8.71 mmol, 3.3 equiv) in CH₂Cl₂ (5.0 mL) [note that the isocyanate solution was delivered into the reaction flask by filtration through a cotton pipette plug to remove a small amount of an insoluble urea impurity]. After complete addition, the ice bath was removed and the mixture was stirred at room temperature for 30 min. MeOH (5 mL) was added and the mixture was stirred for 5 min to quench any unreacted isocyanate. The mixture was concentrated in vacuo. To the residue was added petroleum ether/Et₂O (1:1, 20 mL) and the suspension was sonicated for ~5 min until the gum turned to a fine white powder, then the solid was collected by filtration, washed with petroleum ether/Et₂O (1:1, 20 mL) and dried to give the intermediate tris-urea (2.122 g, 84%) as an off-white solid. TLC –
R_f = 0.26 (SiO_2, 5:95 MeOH:CH_2Cl_2). **Step 2** (trifluoroacetamide hydrolysis): The product from **Step 1** (2.122 g, 2.22 mmol, 1.0 equiv) was dissolved in a mixture of lab grade THF (11.1 mL) and EtOH (22.2 mL). A solution of NaOH (711.0 mg, 17.78 mmol, 8.0 equiv) in water (11.1 mL) was added and the mixture was stirred at room temperature under air for 2 h. Most of the solvents were removed *in vacuo*, then water (15 mL) was added. The product was extracted with CH_2Cl_2 (50 mL + 30 mL) then the combined organic extracts were dried (Na_2SO_4) and concentrated. Flash chromatography (Biotage, 50 g Sfär Duo column, MeOH/[35% aqueous NH_3]/CH_2Cl_2 gradient from 0:0:100 to 10:2:88) gave the title compound (1.315 g, 78%, or 65% over two steps) as a white solid. TLC – R_f = 0.05 (SiO_2, 10:2:88 MeOH:[35% aqueous NH_3]:CH_2Cl_2).

**1H NMR** (500 MHz, CDCl_3) δH 0.95 (t, J = 7.4, 6H, 2 x C_H_3), 0.96 (t, J = 7.4, 3H, C_H_3), 1.46 (dq, J = 7.4, 2H, 2 x CH_2CH_3), 1.69-1.75 (m, 6H, 3 x CH_2CH_2CH_3), 1.79 (s, 4H, 2 x NH_2), 2.86 (t, J = 4.8, 4H, 2 x CH_2NH_2), 3.19-3.41 (m, 8H, 4 x NC_H_2), 3.45-3.50 (m, 4H, 2 x NCH_2), 3.89 (t, J = 6.6, 4H, 2 x OCH_2), 3.90 (t, J = 6.5, 2H, OCH_2), 6.79 (d, J = 9.0, 4H, 4 x ArH), 6.80 (d, J = 8.9, 2H, 2 x ArH), 7.32 (d, J = 7.5, 4H, 4 x ArH), 7.56 (d, J = 8.9, 2H, 2 x ArH), 9.02 (s, 1H, NH), 9.87 (s, 2H, 2 x NH).

**13C NMR** (126 MHz, CDCl_3) δC 13.9 (3 x C_H_3), 19.3 (3 x CH_2CH_3), 31.4 (3 x CH_2CH_2CH_3), 41.7 (2 x NCH_2), 47.0 (2 x NCH_2), 47.4 (2 x NCH_2), 52.3 (2 x NCH_2), 68.1 (3 x OCH_2), 114.6 (2 x ArC), 114.7 (4 x ArC), 120.8 (2 x ArC), 121.1 (4 x ArC), 133.3 (ArC), 133.4 (2 x ArC), 154.6 (2 x ArC), 154.6 (ArC), 156.3 (CO), 158.0 (2 x CO).

**HR-MS** (ESI, positive ion mode) – m/z for [C_{41}H_{62}N_8O_6+H]^+ = 763.4865. Found 763.4830.

**1-(3,5-Bis(trifluoromethyl)anilinylcarbonyl)-4,7,10-tris(4-n-butyloxyanilinylcarbonyl)-1,4,7,10,13-pentaazatridecane, 1-2**

To a solution of 1-1 (695.0 mg, 0.91 mmol, 2.0 equiv) in lab grade CH_2Cl_2 (6.6 mL) at −10 °C (ice/salt bath) under N_2 was added dropwise over 80 min a solution of 3,5-bis(trifluoromethyl)phenyl isocyanate (116.2 mg, 0.46 mmol, 1.0 equiv) in CH_2Cl_2 (2.5 mL) while maintaining the cold bath temperature between −10 °C and 0 °C. After complete addition, the cold bath was allowed to warm to room temperature and the mixture was stirred for a further 2.5 h, before being concentrated *in vacuo*. Flash chromatography (Biotage, 25 g Sfär Duo column, MeOH/[35% aqueous NH_3]/CH_2Cl_2 gradient from 0:0:100 to 10:2:88) gave the title compound (261.6 mg, 56% based on the isocyanate) as a white solid. Further elution from the chromatography column returned unreacted 1-1 (424.1 mg, 61% based on total diamine used). **Data for 1-2**: TLC – R_f = 0.36 (SiO_2, 10:2:88 MeOH:[35% aqueous NH_3]:CH_2Cl_2).

**1H NMR** (500 MHz, CDCl_3) δH 0.93 (t, J = 7.4, 3H, CH_3), 0.96 (t, J = 7.4, 3H, CH_3),
0.96 (t, J = 7.4, 3H, CH₃), 1.38-1.51 (m, 6H, 3 x CH₂CH₃), 1.63-1.76 (m, 6H, 3 x CH₂CH₃), 1.84 (s, 2H, NH₂), 2.91 (t, J = 4.5, 2H, NCH₂), 3.31-3.57 (m, 14H, 7 x NCH₂), 3.76 (t, J = 6.4, 2H, OCH₂), 3.85-3.92 (m, 4H, 2 x OCH₂), 6.72 (d, J = 8.9, 2H, ArH), 6.77 (d, J = 9.0, 2H, ArH), 6.80 (d, J = 9.6, 2H, ArH), 6.87 (s, 1H, NH), 7.27 (d, J = 8.5, 2H, ArH), 7.36 (s, 1H, ArH), 7.44 (d, J = 8.9, 2H, ArH), 7.53 (d, J = 9.0, 2H, ArH), 7.62 (s, 2H, 2 x ArH), 8.42 (s, 1H, NH), 9.01 (s, 1H, NH), 9.16 (s, 1H, NH).

13C NMR (126 MHz, CDCl₃) δ C 13.9 (C₃H₃), 14.0 (2 x C₃H₃), 19.3 (C₆H₂CH₃), 19.3 (2 x C₆H₂CH₃), 31.4 (C₆H₂CH₂CH₃), 31.5 (2 x C₆H₂CH₂CH₃), 39.1 (NCH₂), 41.9 (NCH₂), 47.0 (2 x NCH₂), 48.1 (NCH₂), 48.2 (NCH₂), 48.3 (NCH₂), 53.0 (NCH₂), 67.9 (OCH₂), 68.1 (OCH₂), 114.8 (2 x ArC), 114.8 (2 x ArC), 114.9 (2 x ArC), 118.0 (2 x ArC), 121.1 (2 x ArC), 121.6 (2 x ArC), 122.1 (2 x ArC), 123.4 (q, J = 273.4, 2 x CF₃), 131.7 (q, J = 33.1, 2 x ArC), 132.3 (ArC), 132.8 (3 x ArC), 141.2 (ArC), 155.0 (ArC), 155.1 (ArC), 155.4 (ArC), 156.4 (CO), 157.0 (CO), 157.0 (CO), 158.9 (CO).

19F NMR (377 MHz, CDCl₃) δ F −62.7 (2 x CF₃).

HR-MS (ESI, positive ion mode) – m/z for [C₅₀H₆₅F₆N₉O₇+H]+ = 1018.4984. Found 1018.4950.

1-(3,5-Bis(trifluoromethyl)anilinylcarbonyl)-13-Benzyl-4,7,10-tris(4-n-butyloxyanilinylcarbonyl)-1,4,7,10,13-pentaazatridecane, 1-3

To a solution of 1-2 (642.8 mg, 0.63 mmol, 1.0 equiv) in lab grade THF (3.2 mL) was added a solution of benzaldehyde (67.0 mg, 0.63 mmol, 1.0 equiv) in lab grade MeOH (3.2 mL) and the mixture was stirred under air at room temperature for 20.5 h. The mixture was cooled to 0 °C and solid NaBH₄ (47.8 mg, 1.26 mmol, 2.0 equiv) was added, then the mixture was allowed to warm to room temperature in the cold bath with stirring over 3.5 h. 1 M K₂CO₃ (10 mL) was added and most of the organic solvents were removed in vacuo. Water (5 mL) was added and the product was extracted with CH₂Cl₂ (40 mL + 25 mL) then the combined organic extracts were dried (Na₂SO₄) and concentrated. Flash chromatography (Biotage, 25 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 10:90) gave the title compound (573.7 mg, 82%) as a white solid.

TLC – Rf = 0.43 (SiO₂, 10:90 MeOH:CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δ H 0.94 (t, J = 7.4, 3H, CH₃), 0.97 (t, J = 7.4, 3H, CH₃), 0.98 (t, J = 7.4, 3H, CH₃), 1.38-1.52 (m, 6H, 3 x CH₂CH₃), 1.64-1.77 (m, 6H, 3 x CH₂CH₂CH₃), 1.90 (s, 1H, NH), 2.89 (t, J = 4.0, 2H, NCH₂), 3.34-3.45 (m, 6H, 3 x NCH₂), 3.46-3.57 (m, 8H, 4 x NCH₂), 3.75 (t, J = 6.2, 2H, NCH₂), 3.83 (s, 2H, CH₂Ar), 3.86-3.92 (m, 4H, 2 x OCH₂), 6.73 (d, J = 8.9, 2H, 2 x ArH), 6.76 (d, J = 9.0, 2H, 2 x ArH), 6.78 (d, J = 9.0, 2H, 2 x ArH), 6.87 (s, 1H, NH), 7.13 (d, J = 8.9, 2H, 2 x ArH), 7.26 (d, J = 9.0, 2H, 2 x ArH), 7.36 (d, J = 8.5, 2H, ArH), 7.44 (d, J = 8.9, 2H, ArH), 7.53 (d, J = 9.0, 2H, ArH), 7.62 (s, 2H, 2 x ArH), 8.42 (s, 1H, NH), 9.01 (s, 1H, NH), 9.16 (s, 1H, NH), 10.20 (s, 1H, NH).
7.29-7.34 (m, 3H, 3 x ArH), 7.37 (s, 1H, ArH), 7.45 (d, J = 9.0, 2H, 2 x ArH), 7.53 (d, J = 9.0, 2H, 2 x ArH), 7.61 (s, 2H, 2 x ArH), 8.39 (s, 1H, NH), 9.04 (s, 1H, NH), 9.13 (s, 1H, NH), 10.12 (s, 1H, NH).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$C 13.9 ($\text{C}_3\text{H}_3$), 14.0 (2 x $\text{C}_3\text{H}_3$), 19.3 (CH$_2$CH$_3$), 19.4 (2 x CH$_2$CH$_3$), 31.4 (CH$_2$CH$_2$CH$_3$), 31.5 (2 x CH$_2$CH$_2$CH$_3$), 39.1 (NCH$_2$), 47.0 (2 x NCH$_2$), 48.4 (3 x NCH$_2$), 49.7 (NCH$_2$), 51.2 (NCH$_2$), 54.4 (CH$_2$Ar), 67.9 (OCH$_3$), 68.1 (OCH$_3$), 68.1 (OCH$_3$), 114.8 (6 x ArC), 118.1 (2 x ArC), 121.3 (2 x ArC), 121.6 (2 x ArC), 122.2 (2 x ArC), 123.5 (q, J = 274.0, 2 x CF$_3$), 127.8 (ArC), 128.5 (2 x ArC), 128.9 (2 x ArC), 131.7 (q, J = 33.0, 2 x ArC), 132.2 (2 x ArC), 132.8 (ArC), 138.7 (ArC), 141.2 (ArC), 155.0 (ArC), 155.1 (ArC), 155.4 (ArC), 156.4 (CO), 157.0 (CO), 157.1 (CO), 158.8 (CO).

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$F $-$63.2 (2 x CF$_3$).

HR-MS (ESI, positive ion mode) – m/z for [C$_{57}$H$_{71}$F$_6$N$_9$O$_7$+H]$^+$ = 1108.5453. Found 1108.5441.

1-Benzyl-1-(3,5-bis(trifluoromethyl)anilinylthiocarbonyl)-4,7,10-tris(4-n-butyloxyanilinylcarbonyl)-13-(3,5-bis(trifluoromethyl)anilinylcarbonyl)-1,4,7,10,13-pentaazatridecane, 1

To a suspension of 1-3 (110.8 mg, 0.10 mmol, 1.0 equiv) in lab grade CH$_2$Cl$_2$ (2.0 mL) at 0 °C under air was added a solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (27.1 mg, 0.10 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (1.0 mL) and the mixture was allowed to warm to room temperature in the cold bath with stirring over 1.5 h. MeOH (1 mL) was added and the mixture was stirred for a further 2 min before being concentrated in vacuo. Flash chromatography (Biotage, 5 g Sfär Duo column, MeOH/CH$_2$Cl$_2$ gradient from 0:100 to 6:94) gave the title compound (132.9 mg, 96%) as a white solid. TLC – Rf = 0.46 (SiO$_2$, 5:95 MeOH:CH$_2$Cl$_2$).

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$H 0.93-0.98 (m, 9H, 3 x $\text{C}_3\text{H}_3$), 1.41-1.49 (m, 6H, 3 x $\text{C}_3\text{H}_2$CH$_3$), 1.68-1.75 (m, 6H, 3 x $\text{C}_3\text{H}_2$CH$_2$CH$_3$), 3.23-3.29 (m, 2H, NC$_2$H$_2$), 3.39 -3.53 (m, 12H, 6 x NC$_2$H$_2$), 3.72-3.83 (m, 2H, NC$_2$H$_2$), 3.83-3.91 (m, 6H, 3 x OC$_2$H$_2$), 5.33 (s, 2H, C$_2$H$_2$Ar), 5.62 (s, 1H, NH), 6.74-6.80 (m, 6H, 6 x ArH), 7.31-7.37 (m, 3H, 3 x ArH), 7.38-7.43 (m, 2H, 2 x ArH), 7.45-7.52 (m, 7H, 7 x ArH), 7.65 (s, 1H, ArH), 7.83 (s, 2H, 2 x ArH), 8.45 (s, 2H, 2 x ArH), 8.55 (s, 1H, NH), 8.94 (s, 1H, NH), 9.17 (s, 1H, NH), 10.83 (s, 1H, NH). $^{13}$C NMR (126 MHz, CD$_2$Cl$_2$) $\delta$C 14.0 (3 x $\text{C}_3\text{H}_3$), 19.6 (3 x CH$_2$CH$_3$), 31.7 (CH$_2$CH$_2$CH$_3$), 31.8 (2 x CH$_2$CH$_2$CH$_3$), 40.2 (NCH$_2$), 47.6-49.0 (7 x NCH$_2$), 56.4 (CH$_2$Ar), 68.0 (OCH$_3$), 68.1 (OCH$_3$), 68.1 (OCH$_3$), 114.9 (6 x ArC), 116.1 (ArC), 118.6 (2 x ArC), 121.6 (4 x ArC), 122.1 (2 x ArC), 123.8 (q, J = 271.6, 4 x CF$_3$), 124.7 (2 x ArC) 124.8 (ArC), 127.0 (ArC), 127.5 (2 x ArC), 128.2 (ArC), 129.3 (2 x ArC), 132.2 (q, J = 33.1, 4 x ArC), 132.8 (3 x ArC),
137.2 (ArC), 141.0 (ArC), 142.9 (ArC), 155.6 (3 x ArC), 156.5 (CO), 157.3 (CO), 157.4 (2 x CO), 182.0 (CS).

1^{19}F NMR (377 MHz, CD$_2$Cl$_2$) $\delta_F -63.3$ (2 x C$_3$F), $\delta_F -63.1$ (2 x C$_3$F).

HR-MS (ESI, positive ion mode) – $m/z$ for [C$_{66}$H$_{74}$F$_{12}$N$_{10}$O$_7$S$^+$Na$^+$] = 1401.5163. Found 1401.5156.

1-Benzyl-1-(dimethylaminocarbonyl)-4,7,10-tris(4-n-butyloxyanilinylcarbonyl)-13-(3,5-bis(trifluoromethyl)anilinylthiocarbonyl)-1,4,7,10,13-pentaazatridecane, 2

To neat 1-3 (76.1 mg, 0.069 mmol, 1.0 equiv) was added a solution of dimethylcarbamoyl chloride (8.9 mg, 0.082 mmol, 1.2 equiv) and Et$_3$N (10.4 mg, 0.10 mmol, 1.5 equiv) in lab grade 1,2-DCE (0.7 mL). The vial (sealed with cap) was placed in a sand bath at 45 °C and stirred at this temperature under air for 22 h, before being concentrated in vacuo. Flash chromatography (Biotage, 5 g Sfär Duo column, MeOH/CH$_2$Cl$_2$ gradient from 0:100 to 7:93) gave the title compound (78.8 mg, 97%) as a white solid. TLC – $R_f = 0.43$ (SiO$_2$, 5:95 MeOH:CH$_2$Cl$_2$).

1H NMR (500 MHz, CD$_2$Cl$_2$) $\delta_H$ 0.94 (t, $J = 7.6$, 3H, C$_3$H$_3$), 0.97 (t, $J = 7.4$, 3H, C$_3$H$_3$), 0.98 (t, $J = 7.3$, 3H, CH$_3$), 1.38-1.53 (m, 6H, 3 x C$_2$H$_2$CH$_3$), 1.63-1.78 (m, 6H, 3 x OCH$_2$C$_2$H$_5$), 2.87 (s, 6H, 2 x NC$_6$H$_4$), 3.26 (t, $J = 7.0$, 2H, NCH$_2$), 3.33-3.53 (m, 14H, 7 x NC$_6$H$_4$), 3.77 (t, $J = 6.2$, 2H, OCH$_2$), 4.42 (s, 2H, C$_2$H$_2$Ar), 6.73 (d, $J = 8.6$, 2H, 2 x ArH), 6.79 (d, $J = 8.8$, 2H, 2 x ArH), 6.84 (d, $J = 8.9$, 2H, 2 x ArH), 7.25-7.32 (m, 2H, 2 x ArH), 7.37 (s, 1H, ArH), 7.37-7.41 (m, 3H, 3 x ArH), 7.46 (d, $J = 7.7$, 2H, 2 x ArH), 7.53 (d, $J = 8.9$, 2H, 2 x ArH), 7.59 (d, $J = 8.7$, 2H, 2 x ArH), 7.68 (s, 2H, 2 x ArH), 8.42 (s, 1H, NH), 9.10 (s, 1H, NH), 9.17 (s, 1H, NH), 9.24 (s, 1H, NH).

13C NMR (126 MHz, CD$_2$Cl$_2$) $\delta_C$ 14.0 (C$_3$H$_3$), 14.1 (2 x C$_3$H$_3$), 19.6 (CH$_2$CH$_3$), 19.6 (CH$_2$CH$_3$), 19.7 (CH$_2$CH$_3$), 31.7 (OCH$_2$CH$_2$), 31.8 (2 x OCH$_2$CH$_2$), 38.9 (2 x NCH$_2$), 39.6 (NCH$_2$), 47.1 (NCH$_2$), 47.3 (NCH$_2$), 47.5 (NCH$_2$), 47.6 (NCH$_2$), 48.5 (NCH$_2$), 48.6 (NCH$_2$), 49.2 (NCH$_2$), 54.5 (CH$_2$Ar), 68.2 (OCH$_2$), 68.3 (OCH$_2$), 68.4 (OCH$_2$), 114.8 (2 x ArC), 114.9 (2 x ArC), 114.9 (2 x ArC), 118.2 (ArC), 120.5 (2 x ArC), 121.8 (2 x ArC), 122.3 (2 x ArC), 123.9 (q, $J = 272.3$, 2 x CF$_3$), 127.0 (2 x ArC), 127.9 (ArC), 129.3 (2 x ArC), 131.8 (q, $J = 32.4$, 2 x ArC), 132.9 (ArC), 133.4 (2 x ArC), 133.5 (2 x ArC), 137.6 (ArC), 142.1 (ArC), 155.3 (ArC), 155.3 (ArC), 155.6 (ArC), 156.2 (CO), 157.3 (CO), 157.3 (CO), 165.9 (CO).

19F NMR (377 MHz, CD$_2$Cl$_2$) $\delta_F -63.2$ (2 x CF$_3$).

HR-MS (ESI, positive ion mode) – $m/z$ for [C$_{66}$H$_{75}$F$_{12}$N$_{10}$O$^+$_Na$^+$] = 1201.5644. Found 1201.5666.
**N-(3,5-Bis(trifluoromethyl)phenyl)-N′-butyl urea, 3**

To a solution of BuNH₂ (36.6 mg, 0.50 mmol, 1.0 equiv) in lab grade CH₂Cl₂ (3.0 mL) at 0 °C under air was added a solution of 3,5-bis(trifluoromethyl)phenyl isocyanate (127.6 mg, 0.50 mmol, 1.0 equiv) in CH₂Cl₂ (2.0 mL) and the resulting suspension was allowed to warm in the cold bath with stirring over 1 h. MeOH (~1 mL) was added and the mixture was stirred for a further 20 min before being concentrated *in vacuo*. The resulting solid was re-dissolved in CH₂Cl₂ (5 mL) by briefly warming at 40 °C on a rotary evaporator (atmospheric pressure to avoid significant loss of solvent). The resulting solution was placed in a freezer overnight. Petroleum ether (~5 mL) was added to promote further precipitation and the mixture was placed in the freezer again overnight. The resulting precipitate was collected by gravity filtration, washed with petroleum ether (~10 mL) and dried to give the title compound (127.6 mg, 78%) as a white solid. **TLC** – *Rf = 0.52 (SiO₂, 2.5:97.5 MeOH:CH₂Cl₂).** Spectroscopic data matched that previously reported.²

**1,4-Dibenzyl-1-(4-methoxyanilinylcarbonyl)-1,4-diazabutane, 4-1**

To a solution of *N*,*N′*-dibenzylethylenediamine (480.7 mg, 2.00 mmol, 2.0 equiv) in lab grade CH₂Cl₂ (5 mL) at room temperature under air was added a solution of 4-methoxyphenyl isocyanate (149.1 mg, 1.00 mmol, 1.0 equiv) in CH₂Cl₂ (5 mL) and the mixture was stirred for 3 h, before being concentrated *in vacuo*. Flash chromatography (Biotage, 10 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 10:90), gave the desired product containing a minor higher-*Rf* impurity (presumably the corresponding bis-urea). To this was added ~0.3 M HCl (50 mL) and the mixture was briefly sonicated to promote protonation of the immiscible product. EtOAc (40 mL) was added and the phases were separated. The organic phase was further extracted with ~0.3 M HCl (15 mL) and the combined aqueous extracts were brought to pH >10 by the addition of solid NaOH. The product was extracted with CH₂Cl₂ (40 mL + 20 mL), dried (Na₂SO₄) and concentrated to give an initial portion of the pure title compound (179.9 mg). TLC analysis showed significant product (freebase) still present in the original EtOAc organic phase. Therefore, 1 M HCl (30 mL) was added and the biphasic solution was stirred vigorously at room temperature under air for 22 h, resulting in a homogenous solution (presumably due to hydrolysis of EtOAc). The solvents were removed *in vacuo*. The residue was taken up in water (75 mL) and washed with EtOAc (50 mL), then the aqueous layer was brought to pH >10 by the addition of solid NaOH. The product was extracted with CH₂Cl₂ (40 mL + 20 mL), dried (Na₂SO₄) and concentrated to give a second portion of the pure title compound (198.4 mg; total yield = 378.3 mg, 97%) as a colourless gum that solidified upon storage in a freezer. **TLC** –
Rf = 0.55 (SiO2, 7.5:92.5 MeOH:CH2Cl2). 1H NMR (400 MHz, CDCl3) δH 2.74-2.77 (m, 2H, NC\textsubscript{H}\textsubscript{2}), 3.38-3.41 (m, 2H, NC\textsubscript{H}\textsubscript{2}), 3.80 (s, 3H, OC\textsubscript{H}\textsubscript{3}), 3.83 (s, 2H, C\textsubscript{H}\textsubscript{2}Ar), 4.59 (s, 2H, C\textsubscript{H}\textsubscript{2}Ar), 6.81 (d, J = 9.0, 2H, 2 x Ar\textsubscript{H}), 7.22 (d, J = 9.0, 2H, 2 x Ar\textsubscript{H}), 7.26-7.38 (m, 10H, 10 x Ar\textsubscript{H}), 9.63 (s, 1H, NH). 13C NMR (101 MHz, CDCl\textsubscript{3}) δC 48.8 (N\textsubscript{C}H\textsubscript{2}), 48.9 (N\textsubscript{C}H\textsubscript{2}), 51.2 (C\textsubscript{H}2Ar), 54.3 (C\textsubscript{H}2Ar), 55.7 (O\textsubscript{C}H\textsubscript{3}), 114.1 (2 x Ar\textsubscript{C}), 121.1 (2 x Ar\textsubscript{C}), 127.4 (Ar\textsubscript{C}), 127.6 (Ar\textsubscript{C}), 128.4 (2 x Ar\textsubscript{C}), 128.7 (2 x Ar\textsubscript{C}), 133.6 (Ar\textsubscript{C}), 138.7 (Ar\textsubscript{C}), 139.0 (Ar\textsubscript{C}), 151.5 (Ar\textsubscript{C}), 158.0 (CO). HR-MS (ESI, positive ion mode) – m/z for [C\textsubscript{24}H\textsubscript{27}N\textsubscript{3}O\textsubscript{2}+H]\textsuperscript{+} = 390.2176. Found 390.2180.

1,4-Dibenzyl-1-(3,5-bis(trifluoromethyl)anilinylthiocarbonyl)-4-(4-methoxyanilinylcarbonyl)-1,4-diazabutane, 4

To a solution of 4-I (58.4 mg, 0.15 mmol, 1.0 equiv) in lab grade CH\textsubscript{2}Cl\textsubscript{2} (0.5 mL) at 0 °C under air was added a solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (40.7 mg, 0.15 mmol, 1.0 equiv) in CH\textsubscript{2}Cl\textsubscript{2} (1.0 mL) and the mixture was allowed to warm in the cold bath with stirring over 30 min. The solution was concentrated in vacuo to give the title compound (101.0 mg, >99 %) as a white solid (note: residual CH\textsubscript{2}Cl\textsubscript{2} accounted for the 2% extra mass beyond the theoretical yield of 99.1 mg). TLC – Rf = 0.83 (SiO2, 2.5:97.5 MeOH:CH2Cl2). 1H NMR (500 MHz, CD\textsubscript{2}Cl\textsubscript{2}) δH 3.42-3.48 (m, 2H, NC\textsubscript{H}\textsubscript{2}), 3.71 (t, J = 7.5, 2H, NC\textsubscript{H}\textsubscript{2}), 3.74 (s, 3H, OC\textsubscript{H}\textsubscript{3}), 4.46 (s, 2H, C\textsubscript{H}\textsubscript{2}Ar), 5.20 (s, 2H, C\textsubscript{H}\textsubscript{2}Ar), 6.45 (s, 1H, NH), 6.78 (d, J = 8.9, 2H, 2 x Ar\textsubscript{H}), 7.16 (d, J = 8.9, 2H, 2 x Ar\textsubscript{H}), 7.24 (d, J = 7.4, 2H, 2 x Ar\textsubscript{H}), 7.29-7.43 (m, 8H, 8 x Ar\textsubscript{H}), 7.63 (s, 1H, Ar\textsubscript{H}), 8.43 (s, 2H, 2 x Ar\textsubscript{H}), 10.65 (s, 1H, NH). 13C NMR (126 MHz, CD\textsubscript{2}Cl\textsubscript{2}) δC 48.1 (2 x N\textsubscript{C}H\textsubscript{2}), 55.9 (O\textsubscript{C}H\textsubscript{3}), 56.5 (C\textsubscript{H}2Ar), 114.5 (2 x Ar\textsubscript{C}), 117.8 (Ar\textsubscript{C}), 122.6 (2 x Ar\textsubscript{C}), 124.1 (q, J = 271.4, 2 x CF\textsubscript{3}), 124.8 (2 x Ar\textsubscript{C}), 127.3 (2 x Ar\textsubscript{C}), 128.3 (2 x Ar\textsubscript{C}), 128.4 (2 x Ar\textsubscript{C}), 128.9 (Ar\textsubscript{C}), 129.3 (2 x Ar\textsubscript{C}), 129.9 (2 x Ar\textsubscript{C}), 131.3 (q, J = 33.2, 2 x Ar\textsubscript{C}), 131.5 (Ar\textsubscript{C}), 136.6 (Ar\textsubscript{C}), 137.4 (Ar\textsubscript{C}), 143.2 (Ar\textsubscript{C}), 156.8 (Ar\textsubscript{C}), 157.3 (CO), 181.9 (CS). 19F NMR (377 MHz, CD\textsubscript{2}Cl\textsubscript{2}) δF –63.0 (2 x CF\textsubscript{3}). HR-MS (ESI, positive ion mode) – m/z for [C\textsubscript{33}H\textsubscript{30}F\textsubscript{6}N\textsubscript{4}O\textsubscript{2}S+Na]\textsuperscript{+} = 683.1886. Found 683.1868.

1,4-Dibenzyl-1-(dimethylaminocarbonyl)-1,4-diazabutane, 5-I

To neat N,N'-dibenzylethylenediamine (240.4 mg, 1.00 mmol, 2.0 equiv) was added a solution of dimethylcarbamoyl chloride (53.8 mg, 0.50 mmol, 1.0 equiv) and Et\textsubscript{3}N (91 μL, 0.65 mmol, 1.3 equiv) in lab grade 1,2-DCE (2.0 mL). The vial (with cap) was placed in a sand bath at 45 °C and stirred at this temperature under air for 30 h. 1 M K\textsubscript{2}CO\textsubscript{3} (20 mL)
was added and the product was extracted with CH₂Cl₂ (30 mL + 20 mL) then the combined organic extracts were dried (Na₂SO₄) and concentrated. To remove the di-urea side product, the residue was dissolved in Et₂O (10 mL) and 1 M aqueous HCl (5 mL) and water (10 mL) were added. The biphasic reaction was stirred at room temperature for 20 min, then diluted with Et₂O (25 mL) and 1 M aqueous HCl (3 mL) and water (20 mL). The organic phase was separated. The aqueous phase was basified (to pH > 12) with NaOH pellets, then the product was extracted with CH₂Cl₂ (30 mL + 20 mL). The combined organic extracts were dried (Na₂SO₄) and concentrated. Flash chromatography (Biotage, 10 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 6.5:93.5) gave the title compound (62.7 mg, 40% based on carbamoyl chloride) as a pale-yellow oil.

TLC – Rf = 0.30 (SiO₂, 7.5:92.5 MeOH:CH₂Cl₂).

1H NMR (500 MHz, CDCl₃) δ H 2.79 (t, J = 6.4, 2H, NC₂H₂), 2.87 (s, 6H, 2 x NC₃H₃), 3.26 (t, J = 6.4, 2H, NC₂H₂), 3.77 (s, 2H, CH₂Ar), 4.40 (s, 2H, CH₂Ar), 7.22-7.35 (m, 10H, 10 x ArH).

13C NMR (126 MHz, CDCl₃) δ C 38.8 (2 x NCH₃), 46.7 (NCH₂), 47.5 (NCH₂), 52.1 (CH₂Ar), 53.8 (CH₂Ar), 127.0 (ArC), 127.2 (ArC), 127.5 (2 x ArC), 128.1 (2 x ArC), 128.4 (2 x ArC), 128.6 (2 x ArC), 138.2 (ArC), 140.3 (ArC), 165.6 (CO).

HR-MS (ESI, positive ion mode) – m/z for [C_{19}H_{25}N₃O+H]+ = 312.2070. Found 312.2085.

1,4-Dibenzyl-1-(dimethylaminocarbonyl)-4-(4-n-butyloxyanilinylcarbonyl)-1,4-diazabutane, 5

To a solution of 5-1 (42.4 mg, 0.14 mmol, 1.0 equiv) in lab grade CH₂Cl₂ (0.4 mL) at room temperature under air was added a solution of 4-butoxyphenyl isocyanate (26.0 mg, 0.14 mmol, 1.0 equiv) in CH₂Cl₂ (1.0 mL) [note that the isocyanate solution was delivered into the reaction vial by filtration through a cotton pipette plug to remove a trace amount of an insoluble urea impurity]. After stirring for 50 min, MeOH (~1 mL) was added and the mixture was stirred for 5 min to quench any unreacted isocyanate, before being concentrated in vacuo. Flash chromatography (Biotage, 5 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 2.5:97.5) gave the title compound (65.0 mg, 95%) as a white solid.

TLC – Rf = 0.46 (SiO₂, 2.5:97.5 MeOH:CH₂Cl₂).

1H NMR (500 MHz, CD₂Cl₂) δ H 0.98 (t, J = 7.4, 3H, CH₃), 1.49 (dq, J = 7.6, 7.6, 2H, CH₂CH₃), 1.71-1.77 (m, 2H, OCH₂CH₂), 2.84 (s, 6H, 2 x NCH₃), 3.00 (t, J = 7.4, 2H, NCH₂), 3.26 (t, J = 7.4, 2H, NCH₂), 3.94 (t, J = 6.5, 2H, OCH₂), 4.28 (s, 2H, CH₂Ar), 4.44 (s, 2H, CH₂Ar), 6.82 (d, J = 8.9, 2H, 2 x ArH), 7.15-7.35 (m, 10H, 10 x ArH), 7.56 (d, J = 8.9, 2H, 2 x ArH), 8.78 (s, 1H, NH).

13C NMR (126 MHz, CD₂Cl₂) δ C 14.2 (CH₃), 19.8 (CH₂CH₃), 32.0 (OCH₂CH₂), 39.1 (2 x NCH₃), 45.0 (NCH₂), 47.1 (NCH₂), 51.2 (CH₂Ar), 54.7 (CH₂Ar), 68.5 (OCH₂), 114.8 (2 x ArC), 121.4 (2 x ArC), 127.3 (2 x ArC), 127.5 (ArC), 127.9 (ArC), 128.2 (2 x ArC), 128.8 (2 x ArC), 129.2 (2 x ArC), 134.3 (ArC), 137.7 (ArC), 139.5 (ArC), 154.9 (ArC), 156.2 (CO), 165.6 (CO). HR-MS (ESI, positive ion mode) – m/z for [C_{30}H_{38}N₄O₃+H]+ = 503.3017. Found 503.3019.
1,13-Dibenzyl-4,7,10-tris(4-n-butyloxyanilinylcarbonyl)-1,4,7,10,13-pentaazatridecane, 6-1

To a solution of 1-1 (201.3 mg, 0.26 mmol, 1.0 equiv) in lab grade MeOH (1.3 mL) was added a solution of benzaldehyde (56.0 mg, 0.53 mmol, 2.0 equiv) in MeOH (1.3 mL) and the mixture was stirred under air at room temperature for 17 h. To the cloudy mixture was added 10 drops of THF via a pipette, then the mixture was cooled to 0 °C and solid NaBH₄ (39.9 mg, 1.06 mmol, 4.0 equiv) was added. The mixture was allowed to warm to room temperature in the cold bath with stirring over 3 h. 1 M K₂CO₃ (10 mL) was added and the product was extracted with CH₂Cl₂ (25 mL + 15 mL) then the combined organic extracts were dried (Na₂SO₄) and concentrated. Flash chromatography (Biotage, 5 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 10:90) gave the title compound (185.6 mg, 75%) as a white foam. TLC – Rf = 0.38 (SiO₂, 10:90 MeOH:CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δ_H 1.03 (t, J = 7.4, 9H, 3 x C₃H₃), 1.50-1.58 (m, 6H, 3 x C₂H₂CH₃), 1.76-1.82 (m, 6H, 3 x C₂H₂CH₂CH₃), 2.00 (s, 2H, 2 x N₃), 2.86-2.90 (m, 4H, 2 x NCH₂), 3.39-3.47 (m, 8H, 4 x NCH₂), 3.48-3.55 (m, 4H, 2 x NCH₂), 3.83 (s, 4H, 2 x CH₂Ar), 3.96 (t, J = 6.5, 6H, 3 x OCH₂), 6.81 (d, J = 8.9, 4H, 4 x ArH), 6.86 (d, J = 9.0, 2H, 2 x ArH), 7.22-7.38 (m, 14H, 14 x ArH), 7.64 (d, J = 8.9, 2H, 2 x ArH), 9.03 (s, 1H, NH), 9.91 (s, 2H, 2 x NH). ¹³C NMR (126 MHz, CDCl₃) δ_C 13.9 (3 x CH₃), 19.2 (3 x CH₂CH₃), 31.4 (3 x CH₂CH₂CH₃), 46.8 (2 x NCH₂), 47.6 (2 x NCH₂), 49.4 (2 x NCH₂), 50.4 (2 x NCH₂), 54.1 (2 x CH₂Ar), 67.9 (OCH₂), 68.0 (2 x OCH₂), 114.6 (2 x ArC), 114.7 (4 x ArC), 120.9 (4 x ArC), 121.0 (2 x ArC), 127.4 (2 x ArC), 128.3 (4 x ArC), 128.6 (4 x ArC), 133.1 (2 x ArC), 133.4 (ArC), 139.0 (2 x ArC), 154.5 (3 x ArC), 156.2 (CO), 157.9 (2 x CO). HR-MS (ESI, positive ion mode) – m/z for [C₅H₈N₄O₆+H]⁺ = 943.5804. Found 943.5782.
To neat 6-1 (219.8 mg, 0.23 mmol, 2.0 equiv) was added a solution of dimethylcarbamoyl chloride (12.5 mg, 0.12 mmol, 1.0 equiv) in lab grade 1,2-DCE (1.2 mL) followed by 3 drops of Et₃N from a 21-gauge needle (~15 mg, 0.15 mmol, 1.3 equiv). The vial (with cap) was placed in a pre-heated sand bath at 45 °C and stirred at this temperature under air for 24 h. 1 M K₂CO₃ (20 mL) was added and the product was extracted with CH₂Cl₂ (30 mL + 20 mL) then the combined organic extracts were dried (Na₂SO₄) and concentrated. Flash chromatography (Biotage, 10 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 10:90) gave the title compound (67.8 mg, 57% based on carbamoyl chloride) as a white foam. Further elution from the chromatography column returned unreacted 6-1 (95.2 mg, 43% based on total diamine used). Data for 6-2: TLC – Rf = 0.36 (SiO₂, 7.5:92.5 MeOH:CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δH 0.98 (t, J = 7.3, 9H, 3 x CH₃), 1.46-1.55 (m, 6H, 3 x CH₂CH₃), 1.73-1.80 (m, 6H, 3 x CH₂CH₂CH₃), 2.04 (s, 1H, NH), 2.87 (s, 6H, 2 x NCH₃), 2.89 (t, J = 4.6, 2H, NCH₂), 3.23 (t, J = 7.4, 2H, NCH₂), 3.35-3.49 (m, 12H, 6 x NCH₂), 3.83 (s, 2H, CH₂Ar), 3.92-3.97 (m, 6H, 3 x OCH₂), 4.41 (s, 2H, CH₂Ar), 6.78 (d, J = 8.8, 2H, 2 x ArH), 6.81 (d, J = 8.9, 2H, 2 x ArH), 6.85 (d, J = 9.0, 2H, 2 x ArH), 7.23 (d, J = 8.8, 2H, 2 x ArH), 7.26-7.38 (m, 10H, 10 x ArH), 7.56 (d, J = 8.9, 2H, 2 x ArH), 7.60 (d, J = 9.0, 2H, 2 x ArH), 8.91 (s, 1H, NH), 8.99 (s, 1H, NH), 9.77 (s, 1H, NH). ¹³C NMR (126 MHz, CDCl₃) δC 14.0 (3 x CH₃), 19.4 (3 x CH₂CH₃), 31.5 (2 x CH₂CH₂CH₃), 31.6 (CH₂CH₂CH₂), 38.9 (2 x NCH₃), 46.5 (NCH₂), 46.9 (NCH₂), 47.0 (NCH₂), 47.4 (NCH₂), 47.8 (NCH₂), 49.5 (2 x NCH₂), 50.4 (NCH₂), 54.1 (CH₂Ar), 54.3 (CH₃Ar), 68.1 (3 x OCH₂), 114.7 (2 x ArC), 114.8 (4 x ArC), 121.0 (2 x ArC), 121.1 (4 x ArC), 126.9 (2 x ArC), 127.6 (2 x ArC), 127.7 (ArC), 128.4 (2 x ArC), 128.8 (2 x ArC), 129.1 (ArC), 133.2 (ArC), 133.5 (2 x ArC), 137.1 (ArC), 138.9 (ArC), 154.7 (3 x ArC), 156.3 (CO), 156.4 (CO), 158.0 (CO), 165.5 (CO). HR-MS (ESI, positive ion mode) – m/z for [C₅₈H₇₉N₉O₇+H]⁺ = 1014.6175. Found 1014.6159.
1,13-Dibenzyl-1-(dimethylaminocarbonyl)-13-(3,5-bis(trifluoromethyl)anilinylthiocarbonyl)-4,7,10-tris(4-n-butyloxyanilinylcarbonyl)-1,4,7,10,13-pentaazatridecane, 6

To a solution of 6-2 (32.6 mg, 0.032 mmol, 1.0 equiv) in lab grade CH₂Cl₂ (0.5 mL) at 0 °C under air was added a solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (8.7 mg, 0.032 mmol, 1.0 equiv) in CH₂Cl₂ (0.5 mL) and the mixture was allowed to warm to room temperature in the cold bath with stirring over 2.5 h. MeOH (0.5 mL) was added and the mixture was stirred for a further 10 min before being concentrated in vacuo. Flash chromatography (Biotage, 5 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 4:96) gave the title compound (38.2 mg, 92%) as a white solid.

TLC – Rf = 0.35 (SiO₂, 2.5:97.5 MeOH:CH₂Cl₂).

1H NMR (500 MHz, CD₂Cl₂) δ H 0.96-1.01 (m, 9H, 3 x CH₃), 1.46-1.54 (m, 6H, 3 x CH₂CH₃), 1.72-1.80 (m, 6H, 3 x CH₂CH₂CH₃), 2.88 (s, 6H, 2 x NCH₃), 3.22-3.45 (m, 14H, 7 x NCH₂), 3.70 (t, J = 7.3, 2H, NCH₂), 3.91-3.98 (m, 6H, 3 x OCH₂), 4.41 (s, 2H, CH₂Ar), 5.33 (s, 2H, CH₂Ar), 6.81 (d, J = 8.9, 2H, 2 x ArH), 6.82 (d, J = 9.0, 2H, 2 x ArH), 6.87 (d, J = 9.0, 2H, 2 x ArH), 7.28-7.44 (m, 10H, 10 x ArH), 7.61 (d, J = 9.0, 2H, 2 x ArH), 7.63 (d, J = 9.0, 2H, 2 x ArH), 7.65 (s, 1H, ArH), 8.55 (s, 2H, 2 x ArH), 9.13 (s, 1H, NH), 9.28 (s, 1H, NH), 9.35 (s, 1H, NH), 10.93 (s, 1H, NH). 13C NMR (126 MHz, CD₂Cl₂) δc 14.2 (3 x CH₃), 19.8 (3 x CH₂CH₃), 31.9 (CH₂CH₂CH₃), 32.0 (2 x CH₂CH₂CH₃), 39.0 (2 x NCH₃), 47.6 (NCH₂), 47.7 (NCH₂), 47.9 (2 x NCH₂), 48.3 (NCH₂), 48.5 (NCH₂), 49.1 (NCH₂), 49.7 (NCH₂), 54.6 (CH₂Ar), 56.6 (CH₂Ar), 68.0 (3 x OCH₂), 115.0 (6 x ArC), 117.6 (ArC), 121.4 (2 x ArC), 121.6 (2 x ArC), 121.7 (2 x ArC), 124.1 (q, J = 273.1, 2 x CF₃), 124.7 (2 x ArC), 127.0 (2 x ArC), 127.9 (2 x ArC), 128.0 (ArC), 128.1 (ArC), 129.2 (2 x ArC), 129.5 (2 x ArC), 131.3 (q, J = 33.2, 2 x ArC), 133.4 (ArC), 133.5 (ArC), 133.6 (ArC), 133.7 (ArC), 137.8 (ArC), 143.5 (ArC), 155.4 (ArC), 155.5 (2 x ArC), 157.2 (CO), 157.3 (CO), 157.4 (CO), 166.0 (CO), 182.1 (CS). 19F NMR (377 MHz, CD₂Cl₂) δF −63.0 (2 x CF₃). HR-MS (ESI, positive ion mode) – m/z for [C₆H₄F₃N₁₀O₇S+Na⁺] = 1307.5885. Found 1307.5868.
1,16-Bis(trifluoroacetyl)-1,4,7,10,13,16-hexaazahexadecane, 7-1

To a solution of pentaethylenehexamine (2.324 g, 10.00 mmol, 1.0 equiv) in lab grade MeOH (200 mL) under N₂ at −78 °C (liquid N₂/EtOAc cold bath) was added a solution of ethyl trifluoroacetate (2.842 g, 20.00 mmol, 2.0 equiv) in MeOH (5 mL) and the mixture was allowed to warm to room temperature in the cold bath with stirring over 19 h, before being concentrated in vacuo. Flash chromatography (Biotage, 25 g Sfär Duo column, MeOH/[35% aqueous NH₃]/CH₂Cl₂ gradient from 0:0:100 to 10:2:88) gave the title compound (1.135 g, 27%) as a pale yellow oil containing several minor impurities. The ¹H NMR spectrum of the major product was consistent with that reported previously.³ This material was used in the next step without further purification. TLC – Rf = 0.08 (SiO₂, 15:3:82 MeOH/[35% aqueous NH₃]/CH₂Cl₂, ninhydrin stain).

4,7,10,13-Tetrakis(4-n-butyloxyanilinylcarbonyl)-1,4,7,10,13,16-hexaazahexadecane, 7-2

Step 1 (tetrakis-urea formation): To a solution of 7-1 (1.135 g, 2.67 mmol, 1.0 equiv) in lab grade CH₂Cl₂ (21.7 mL) at 0 °C under air was added over 5 min a solution of 4-butoxy phenyl isocyanate (2.13 mL, 11.77 mmol, 4.4 equiv) in CH₂Cl₂ (5.0 mL) [note that the isocyanate solution was delivered into the reaction flask by filtration through a cotton pipette plug to remove a small amount of an insoluble urea impurity]. After complete addition, the ice bath was removed and the mixture was stirred at room temperature for 20 min. MeOH (~3 mL) was added and the mixture was stirred for 15 min to quench any unreacted isocyanate. After standing at room temperature for 1.5 h, the suspension was gravity filtered to remove an unknown precipitate, and the filter cake was rinsed with further CH₂Cl₂ (~10 mL). The filtrate was concentrated in vacuo. To the solid residue was added 1:1 Et₂O/petroleum ether (100 mL) and the suspension was placed inside a sonicator for 10 min, before being gravity filtered to collect the undissolved product. The flask and filter cake were rinsed/washed with further 1:1 Et₂O/petroleum ether (70 mL) and the cake was air dried to give the crude intermediate tetrakis-urea (2.481 g, 78%) as a pale yellow solid. TLC – Rf = 0.39 (SiO₂, 5:95 MeOH/CH₂Cl₂). Step 2 (trifluoroacetamide hydrolysis): The product from Step 1 (2.481 g, 2.09 mmol, 1.0 equiv) was suspended in a mixture of lab grade THF (10.4 mL), EtOH (20.9 mL) and DMF (20 drops from a Pasteur pipette). A solution of NaOH (667.5 mg, 16.69 mmol, 8.0 equiv) in water (10.4 mL) was added and the solution was stirred at room temperature under air for 2 h. Most of the solvents were removed in vacuo, then water (20 mL) was added. The product was extracted with CH₂Cl₂ (50 mL + 30 mL) then the
combined organic extracts were dried (Na₂SO₄) and concentrated. Two iterative rounds of flash chromatography (Biotage, 25 g Sfär Duo column (first purification), 50 g Sfär Duo column (second purification), MeOH/[35% aqueous NH₃]/CH₂Cl₂ gradient from 0:0:100 to 10:2:88 for both purifications) gave the title compound (895.7 mg, 43% or 34% over two steps) as a white foamy solid. TLC – Rf = 0.13 (SiO₂, 10:2:88 MeOH/[35% aqueous NH₃]/CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δ: 0.96 (t, J = 7.4, 6H, 2 x CH₃), 0.97 (t, J = 7.3, 6H, 2 x CH₃), 1.41-1.52 (m, 8H, 4 x C₂H₅), 1.67-1.78 (m, 8H, 4 x OCH₂CH₂), 2.87 (t, J = 4.5, 4H, 2 x NCH₃), 3.30-3.51 (m, 16H, 8 x NCH₂), 3.91 (t, J = 6.4, 4H, 2 x OCH₂), 3.92 (t, J = 6.4, 4H, 2 x OCH₂), 6.80 (d, J = 8.9, 4H, 4 x ArH), 6.81 (d, J = 9.0, 4H, 4 x ArH), 7.30 (d, J = 8.0, 4H, 4 x ArH), 7.60 (d, J = 8.9, 4H, 4 x ArH), 9.09 (s, 2H, 2 x NH), 10.06 (s, 2H, 2 x NH). ¹³C NMR (126 MHz, CDCl₃) δ: 13.9 (2 x C₂H₅), 19.3 (4 x C₂H₅), 31.4 (2 x OCH₂CH₂), 31.5 (2 x OCH₂CH₂), 41.8 (2 x NCH₃), 47.1 (2 x NCH₃), 47.9 (4 x NCH₂), 52.7 (2 x NCH₂), 68.0 (2 x OCH₂), 68.1 (2 x OCH₂), 114.7 (4 x ArC), 114.8 (4 x ArC), 120.7 (4 x ArC), 121.1 (4 x ArC), 133.2 (2 x ArC), 133.4 (2 x ArC), 154.6 (2 x ArC), 154.7 (2 x ArC), 156.4 (2 x CO), 158.4 (2 x CO). HR-MS (ESI, positive ion mode) – m/z for [C₅₄H₈₀N₁₀O₈+H⁺]⁺ = 997.6233. Found 997.6218.

1-(3,5-Bis(trifluoromethyl)anilinylcarbonyl)-4,7,10,13-tetrakis(4-n-butyloxyanilinylcarbonyl)-1,4,7,10,13,16-hexaazahexadecane, 7-3

To a solution of 7-2 (434.2 mg, 0.44 mmol, 1.0 equiv) in lab grade CH₂Cl₂ (6.2 mL) at –10 °C (ice/salt bath) under N₂ was added dropwise over 70 min a solution of 3,5-bis(trifluoromethyl)phenyl isocyanate (111.1 mg, 0.44 mmol, 1.0 equiv) in CH₂Cl₂ (2.5 mL) while maintaining the cold bath temperature between –10 °C and 0 °C. After complete addition, the cold bath was allowed to warm to room temperature and the mixture was stirred for a further 1 h, before being concentrated in vacuo. Flash chromatography (Biotage, 25 g Sfär Duo column, MeOH/[35% aqueous NH₃]/CH₂Cl₂ gradient from 0:0:100 to 10:2:88) gave the title compound (286.3 mg, 53%) as a white solid. [Further elution from the chromatography column returned unreacted 7-2 (71.3 mg, 16% recovered)]. Data for 7-3: TLC – Rf = 0.38 (SiO₂, 10:2:88 MeOH/[35% aqueous NH₃]/CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δ: 0.92-0.99 (m, 12H, 4 x CH₃), 1.38-1.51 (m, 8H, 4 x CH₂CH₃), 1.62-1.77 (m, 8H, 4 x OCH₂CH₂), 2.91-2.96 (m, 2H, NCH₃), 3.31-3.59 (m, 18H, 9 x NCH₂), 3.72-3.79 (m, 2H, OCH₂), 3.87-3.94 (m, 6H, 3 x OCH₂), 6.73 (d, J = 8.6, 2H, 2 x ArH), 6.78-6.84 (m, 6H, 6 x ArH), 6.97 (s, 1H, NH), 7.29 (d, J = 8.8, 2H, 2 x ArH), 7.37 (s, 1H, ArH), 7.47 (d, J = 8.6, 2H, 2 x ArH), 7.54-7.65 (m, 6H, 6 x ArH), 8.35 (s, 1H, NH), 9.21 (s, 1H, NH), 9.28 (s, 2H, 2 x ArH).
1-Benzyl-4,7,10,13,16-pentakis(4-n-butyloxyanilinylcarbonyl)-19-(3,5-bis(trifluoromethyl)anilinylcarbonyl)-1,4,7,10,13,16,19-heptaazanonadecane, 7-4

**Step 1 (reductive amination):** To a solution of 7-3 (494.4 mg, 0.39 mmol, 1.0 equiv) in lab grade THF (2.0 mL) was added a solution of N-benzyl-N-Boc-2-aminoacetaldehyde (98.4 mg, 0.39 mmol, 1.0 equiv) in lab grade MeOH (2.0 mL) and the mixture was stirred under air at room temperature for 19 h. The mixture was cooled to 0 °C and solid NaBH₄ (30.0 mg, 0.79 mmol, 2.0 equiv) was added and the cold bath was allowed to warm to room temperature with stirring over 3 h. 1 M K₂CO₃ (10 mL) was added and most organic solvent was removed *in vacuo*. The mixture was diluted with water (10 mL) and the product was extracted with CH₂Cl₂ (2 × 20 mL) then the combined organic extracts were dried (Na₂SO₄) and concentrated. Flash chromatography (Biotage, 25 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 8:92) gave the product (358.7 mg, 61%) as a white solid. TLC – Rₖ = 0.34 (7.5:92.5 MeOH/CH₂Cl₂). **Step 2 (urea formation):** The product from **Step 1** (358.7 mg, 0.24 mmol, 1.0 equiv) was dissolved in lab grade CH₂Cl₂ (1.0 mL) and a solution of 4-butoxyphenyl isocyanate (46.2 mg, 0.24 mmol, 1.0 equiv) in CH₂Cl₂ (1.4 mL) was added [note that the isocyanate solution was delivered into the reaction flask by filtration through a cotton pipette plug to remove a small amount of an insoluble urea impurity]. The mixture was stirred at room temperature under air for 1.5 h. MeOH (~0.5 mL) was added and the mixture was stirred for 5 min to quench any unreacted isocyanate, before being concentrated *in vacuo*. Flash chromatography (Biotage, 25 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 3.5:96.5) gave the product (360.4 mg, 89% or 54% over two steps) as a white
solid. **Step 3** (*Boc deprotection*): The product from Step 2 (360.4 mg, 0.21 mmol, 1.0 equiv) was dissolved in lab grade CH₂Cl₂ (2.1 mL) and TFA (0.25 mL, 3.22 mmol, 15.0 equiv) was added. The mixture was stirred under air at room temperature for 27.5 h. After cooling to 0 °C, saturated NaHCO₃ (20 mL) was slowly added to the open flask with stirring. After complete addition, the cold bath was removed and the mixture was stirred for a further 5 min. After further dilution with saturated NaHCO₃ (10 mL), the product was extracted with CH₂Cl₂ (30 mL + 20 mL) and the combined organic extracts were dried (Na₂SO₄) and concentrated. Flash chromatography (Biotage, 25 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 7.5:92.5) gave the title compound (313.2 mg, 92% or 50% over three steps) as a white solid. **TLC** – *R*ᵣ = 0.46 (SiO₂, 7.5:92.5 MeOH:CH₂Cl₂). **¹H NMR** (500 MHz, CD₂Cl₂) δH 0.93-1.00 (m, 15H, 5 x CH₃), 1.42-1.52 (m, 10H, 5 x CH₂CH₃), 1.66-1.77 (m, 10H, 5 x OCH₂CH₂), 2.84-2.88 (m, 2H, NCH₂), 3.31-3.58 (m, 22H, 11 x NCH₂), 3.79-3.86 (m, 4H, OCH₂, CH₂Ar), 3.87-3.95 (m, 6H, 3 x OCH₂), 5.33 (s, 1H, NH), 6.64 (s, 1H, NH), 6.73-6.85 (m, 10H, 10 x ArH), 7.14 (d, *J* = 6.5, 2H, 2 x ArH), 7.25-7.34 (m, 5H, 5 x ArH), 7.41 (s, 1H, ArH), 7.51 (d, *J* = 7.9, 2H, 2 x ArH), 7.54-7.62 (m, 6H, 6 x ArH), 7.75 (s, 2H, 2 ArH), 8.47 (s, 1H, NH), 9.00-9.35 (m, 4H, 4 x NH), 10.18 (s, 1H, NH). **¹³C NMR** (126 MHz, CD₂Cl₂) δC 14.0 (4 x CH₃), 19.6 (CH₂CH₃), 19.6 (4 x CH₂CH₃), 31.8 (OCH₂CH₂), 31.8 (4 x OCH₂CH₂), 39.8 (NCH₂), 47.5 (2 x NCH₂), 48.0 (2 x NCH₂), 48.7 (3 x NCH₂), 49.9 (NCH₂), 51.4 (NCH₂), 54.2 (NCH₂), 54.5 (CH₂Ar), 68.3 (OCH₂), 68.3 (OCH₂), 68.4 (3 x OCH₂), 114.9 (10 x ArC), 118.2 (ArC), 121.6 (2 x ArC), 121.6 (6 x ArC), 122.1 (2 x ArC), 123.8 (q, *J* = 272.7, 2 x CF₃), 127.9 (ArC), 128.7 (2 x ArC), 129.0 (2 x ArC), 131.9 (q, *J* = 32.6, 2 x ArC), 133.0 (2 x ArC), 133.1 (2 x ArC), 133.3 (ArC), 133.4 (ArC), 133.4 (ArC), 139.4 (ArC), 141.9 (2 x ArC), 155.3 (ArC), 155.4 (2 x ArC), 155.4 (ArC), 155.6 (ArC), 156.6 (CO), 157.2 (3 x CO), 157.3 (CO), 159.1 (CO). **¹⁹F NMR** (377 MHz, CD₂Cl₂) δF −63.0 (2 x CF₃). **HR-MS** (Nanospray, positive ion mode) – *m/z* for [C₈₃H₁₀₇F₆N₁₃O₁₁+H]⁺ = 1576.8195. Found 1576.8208.
1-Benzyl-1-(3,5-bis(trifluoromethyl)anilinylthiocarbonyl)-4,7,10,13,16-pentakis(4-n-butyloxyanilinylcarbonyl)-19-(3,5-bis(trifluoromethyl)anilinylcarbonyl)-1,4,7,10,13,16,19-heptaazanonadecane, 7

To neat 7-4 (63.1 mg, 0.040 mmol, 1.0 equiv) was added a solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (10.8 mg, 0.040 mmol, 1.0 equiv) in lab grade CH2Cl2 (0.8 mL) and the mixture was stirred at room temperature under air for 2 h, before being concentrated in vacuo. Flash chromatography (Biotage, 5 g Sfär Duo column, MeOH/CH2Cl2 gradient from 0:100 to 5:95) gave the title compound (65.4 mg, 88%) as a white solid.

TLC – Rf = 0.53 (SiO2, 7.5:92.5 MeOH:CH2Cl2).

$^1$H NMR (500 MHz, CD2Cl2) $\delta$H 0.93-0.99 (m, 15H, 5 x CH$_3$), 1.41-1.51 (m, 10H, 5 x CH$_2$CH$_3$), 1.67-1.76 (m, 10H, 5 x OCH$_2$CH$_2$), 3.09-3.17 (m, 2H, NC$_2$H$_4$), 3.28-3.33 (m, 2H, NCH$_2$H$_2$), 3.35-3.57 (m, 18H, 9 x NC$_2$H$_4$), 3.70-3.79 (m, 2H, NC$_2$H$_4$), 3.84-3.94 (m, 10H, 5 x OCH$_2$), 5.23 (s, 2H, C$_2$HAr), 5.60 (s, 1H, NH), 6.74-6.84 (m, 10H, 10 x ArH), 7.27-7.42 (m, 5H, 5 x ArH), 7.46-7.56 (m, 11H, 11 x ArH), 7.64 (s, 1H, ArH), 7.69 (s, 1H, NH), 7.82 (s, 2H, 2 x ArH), 8.44 (s, 2H, 2 x ArH), 8.59 (s, 1H, NH), 8.92 (s, 2H, 2 x NH), 9.06 (s, 1H, NH), 9.21 (s, 1H, NH), 10.84 (s, 1H, NH). $^{13}$C NMR (126 MHz, CD$_2$Cl$_2$) $\delta$C 14.0 (CH$_3$), 14.0 (4 x CH$_3$), 19.6 (CH$_2$CH$_3$), 19.6 (4 x CH$_2$CH$_3$), 31.7 (OCH$_2$CH$_2$), 31.8 (4 x OCH$_2$CH$_2$), 40.2 (NCH$_2$), 47.9 (3 x NCH$_2$), 48.2 (2 x NCH$_2$), 48.6 (4 x NCH$_2$), 49.0 (2 x NCH$_2$), 56.2 (CH$_2$Ar), 68.3 (3 x OCH$_2$), 68.4 (OCH$_2$), 68.5 (OCH$_2$), 114.8 (2 x ArC), 114.9 (2 x ArC), 114.9 (2 x ArC), 115.0 (2 x ArC), 115.0 (2 x ArC), 115.9 (ArC) 118.5 (ArC), 121.4 (2 x ArC), 122.0 (8 x ArC), 123.8 (q, J = 272.8, 4 x CF$_3$), 127.6 (2 x ArC), 128.2 (ArC), 129.3 (2 x ArC), 132.1 (q, J = 32.9, 4 x ArC), 132.9 (4 x ArC), 133.0 (3 x ArC), 133.0 (2 x ArC), 137.0 (ArC), 141.0 (ArC), 143.0 (ArC), 155.6 (5 x ArC), 156.5 (CO), 157.2 (CO), 157.3 (2 x CO), 157.4 (2 x CO), 181.8 (CS). $^{19}$F NMR (377 MHz, CD$_2$Cl$_2$) $\delta$F −63.1 (2 x CF$_3$), −63.3 (2 x CF$_3$). HR-MS (Nanospray, positive ion mode) – m/z for [C$_{92}$H$_{110}$F$_{12}$N$_{14}$O$_{11}$S+H]$^+$ = 1847.8086. Found 1847.8060.
4-Chloropyridinium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate, S8

To a glass vial (not pre-dried) was added 4-chloropyridinium chloride (15.0 mg, 0.10 mmol) and sodium tetrakis-(3,5-bis(trifluoromethyl)phenyl)borate (88.6 mg, 0.10 mmol). Commercially obtained dry MeCN (1.5 mL) was added and the suspension was stirred at room temperature under air (capped vial) for 2 h. The suspension was diluted with CH₂Cl₂ (~2 mL) and stirred for a further 15 min before being filtered through a pipette cotton plug to remove the suspended solids. The reaction vial and cotton plug were further rinsed with CH₂Cl₂ (~3 mL), then the filtrate was concentrated, re-evaporated twice from CH₂Cl₂ (to fully remove MeCN) and dried under high vacuum to give the title compound (95.6 mg, 98%) as an easily handled off-white powder. ¹H NMR (500 MHz, CD₂Cl₂) δH 7.56 (s, 4H, 4 x ArH), 7.72 (pentet, J = 2.2, 8H, 8 x ArH), 8.05 (d, J = 7.0, 2H, 2 x ArH), 8.52 (d, J = 6.9, 2H, 2 x ArH). ¹³C NMR (126 MHz, CD₂Cl₂) δC 118.0 (pentet, J = 4.0, 4 x ArC), 125.1 (q, J = 272.3, 8 x CF₃), 129.4 (qdd, J = 31.5, 5.7, 2.9, 8 x ArC), 129.7 (2 x ArC), 135.3 (8 x ArC), 142.0 129.7 (2 x ArC), 158.8 (ArC), 162.3 (q, J = 49.8, 4 x ArCB).

tert-Butylamino-tris(dimethylamino)phosphonium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate, S9

(No stirring was performed in this reaction.) To a solution of S8 (50.0 mg, 0.051 mmol, 1.0 equiv) in reagent grade CH₂Cl₂ (1 mL) under air at room temperature was added a solution of phosphazene base P₁-t-Bu (12.6 mg, 0.054 mmol, 1.05 equiv) in CH₂Cl₂ (1 mL). The reaction flask was gently swirled by hand for 1 min, then the solvent was blown off using a stream of N₂. The residue was further dried in vacuo to give a pale yellow solid. A cold mixture of water/MeOH (1:1, 8 mL, pre-cooled in an ice bath) was added and the suspension was briefly sonicated (~30 seconds), then gravity filtered. The collected solid was washed with further cold water/MeOH (1:1, 2 mL) and dried in vacuo to give the title compound (22.6 mg, 40%) as a white powder. ¹H NMR (500 MHz, CD₂Cl₂) δH 1.31 (s, 9H, C(CH₃)₃), 2.71 (d, 18H, J = 10.0, 6 x NCH₃), 7.57 (s, 4H, 4 x ArH), 7.72 (s, 8H, 8 x ArH). ¹³C NMR (126 MHz, CD₂Cl₂) δC 31.5 (d, J = 4.4, C(CH₃)₃), 37.9 (d, J = 4.6, 6 x NCH₃), 53.7 (m, C(CH₃)₃), 117.9 (m, 4 x ArC), 125.0 (q, J = 270.9, 8 x CF₃), 129.3 (qq, J = 31.5, 2.9, 8 x ArC), 135.2 (8 x ArC), 162.1 (q, J = 50.6, 4 x ArCB). ¹⁹F NMR (377 MHz, CD₂Cl₂) δF −62.9 (8 x CF₃). ³¹P NMR (162 MHz, CD₂Cl₂) δP 34.7 ([NR₂]₄P⁺).
1-Benzyl-1-(3,5-bis(trifluoromethyl)anilinylthiocarbonyl)-4,7,10-tris(n-butylaminocarbonyl)-13-(3,5-bis(trifluoromethyl)anilinylcarbonyl)-1,4,7,10,13-pentaazatridecane, S10

**Step 1** *(reductive amination)*: To neat S10-1 (78.2 mg, 0.11 mmol, 1.0 equiv) was added a solution of benzaldehyde (11.2 mg, 0.11 mmol, 1.0 equiv) in lab grade MeOH (1.1 mL) and the mixture was stirred under air at room temperature for 21 h. The mixture was cooled to 0 °C and solid NaBH₄ (8.0 mg, 0.21 mmol, 2.0 equiv) was added, then the mixture was allowed to warm to room temperature in the cold bath with stirring arbitrarily over 96 h. 1 M K₂CO₃ (6 mL) was added and the product was extracted with CH₂Cl₂ (25 mL + 15 mL) then the combined organic extracts were dried (Na₂SO₄) and concentrated. Flash chromatography (Biotage, 10 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 10:90) gave the product (38.6 mg, 44%) as a white solid. **TLC** – Rf = 0.15 (SiO₂, 10:90 MeOH:CH₂Cl₂).

**Step 2** *(thiourea formation)*: The product from Step 1 (38.6 mg, 0.046 mmol, 1.0 equiv) was taken up in lab grade CH₂Cl₂ (0.4 mL) and a solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (12.6 mg, 0.046 mmol, 1.0 equiv) in CH₂Cl₂ (1.0 mL) was added. The mixture was stirred at room temperature under air for 1 h, before being concentrated *in vacuo*. Flash chromatography (Biotage, 5 g Sfär Duo column, MeOH/CH₂Cl₂ gradient from 0:100 to 6:94) gave the product (48.4 mg, 95% or 42% over two steps) as a white solid. **TLC** – Rf = 0.29 (SiO₂, 5:95 MeOH:CH₂Cl₂).

**¹H NMR** (500 MHz, CD₂Cl₂) δ H 0.82-0.91 (m, 9H, 3 x CH₃), 1.24-1.37 (m, 6H, 3 x CH₂CH₃), 1.42-1.53 (m, 6H, 3 x NCH₂CH₂), 3.05-3.55 (m, 20H, 10 x NC₂H₂), 3.55-4.07 (m, 2H, NC₂H₂), 5.18 (s, 2H, CH₂Ar), 6.01 (s, 2H, 2 x NH), 6.56 (s, 2H, 2 x NH), 7.29-7.44 (m, 5H, 5 x ArH), 7.47 (s, 1H, ArH), 7.63 (s, 1H, ArH), 7.93 (s, 2H, 2 x ArH), 8.29 (s, 2H, 2 x ArH), 10.93 (s, 1H, NH).

**¹³C NMR** (126 MHz, CD₂Cl₂) δ C 14.0 (3 x CH₃), 14.0 (3 x CH₃), 14.1 (CH₃), 14.1 (CH₃), 20.6 (CH₂CH₃), 20.6 (CH₂CH₃), 20.7 (CH₂CH₃), 32.5 (NCH₂CH₂), 32.6 (NCH₂CH₂), 32.7 (NCH₂CH₂), 40.0 (2 x NCH₂), 41.3 (2 x overlapping NCH₂), 41.3 (2 x overlapping NCH₂), 41.4 (overlapping NCH₂), 41.4 (overlapping NCH₂), 48.0 (2 x NCH₂), 48.1 (overlapping NCH₂), 48.8 (NCH₂), 56.2 (CH₂Ar), 115.7 (2 x ArC), 118.3 (3 x ArC), 124.0 (q, J = 272.6, 4 x CF₃), 125.3 (ArC), 127.6 (2 x ArC), 128.5 (ArC), 129.5 (2 x ArC), 131.5 (q, J = 33.6, 2 x ArC), 132.4 (q, J = 33.1, 2 x ArC), 137.1 (broad ArC), 141.8 (ArC), 142.9 (broad ArC), 156.3 (CO), 159.4 (CO), 159.5 (2 x CO), 182.3 (CS).

**¹⁹F NMR** (377 MHz, CD₂Cl₂) δ F −63.4 (2 x CF₃), −63.2 (2 x CF₃). **HR-MS** (ESI, positive ion mode) – m/z for [C₄₈H₆₂F₁₂N₁₀O₄S+Na]⁺ = 1125.4377. Found 1125.4367.
Conformational Analysis

Figure S1 – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 27 mM, CD$_2$Cl$_2$). Two conformers are present, which differ in the directionality of the hydrogen bond chain. The major conformer 1 (75% at −10 °C) has the thiourea at the hydrogen bond-accepting terminus, while the minor conformer $1'$ (25% at −10 °C) has the thiourea at the hydrogen bond-donating terminus. Selected pairs of rotationally exchanging protons are highlighted in different colours (except for the internal urea N–Hs, which are all coloured yellow), and where the protons in rotational exchange resonate at distinct chemical shifts, the relevant signals are labelled on the spectra as belonging to the major or minor conformer. These assignments were supported by NOESY (EXSY) and ROESY experiments (vide infra). The disappearance of the benzylic methylene signal at ~5.3 ppm (coloured purple) for the major conformer below −20 °C is attributed to the proximal sulfur atom slowing down rotation about the N–CH$_2$Ph bond at lower temperatures, causing signal broadening.
Figure S2 – Additional variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 25 mM, CD$_2$Cl$_2$). Coalescence of the signals from the benzylic methylene protons (coloured purple) of the two conformers is observed at 38 °C.
Figure S3 – (a) $^1$H NMR spectrum of compound 1 at $-10$ °C (500 MHz, 25 mM, CD$_2$Cl$_2$). At this temperature, distinct signals are observed for both conformers because rotation about the urea N–CO bonds is slow on the NMR timescale. Representative signals are labelled on the spectra as belonging to the major or minor conformer, as supported by NOESY (EXSY) and ROESY experiments (vide infra). Comparison of the integration of the resolved thiourea proton of the major conformer ($\delta_H = 11.12$ ppm, coloured blue) with the integration of the resolved benzylic methylene protons of the minor conformer ($\delta_H = 4.90$ ppm, coloured purple) allows the conformer distribution to be quantified as 75:25; (b) A portion of the $^{13}$C NMR spectrum of compound 1 at $-10$ °C (126 MHz, 27 mM, CD$_2$Cl$_2$). The two signals observed in this region are assigned to the thiocarbonyl (C=S) resonances of the major and minor conformers.
Figure S4 – A portion of the HSQC NMR spectrum of compound 1 at −10 °C (27 mM, CD₂Cl₂). The spectrum shows correlations for the benzylic methylene signals of the major and minor conformers.
Figure S5 – NOESY / EXSY spectrum of compound 1 at −10 °C (500 MHz, 25 mM, CD2Cl2). Cross-peaks arising from through space correlations (nOe) appear in the same phase (red) as the cross-peaks from rotational exchange (EXSY correlations), indicating that the nOes are negative.
Figure S6 – Selective one-dimensional NOESY experiments for compound 1 at −10 °C (500 MHz, 25 mM, CD2Cl2). (a) 1H NMR spectrum at −10 °C (for reference); (b) Irradiation of the benzylic methylene of the minor conformer (δH = 4.90 ppm, coloured purple); (c) Irradiation of the thiourea proton of the major conformer (δH = 11.12 ppm, coloured blue); and (d) Irradiation of the thiourea ortho-aryl protons of the major conformer (δH = 8.44 ppm, coloured grey). Signals arising from rotational exchange and through space nOe’s appear in the same phase, indicating that the nOe’s are negative. ‘Exchange nOe’s’ are also observed as a result of excitation transfer between the two conformers due to rotational exchange occurring on the timescale of the nOe build-up.
Figure S7a – ROESY spectrum of compound 1 at −10 °C (500 MHz, 25 mM, CD2Cl2). Cross-peaks arising from through space correlations appear in blue, while cross peaks arising from rotational exchange appear in red (same phase as the diagonal).
Figure S7b – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 10 mM, CD$_2$Cl$_2$). The ratio of 1:1' at −10 °C is 73:27. See also Table S1.
Figure S7c – Variable temperature $^1$H NMR spectra of a mixture of compound 1 (10 mM) and Bu$_3$PO (2 mM) (500 MHz, CD$_2$Cl$_2$). The ratio of 1:1' at $-10$ °C is 82:18. See also Table S1.
Figure S7d – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 2.5 mM, toluene-d8). The signals are broad and unresolved in toluene-d8, precluding conformational analysis.
Figure S7e – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 2.5 mM, CDCl$_3$). The ratio of 1:1' at −10 °C is 48:52. Thus, in CDCl$_3$, the relative populations of conformers 1 and 1' are ‘reversed’ with respect to their populations in CD$_2$Cl$_2$ and all other solvents studied. See also Table S1.
Figure S7f – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 2.5 mM, CD$_2$Cl$_2$). The ratio of 1:1' at −10 °C is 81:19. See also Table S1.
Figure S7g – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 2.5 mM, THF-d8). The ratio of 1:1' at −10 °C is 91:9. See also Table S1.
Figure S7h – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 2.5 mM, acetone-d$_6$). The ratio of 1:1' at −10 °C is >95:5. See also Table S1.
Figure S7i – Variable temperature $^1$H NMR spectra of compound 1 (500 MHz, 2.5 mM, MeCN-d3). The ratio of 1:1' at −10 °C is >95:5. Note that partial precipitation occurred upon cooling in the NMR spectrometer. See also Table S1.
Figure S8 – Variable temperature $^1$H NMR spectra of compound 2 (500 MHz, 25 mM, CD$_2$Cl$_2$). Two conformers are present, which differ only in the local conformation of the disubstituted urea – the global directionality of the hydrogen bond chain is the same in both conformers, with the disubstituted urea occupying the hydrogen bond-accepting terminus. The major conformer 2 (95% at −10 °C) has the disubstituted urea in the syn,syn-conformation and its alkyl N–H participates in a seven-membered hydrogen-bonding ring with the adjacent urea. In the minor conformer 2' (5% at −10 °C), the disubstituted urea is in an anti,syn-conformation and only the aryl N–H participates in intramolecular hydrogen bonding; in this case in a nine-membered ring. Selected pairs of rotationally exchanging protons are highlighted in different colours (except for the internal urea N–Hs, which are all coloured yellow), and where the protons in rotational exchange resonate at distinct chemical shifts, the relevant signals are labelled on the spectra as belonging to the major or minor conformer. These assignments were supported by a NOESY (EXSY) experiments (vide infra).
Figure S9 – Variable temperature 1H NMR spectra of compound 2 at 10-fold dilution (500 MHz, 2.5 mM, CD2Cl2). The chemical shifts of all protons and the ratios of the major and minor conformer at each temperature are identical or similar to those observed at 25 mM, confirming that intermolecular interactions are insignificant at the concentrations used for analysis.
Figure S10 – $^1$H NMR spectrum of compound 2 at −10 °C (500 MHz, 25 mM, CD$_2$Cl$_2$). At this temperature, distinct signals are observed for both conformers because rotation about the urea N–CO bonds is slow on the NMR timescale. Resolved signals are labelled on the spectra as belonging to the major or minor conformer, as supported by a NOESY (EXSY) experiment (vide infra). Comparison of the integration of the resolved aryl N–H signal of the disubstituted urea for the major conformer ($\delta_H = 8.62$ ppm, coloured green) with the integration of the resolved aryl ortho proton signal of the disubstituted urea of the minor conformer ($\delta_H = 8.42$ ppm, coloured orange) allows the conformer distribution to be quantified as 95:5.
Figure S11 – NOESY / EXSY spectrum of compound 2 at −10 °C (500 MHz, 25 mM, CD2Cl2). Cross-peaks arising from through space correlations (nOe) appear in the same phase (red) as the cross peaks from rotational exchange (EXSY correlations), indicating that the nOes are negative.
Figure S12 – Variable temperature $^1$H NMR spectra of compound 7 (500 MHz, 25 mM, CD$_2$Cl$_2$). Like its shorter homologue 1, two conformers are populated for 7, which differ in the directionality of the hydrogen bond chain. The major conformer 7 (74% at −10 °C) has the thiourea at the hydrogen bond-accepting terminus, while the minor conformer 7' (26% at −10 °C) has the thiourea at the hydrogen bond-donating terminus. Selected pairs of rotationally exchanging protons are highlighted in different colours (except for the internal urea N–Hs, which are all coloured yellow), and where the protons in rotational exchange resonate at distinct chemical shifts, the relevant signals are labelled on the spectra as belonging to the major or minor conformer. These assignments were supported by NOESY (EXSY) experiments (vide infra). The disappearance of the benzylic methylene signal at ~5.2 ppm (coloured purple) for the major conformer below −10 °C is attributed to the proximal sulfur atom slowing down rotation about the N–CH$_2$Ph bond at lower temperatures, causing signal broadening.
Figure S13 – $^1$H NMR spectrum of compound 7 at −10 ºC (500 MHz, 25 mM, CD$_2$Cl$_2$). At this temperature, distinct signals are observed for both conformers because rotation about the urea N–CO bonds is slow on the NMR timescale. Representative signals are labelled on the spectra as belonging to the major or minor conformer, as supported by NOESY (EXSY) experiments (vide infra). Comparison of the integration of the resolved thiourea proton of the major conformer ($\delta_{H1} = 11.10$ ppm, coloured blue) with the integration of the resolved benzylic methylene protons of the minor conformer ($\delta_{H1} = 4.81$ ppm, coloured purple) allows the conformer distribution to be quantified as 74:26.
Figure S14 – Selective one-dimensional NOESY experiment for compound 7 at −10 °C (500 MHz, 25 mM, CD$_2$Cl$_2$). (a) $^1$H NMR spectrum at −10 °C (for reference); (b) Irradiation of the thiourea proton of the major conformer ($\delta_{\text{H}} = 11.10$ ppm, coloured blue). Signals arising from rotational exchange and through space nOes appear in the same phase, indicating that the nOes are negative. ‘Exchange nOes’ are also observed as a result of excitation transfer between the two conformers due to rotational exchange occurring on the timescale of the nOe build-up.
Figure S15 – NOESY / EXSY spectrum of compound 7 at −10 ºC (500 MHz, 25 mM, CD2Cl2). Cross-peaks arising from through space correlations (nOe) appear in the same phase as the cross peaks from rotational exchange (EXSY correlations), indicating that the nOes are negative.
Like 1, two conformers are populated for alkyl urea analogue S10, which differ in the directionality of the hydrogen bond chain. The major conformer S10 (72% at −10 °C) has the thiourea at the hydrogen bond-accepting terminus, while the minor conformer S10' (28% at −10 °C) has the thiourea at the hydrogen bond-donating terminus. Selected pairs of rotationally exchanging protons are highlighted in different colours (except for the internal urea N–Hs, which are all coloured yellow), and where the protons in rotational exchange resonate at distinct chemical shifts, the relevant signals are labelled on the spectra as belonging to the major or minor conformer. These assignments were supported by NOESY (EXSY) experiments. The disappearance of the benzylic methylene signal at ~5.2 ppm (coloured purple) for the major conformer below −20 °C is attributed to the proximal sulfur atom slowing down rotation about the N–CH$_2$Ph bond at lower temperatures, causing signal broadening.
Figure S16a – Selective one-dimensional NOESY experiment for compound S10 at −10 °C (500 MHz, 25 mM, CD$_2$Cl$_2$). (Upper) $^1$H NMR spectrum at −10 °C (for reference); (Lower) Irradiation of the thiourea proton of the major conformer ($\delta_H = 11.14$ ppm, coloured blue). Signals arising from rotational exchange and through space nOes appear in the same phase, indicating that the nOes are negative. ‘Exchange nOes’ are also observed as a result of excitation transfer between the two conformers due to rotational exchange occurring on the timescale of the nOe build-up.
Table S1 – Summary of the conformational populations of thioureas 1, 7 and S10 under various conditions. All ratios were measured at –10 °C. The capture and release experiments shown in the manuscript essentially involve the ‘major’ conformer of 1 and 7 (i.e., conformer X, drawn on the left of the equilibrium below). As such, we investigated the effect of various parameters on the conformational population of X. The results show that the length of the oligomer (entry 1 versus entry 2), the identity of the internal ureas (entry 1 versus entry 3) and the concentration (entries 1, 4 and 8) have little effect on the conformer ratio, favouring X in all cases. Adding the ligand (Bu3PO) at the same concentration as the capture and release experiments further shifts the equilibrium in favour of X (entry 4 versus entry 5), consistent with the proposed binding at the BTMP urea. Finally, the conformer ratio was found to be dependent on the solvent (entries 6−11): an almost equal population of the two conformers was observed in CDCl3 (entry 7), while X was strongly favoured by more polar solvents and/or solvents with hydrogen bond-accepting heteroatoms (entries 9–11).

![Diagram of conformers X and X']

| Entry | Compound | n  | R             | Conc. | Solvent | Ratio X:X' | Figure Reference |
|-------|----------|----|---------------|------|---------|------------|------------------|
| 1     | 1        | 1  | 4-butoxyphenyl | 25 mM| CD2Cl2  | 75:25      | Fig. S1           |
| 2     | 7        | 3  | 4-butoxyphenyl | 25 mM| CD2Cl2  | 74:26      | Fig. S12          |
| 3     | S10      | 1  | butyl         | 25 mM| CD2Cl2  | 72:28      | Fig. S16          |
| 4     | 1        | 1  | 4-butoxyphenyl | 10 mM| CD2Cl2  | 73:27      | Fig. S7b          |
| 5     | 1        | 1  | 4-butoxyphenyl | 10 mM| CD2Cl2  | 82:18      | Fig. S7c          |
| 6     | 1        | 1  | 4-butoxyphenyl | 2.5 mM| tluene-d8| nd\(^b\) | Fig. S7d          |
| 7     | 1        | 1  | 4-butoxyphenyl | 2.5 mM| CDCl3   | 48:52      | Fig. S7e          |
| 8     | 1        | 1  | 4-butoxyphenyl | 2.5 mM| CD2Cl2  | 81:19      | Fig. S7f          |
| 9     | 1        | 1  | 4-butoxyphenyl | 2.5 mM| THF-d8  | 91:9       | Fig. S7g          |
| 10    | 1        | 1  | 4-butoxyphenyl | 2.5 mM| acetone-d6| >95:5 | Fig. S7h          |
| 11    | 1        | 1  | 4-butoxyphenyl | 2.5 mM| MeCN-d3  | >95:5      | Fig. S7i          |

\(^a\)Bu3PO (2 mM) was also present. \(^b\)Broad, unresolved signals were observed. \(^c\)Partial precipitation was observed upon cooling in the NMR spectrometer.
Titrations, Binding Constants and Related Experiments

General Points

- **31P NMR parameters for titrations:** proton decoupled $^{31}\text{P}\{^1\text{H}\}$, CH$_2$Cl$_2$, 162 MHz, 128 scans, Bruker spectrometer; ‘non-deuterated CH$_2$Cl$_2$’ was selected as the solvent.

- A 150 mM solution of Ph$_3$PO in CH$_2$Cl$_2$ was used as external standard by placing a capillary tube containing this solution in the NMR tube; capillary tube dimensions (L x I.D. x O.D.) = 100 mm x 0.95 mm x 1.35 mm (pre-sealed at the bottom and, after addition of the Ph$_3$PO solution, sealed at the top using a Bunsen burner). Note that the height of the external standard solution in the capillary tube should be lower (by ca 20%) than the height of the sample solution in the NMR tube to avoid significant broadening of the external standard signal.

- The titrant solutions (containing the disubstituted urea ligand at 20 mM in CH$_2$Cl$_2$) were stored sealed in the fridge between additions, and a new line was marked at the solvent level after each aliquot was taken to check/ensure no solvent loss occurred between additions.

- **Binding constants (K)** for 1−3 with Bu$_3$PO in CH$_2$Cl$_2$ were determined using Bindfit (supramolecular.org) with a 1:1 binding model.$^4$

*General procedure for 31P NMR titrations:* A solution of Bu$_3$PO (2.0 mM in CH$_2$Cl$_2$, 0.50 mL, 1.0 μmol, 1.0 equiv) was added to an NMR tube and a sealed capillary tube containing Ph$_3$PO (150 mM in CH$_2$Cl$_2$) was placed inside. The solvent level in the NMR tube (containing the capillary tube) was marked on a separate NMR tube for reference, then the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum was recorded to obtain the chemical shifts of ‘free’ Bu$_3$PO and the Ph$_3$PO external standard [$\delta_P$ Bu$_3$PO = 47.23 ppm$^5$; $\delta_P$ Ph$_3$PO = 27.67 ppm; all subsequent spectra were referenced to the external standard at 27.67 ppm]. An aliquot of the appropriate ligand solution (1, 2, 3, (3+4)* or (3+5)**, 20 mM in CH$_2$Cl$_2$, 25 μL, 0.5 μmol, 0.5 equiv) was added via a Gilson pipette, followed by a small amount of CH$_2$Cl$_2$ (~0.1 mL) to rinse the upper interior of the NMR tube. The volume in the NMR tube was then re-adjusted to the original level by blowing N$_2$ into the tube using a 120 mm length, 21-gauge needle attached to a N$_2$-filled balloon. During this process, any moisture building up on the exterior of the NMR tube (due to endothermic evaporation) was removed with paper towel. The $^{31}$P NMR spectrum was again recorded. Aliquots of the titrant were then added sequentially using the same procedure and the $^{31}$P NMR spectrum was each time recorded. When the amount of ligand present reached a total of 5.0 equiv, the volume of the added titrant (containing 20 mM of the ligand in CH$_2$Cl$_2$) was increased to 50 μL so that a further 1.0 equiv of the ligand was introduced during each addition (up to a total of 9.0 equiv), again adjusting the solvent
volume as described to ensure a constant concentration of Bu₃PO (2.0 mM). [*Contained 20 mM of 3 and 20 mM of 4; **Contained 20 mM of 3 and 20 mM of 5.]

Figure S16 – Titration of Bu₃PO (2 mM) with 1 (0–9 equiv) as monitored by ³¹P{¹H} NMR spectroscopy (162 MHz, CH₂Cl₂).
### Table S2 – $\delta_P$ of Bu$_3$PO (2 mM, CH$_2$Cl$_2$) with increasing concentration of 1.

| concentration Bu$_3$PO (mM$^{-1}$) | concentration 1 (mM$^{-1}$) | $\delta_P$ (ppm) | $\Delta\delta_P$ (ppm) |
|-----------------------------------|-------------------------------|------------------|------------------------|
| 0.002                             | 0.000                         | 47.23            | 0.00                   |
| 0.002                             | 0.001                         | 49.05            | 1.82                   |
| 0.002                             | 0.002                         | 50.61            | 3.38                   |
| 0.002                             | 0.003                         | 51.53            | 4.30                   |
| 0.002                             | 0.004                         | 51.98            | 4.75                   |
| 0.002                             | 0.005                         | 52.27            | 5.04                   |
| 0.002                             | 0.006                         | 52.43            | 5.20                   |
| 0.002                             | 0.007                         | 52.59            | 5.36                   |
| 0.002                             | 0.008                         | 52.67            | 5.44                   |
| 0.002                             | 0.009                         | 52.74            | 5.51                   |
| 0.002                             | 0.010                         | 52.78            | 5.55                   |
| 0.002                             | 0.012                         | 52.87            | 5.64                   |
| 0.002                             | 0.014                         | 52.91            | 5.68                   |
| 0.002                             | 0.016                         | 52.96            | 5.73                   |
| 0.002                             | 0.018                         | 52.99            | 5.76                   |
Figure S17 – Determination of the binding constant ($K$) of Bu$_3$PO with 1 in CH$_2$Cl$_2$. These results were obtained using Bindfit (supramolecular.org) with a 1:1 binding model. Fit details available at http://app.supramolecular.org/bindfit/view/17f96abe-2b42-4b99-adb9-6cfca405e124.
Figure S18 – Titration of Bu₃PO (2 mM) with 2 (0–9 equiv) as monitored by $^{31}$P{$^1$H} NMR spectroscopy (162 MHz, CH₂Cl₂).

Table S3 – $\delta_P$ of Bu₃PO (2 mM, CH₂Cl₂) with increasing concentration of 2.

| concentration Bu₃PO (molL⁻¹) | concentration 2 (molL⁻¹) | $\delta_P$ (ppm) | $\Delta\delta_P$ (ppm) |
|-----------------------------|--------------------------|------------------|------------------------|
| 0.002                       | 0.000                    | 47.23            | 0.00                   |
| 0.002                       | 0.001                    | 48.04            | 0.81                   |
| 0.002                       | 0.002                    | 48.44            | 1.21                   |
| 0.002                       | 0.003                    | 48.72            | 1.49                   |
| 0.002                       | 0.004                    | 49.01            | 1.78                   |
| 0.002                       | 0.005                    | 49.22            | 1.99                   |
| 0.002                       | 0.006                    | 49.36            | 2.13                   |
| 0.002                       | 0.007                    | 49.47            | 2.24                   |
| 0.002                       | 0.008                    | 49.62            | 2.39                   |
| 0.002                       | 0.009                    | 49.75            | 2.52                   |
| 0.002                       | 0.010                    | 49.86            | 2.63                   |
| 0.002                       | 0.012                    | 50.00            | 2.77                   |
| 0.002                       | 0.014                    | 50.14            | 2.91                   |
| 0.002                       | 0.016                    | 50.28            | 3.05                   |
| 0.002                       | 0.018                    | 50.34            | 3.11                   |
Figure S19 – Determination of the binding constant (K) of Bu₃PO with 2 in CH₂Cl₂. These results were obtained using Bindfit (supramolecular.org) with a 1:1 binding model. Fit details available at http://app.supramolecular.org/bindfit/view/60263b23-2d00-4e27-82da-9237c8ba1127.
Figure S20 – Titration of Bu$_3$PO (2 mM) with 3 (0–9 equiv) as monitored by $^{31}$P{$^1$H} NMR spectroscopy (162 MHz, CH$_2$Cl$_2$).

Table S4 – $\delta_P$ of Bu$_3$PO (2 mM, CH$_2$Cl$_2$) with increasing concentration of 3.

| concentration Bu$_3$PO (molL$^{-1}$) | concentration 3 (molL$^{-1}$) | $\delta_P$ (ppm) | $\Delta \delta_P$ (ppm) |
|--------------------------------------|-------------------------------|-----------------|-------------------------|
| 0.002                                | 0.000                         | 47.23           | 0.00                    |
| 0.002                                | 0.001                         | 48.57           | 1.34                    |
| 0.002                                | 0.002                         | 49.63           | 2.40                    |
| 0.002                                | 0.003                         | 50.35           | 3.12                    |
| 0.002                                | 0.004                         | 50.88           | 3.65                    |
| 0.002                                | 0.005                         | 51.20           | 3.97                    |
| 0.002                                | 0.006                         | 51.41           | 4.18                    |
| 0.002                                | 0.007                         | 51.61           | 4.38                    |
| 0.002                                | 0.008                         | 51.75           | 4.52                    |
| 0.002                                | 0.009                         | 51.84           | 4.61                    |
| 0.002                                | 0.010                         | 51.93           | 4.70                    |
| 0.002                                | 0.012                         | 52.04           | 4.81                    |
| 0.002                                | 0.014                         | 52.13           | 4.90                    |
| 0.002                                | 0.016                         | 52.22           | 4.99                    |
| 0.002                                | 0.018                         | 52.27           | 5.04                    |
Figure S21 – Determination of the binding constant ($K$) of Bu$_3$PO with 3 in CH$_2$Cl$_2$. These results were obtained using Bindfit (supramolecular.org) with a 1:1 binding model. Fit details available at http://app.supramolecular.org/bindfit/view/dee1a1ec-c880-497a-8d71-15c68e0ef1bf.
Figure S22 – Titration of Bu₃PO (2 mM) with 3+4 (0–9 equiv of each) as monitored by $^{31}$P{¹H} NMR spectroscopy (162 MHz, CH₂Cl₂). The titrant consists of a mixture of 3 and 4 in a 1:1 molar ratio – the column to the right of the NMR stack shows the equivalents of both 3 and 4 present at each titration point.

Table S5 – δₚ of Bu₃PO (2 mM, CH₂Cl₂) with increasing concentrations of 3 and 4.

| concentration Bu₃PO (molL⁻¹) | concentration 3 and 4 (molL⁻¹) | δₚ (ppm) | Δδₚ (ppm) |
|-----------------------------|-------------------------------|---------|----------|
| 0.002                       | 0.000                         | 47.23   | 0.00     |
| 0.002                       | 0.001                         | 48.88   | 1.65     |
| 0.002                       | 0.002                         | 49.65   | 2.42     |
| 0.002                       | 0.003                         | 50.36   | 3.13     |
| 0.002                       | 0.004                         | 50.81   | 3.58     |
| 0.002                       | 0.005                         | 51.09   | 3.86     |
| 0.002                       | 0.006                         | 51.32   | 4.09     |
| 0.002                       | 0.007                         | 51.51   | 4.28     |
| 0.002                       | 0.008                         | 51.63   | 4.40     |
| 0.002                       | 0.009                         | 51.75   | 4.52     |
| 0.002                       | 0.010                         | 51.82   | 4.59     |
| 0.002                       | 0.012                         | 51.94   | 4.71     |
| 0.002                       | 0.014                         | 52.03   | 4.80     |
| 0.002                       | 0.016                         | 52.10   | 4.87     |
| 0.002                       | 0.018                         | 52.15   | 4.92     |
Figure S23 – Titration of Bu₃PO (2 mM) with 3+5 (0–9 equiv of each) as monitored by ³¹P{¹H} NMR spectroscopy (162 MHz, CH₂Cl₂). The titrant consists of a mixture of 3 and 5 in a 1:1 molar ratio – the column to the right of the NMR stack shows the equivalents of both 3 and 5 present at each titration point.
Table S6 – $\delta_P$ of Bu$_3$PO (2 mM, CH$_2$Cl$_2$) with increasing concentrations of 3 and 5.

| concentration Bu$_3$PO (molL$^{-1}$) | concentration 3 and 5 (molL$^{-1}$) | $\delta_P$ (ppm) | $\Delta\delta_P$ (ppm) |
|-------------------------------------|-------------------------------------|-----------------|------------------------|
| 0.002                               | 0.000                               | 47.23           | 0.00                   |
| 0.002                               | 0.001                               | 48.75           | 1.52                   |
| 0.002                               | 0.002                               | 49.48           | 2.25                   |
| 0.002                               | 0.003                               | 50.19           | 2.96                   |
| 0.002                               | 0.004                               | 50.60           | 3.37                   |
| 0.002                               | 0.005                               | 50.85           | 3.62                   |
| 0.002                               | 0.006                               | 51.04           | 3.81                   |
| 0.002                               | 0.007                               | 51.21           | 3.98                   |
| 0.002                               | 0.008                               | 51.32           | 4.09                   |
| 0.002                               | 0.009                               | 51.40           | 4.17                   |
| 0.002                               | 0.010                               | 51.49           | 4.26                   |
| 0.002                               | 0.012                               | 51.60           | 4.37                   |
| 0.002                               | 0.014                               | 51.69           | 4.46                   |
| 0.002                               | 0.016                               | 51.76           | 4.53                   |
| 0.002                               | 0.018                               | 51.80           | 4.57                   |
Figure S24 – Evidence of hydrogen bonding between 3 and 5. (a) $^1$H NMR spectrum of compound 5 (400 MHz, 10 mM, CD$_2$Cl$_2$); (b) $^1$H NMR spectrum of compound 3 (400 MHz, 10 mM, CD$_2$Cl$_2$); (c) $^1$H NMR spectrum of 3 and 5 combined in a 1:1 molar ratio (400 MHz, both 10 mM, CD$_2$Cl$_2$); (d) Proposed intermolecular hydrogen bonding between the disubstituted urea in 3 and the available urea carbonyl group of 5.
Figure S25 – Reversible deprotonation and polarity switching of thiourea transmitter 4. (a) $^1$H NMR spectrum of 4 (500 MHz, 42 mM, CD$_2$Cl$_2$) and (b) with the addition of $t$-BuN=P(NMe$_2$)$_3$ (1 equiv) to the same sample to deprotonate the thiourea. (c) Re-protonation after addition of [4-Cl-pyH]$^+\cdot$[BARF]$^-$ (1 equiv) to the same sample. Note that this Figure is an expansion of Figure 3 in the manuscript.
Figure S25d – NOESY spectrum of [t-BuHN–P(NMe₂)₃]⁺·4⁻ at 25 °C (500 MHz, 40 mM, CD₂Cl₂).

An alternative orientation of 4⁻ was also considered, where the N-aryl nitrogen of the thiourea points inwards and hydrogen bonds to the adjacent urea NH instead of the sulfur atom:

In this alternative orientation, an NOE would likely be expected between the urea NH (colored yellow) and the BTMP thiourea ortho-aryl protons (colored grey), as well as between the ortho protons on each of the two N-aryl rings; however, no appreciable NOE was observed in either case. These results tentatively suggest that it is the sulfur that points inwards and hydrogen bonds to the adjacent urea proton – a situation that would also relieve steric interactions between the N-aryl rings.
Figure S26 – Accompanying $^{13}$C NMR evidence for the deprotonation of thiourea transmitter 4. (a) Portion of the $^{13}$C NMR spectrum of 4 (126 MHz, 42 mM, CD$_2$Cl$_2$) showing the thiocarbonyl signal and (b) with the addition of t-BuN=P(NMe$_2$)$_3$ (1 equiv) to the same sample.

General Points for $^{31}$P NMR Capture-and-Release Experiments

- All $^{31}$P NMR experiments: proton decoupled $[^{31}$P{${}^1$H}], CD$_2$Cl$_2$, 162 MHz, 192 scans, Bruker spectrometer.

- A 150 mM solution of Ph$_3$PO in CD$_2$Cl$_2$ was used as external standard by placing a capillary tube containing this solution in the NMR tube; capillary tube dimensions (L x I.D. x O.D.) = 100 mm x 0.95 mm x 1.35 mm (pre-sealed at the bottom and, after addition of the Ph$_3$PO solution, sealed at the top using a Bunsen burner). Note that the height of the external standard solution in the capillary tube should be lower (by ca 20%) than the height of the sample solution in the NMR tube to avoid significant broadening of the external standard signal.

- $^1$H NMR spectra were also acquired for every experiment to confirm correct stoichiometry and, where applicable, chemoselective thiourea deprotonation; hence, why CD$_2$Cl$_2$ was used as the $^{31}$P NMR solvent instead of CH$_2$Cl$_2$ ($^1$H NMR spectra were also acquired with the Ph$_3$PO external standard capillary in the NMR tube).
• The major indicators of deprotonation of the thiourea function in 1, 4, 6 and 7 with t-BuN=P(NMe₂)₃ were the loss of the thiourea NH signal at ca 11 ppm in the ₁H NMR spectrum, as well as a new signal in the ³¹P NMR spectrum (in addition to Bu₃PO) corresponding to [t-BuHN−P(NMe₂)₃]⁺X⁻ at δₚ = 32–35 ppm (X = 1, 4, 6 or 7). For comparison, the conjugate base t-BuN=P(NMe₂)₃ was found to have δₚ = 7.05 ppm under the same conditions (Figure S28).

• The ³¹P NMR chemical shift (δₚ) of the ion pairs [t-BuHN−P(NMe₂)₃]⁺X⁻ (where X = 1, 4, 6 and 7; δₚ = 32–35 ppm) matched closely with that of an in-house prepared tetraarylborate analogue [t-BuHN−P(NMe₂)₃][BARF₄]⁻ (S9) characterized under the same conditions (δₚ = 34.71 ppm; Figure S29).

• Although no attempts have been made to isolate the [t-BuHN−P(NMe₂)₃]⁺ salts of thiourea anions 1⁻, 4⁻, 6⁻ or 7⁻, we have seen no evidence of sensitivity to air or adventitious moisture during the timeframes of NMR analysis of their CD₂Cl₂ solutions. We note, however, that they do undergo slow alkylation at sulfur by the solvent itself (CD₂Cl₂). For this reason, all ₁H and ³¹P NMR spectra of these anions (1⁻, 4⁻, 6⁻ or 7⁻) were acquired within 30 min of adding the base (t-BuN=P(NMe₂)₃). Subsequent re-protonation, where relevant, was then carried out immediately after recording the NMR spectra. With these precautions taken (as described in the general procedure), at most, traces of thiourea alkylation are observed. The rate of alkylation was nonetheless investigated by ¹H NMR using 4⁻ as a representative example (42 mM, CD₂Cl₂, room temperature). After 4 h, the molar ratio of 4⁻/alkylation product was 4.0:1.0. After 20 h, the ratio was 1.0:1.0. After 68 h, >99% consumption of 4⁻ was observed; the alkylation product was isolated in 73% yield (Scheme S7).

Scheme S7 – Thiourea anions are slowly alkylated at sulfur by CD₂Cl₂. The alkylation product of representative thiourea anion 4⁻ was isolated in 73% yield after 72 h at room temperature.

General procedure for ³¹P NMR capture-and-release experiments and controls (Figure 4 in manuscript): First, the δₚ of the Ph₃PO external standard (relative to ‘free’ Bu₃PO; δₚ = 47.23 ppm)⁵ was determined: an aliquot of Bu₃PO (2.0 mM in CD₂Cl₂, 0.50 mL, 1.0 μmol, 1.0 equiv) was added to an NMR tube and a sealed capillary tube containing Ph₃PO (150 mM in CD₂Cl₂) was placed inside. The ³¹P {¹H} NMR spectrum was recorded [δₚ Bu₃PO = 47.23 ppm; δₚ Ph₃PO = 27.38 ppm; all subsequent spectra were referenced to the external standard at 27.38 ppm]. Then, for the capture-and-release studies
and controls, the appropriate ligand (1, 3, (3+4)*, 4, 5, or 6; 5.0 μmol, 5.0 equiv) was weighed into a 1.7 mL vial. To this was added a solution of B₃PO (2.0 mM in CD₂Cl₂, 0.5 mL, 1.0 μmol, 1.0 equiv). The resulting solution was transferred quantitatively to an NMR tube and a sealed capillary tube containing Ph₃PO (150 mM in CD₂Cl₂) was placed inside. ¹H and ³¹P{¹H} NMR spectra were acquired. Next, under air, a solution of t-BuN=P(NMe₂)₃ (200 mM in CD₂Cl₂, 25 μL, 5.0 μmol, 5.0 equiv) was added via a Gilson pipette (the concentration of B₃PO drops slightly from 2.0 mM to 1.9 mM after this step). ¹H and ³¹P{¹H} NMR experiments were again acquired, within 30 min of adding the base. [*5.0 μmol of 3 and 5.0 μmol of 4 was used.]
Table S7 – Summary of the $^{31}$P{H} NMR chemical shift ($\delta_P$) of Bu$_3$PO (162 MHz, CD$_2$Cl$_2$) upon treatment with each of 1, 2, 3, (3+4), (3+5), 4, 5, 6 and 7 (5 equiv), followed by t-BuN=P(NMe$_2$)$_3$ (5 equiv) where applicable. Spectra of mixtures containing Bu$_3$PO + ligand were recorded at 2.0 mM of Bu$_3$PO; spectra of mixtures containing Bu$_3$PO + ligand + t-BuN=P(NMe$_2$)$_3$ were recorded at 1.9 mM in Bu$_3$PO.

| Ligand | $^{31}$P{H} NMR: $\delta_P$ Bu$_3$PO (ppm) | Note: $\delta_P$ free Bu$_3$PO = 47.23 ppm |
|--------|--------------------------------------------|-------------------------------------------|
| no ligand (Bu$_3$PO alone) | 47.23 | 47.29 |
| [t-BuHN−P(NMe$_2$)$_3$]$^-$[BAr$_4^-$(S9)] | 47.51 | - |
| 1 | 52.66 | 48.31 |
| 2 | 49.86 (data obtained from titration in CH$_2$Cl$_2$) | - |
| 3 | 51.99 | 51.25 |
| 4 | 51.81 | 50.10 |
| 5 | 51.49 (data obtained from titration in CH$_2$Cl$_2$) | - |
| 6 | 47.60 | 47.16 |
| 7 | 47.51 | - |
| 8 | 47.27 | 47.17 |
| 9 | 52.51 (data from first cycle only) | 48.04 (data from first cycle only; obtained at 2.0 mM) |
Figure S27 – $^{31}$P{$^1$H} NMR spectrum of Bu$_3$PO (162 MHz, 2.0 mM, CD$_2$Cl$_2$).

Figure S28 – $^{31}$P{$^1$H} NMR spectrum of a mixture of Bu$_3$PO (1.9 mM) and $t$-BuN=P(NMe$_2$)$_3$ (5 equiv, 9.5 mM) (162 MHz, CD$_2$Cl$_2$).
Figure S29 – $^{31}$P{1H} NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and [t-BuHN–P(NMe$_2$)$_3$]$^+$–[BArF$_4$]$^-$ (5 equiv, 10 mM) (162 MHz, CD$_2$Cl$_2$). This experiment also provides further evidence that [t-BuHN–P(NMe$_2$)$_3$]$^+$ does not hydrogen bond to Bu$_3$PO to any significant extent – even when it is paired with the prototypical non-coordinating counterion [BArF$_4$]$^-$ because the $\Delta\delta_P$ of Bu$_3$PO (relative to Bu$_3$PO alone) was minimal ($\Delta\delta_P$ Bu$_3$PO = +0.28 ppm).

Figure S30 – (a) $^{31}$P{1H} NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and 1 (5 equiv, 10 mM) (162 MHz, CD$_2$Cl$_2$) and (b) after addition of t-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (1.9 mM) and [t-BuHN–P(NMe$_2$)$_3$]$^+$·1$^-$ (9.5 mM).
Figure S31 – (a) Accompanying $^1$H NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and 1 (5 equiv, 10 mM) (400 MHz, CD$_2$Cl$_2$) and (b) after addition of t-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (1.9 mM) and [t-BuHN−P(NMe$_2$)$_3$]$^+$.1$^-$ (9.5 mM). Deprotonation of 1 in (b) is indicated by the loss of the thiourea proton signal at $\delta_H = 10.82$ ppm. (The spectra also contain signals in the aromatic region arising from the Ph$_3$PO external standard).
Figure S32 — (a) $^{31}$P{$^1$H} NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and 3 (5 equiv, 10 mM) (162 MHz, CD$_2$Cl$_2$) and (b) after addition of t-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (1.9 mM), 3 (9.5 mM) and t-BuN=P(NMe$_2$)$_3$ (9.5 mM). The broad signal at δ$_P$ = 11.3–13.5 ppm is attributed to an equilibrium between t-BuN=P(NMe$_2$)$_3$ and [t-BuHN−P(NMe$_2$)$_3$]$^-$ arising from partial deprotonation of 3 (presumably at the aryl N−H). Presumably, this equilibrium strongly favours the freebase form because the observed δ$_P$ is much closer to that of the freebase (t-BuN=P(NMe$_2$)$_3$, δ$_P$ = 7.05 ppm) than the conjugate acid ([t-BuHN−P(NMe$_2$)$_3$]$^-$ = 32–35 ppm; counterion dependent).
Figure S33 – (a) $^{31}$P\footnote{H} NMR spectrum of a mixture of Bu$_3$PO (2.0 mM), 3 (5 equiv, 10 mM) and 4 (5 equiv, 10 mM) (162 MHz, CD$_2$Cl$_2$) and (b) after addition of $t$-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (1.9 mM), 3 (9.5 mM) and $[t$-BuHN−P(NMe$_2$)$_3$]$^-$ (9.5 mM).
Figure S34 – (a) Accompanying $^1$H NMR spectrum of a mixture of Bu$_3$PO (2.0 mM), 3 (5 equiv, 10 mM) and 4 (5 equiv, 10 mM) (400 MHz, CD$_2$Cl$_2$) and (b) after addition of $t$-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (1.9 mM), 3 (9.5 mM) and [[$t$-BuN=P(NMe$_2$)$_3$]$\cdot$4$^{-}$ (9.5 mM). Deprotonation of 4 in (b) is indicated by the loss of the thiourea proton signal at $\delta_H = 10.49$ ppm. (The spectra also contain signals in the aromatic region arising from the Ph$_3$PO external standard.)
Figure S35 – (a) $^{31}$P{$^{1}$H} NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and 4 (5 equiv, 10 mM) (162 MHz, CD$_2$Cl$_2$) and (b) after addition of $t$-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (1.9 mM), and [[$t$-BuHN$^-$P(NMe$_2$)$_3$]$^+$4$^-$ (9.5 mM).
Figure S36 – (a) Accompanying $^1$H NMR spectrum of a mixture of $\text{Bu}_3\text{PO}$ (2.0 mM) and 4 (5 equiv, 10 mM) (400 MHz, CD$_2$Cl$_2$) and (b) after addition of $t$-BuN=P(NMe$_2$)$_2$ (5 equiv) to the same sample, generating a mixture of $\text{Bu}_3\text{PO}$ (1.9 mM) and $[t$-BuHN=P(NMe$_2$)$_2$]$^-$ (9.5 mM). Deprotonation of 4 in (b) is indicated by the loss of the thiourea proton signal at $\delta_H = 10.51$ ppm. (The spectra also contain signals in the aromatic region arising from the Ph$_3$PO external standard).
Figure S37 – $^{31}$P{1H} NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and 5 (5 equiv, 10 mM) (162 MHz, CD$_2$Cl$_2$).

Figure S38 – (a) $^{31}$P{1H} NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and 6 (5 equiv, 10 mM) (162 MHz, CD$_2$Cl$_2$) and (b) after addition of $t$-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (1.9 mM), and [t-BuHN=P(NMe$_2$)$_3$]$^+$.6$^-$(9.5 mM).
Figure S39 – (a) Accompanying ¹H NMR spectrum of a mixture of Bu₃PO (2.0 mM) and 6 (5 equiv, 10 mM) (400 MHz, CD₂Cl₂) and (b) after addition of t-BuN=P(NMe₂)₃ (5 equiv) to the same sample, generating a mixture of Bu₃PO (1.9 mM) and [t-BuHN−P(NMe₂)₃]⁺·6⁻ (9.5 mM). Deprotonation of 6 in (b) is indicated by the loss of the thiourea proton signal at δH = 10.89 ppm. (The spectra also contain signals in the aromatic region arising from the Ph₃PO external standard.)

Additional Points for ³¹P NMR Capture-and-Release Cycles with Compound 7

- The ³¹P NMR spectrum of ‘free’ Bu₃PO with the Ph₃PO external standard was previously recorded as described in the general procedure for ³¹P NMR capture-and-release experiments and controls: δP Bu₃PO = 47.23 ppm; δP Ph₃PO = 27.38 ppm; all spectra were referenced to the external standard at 27.38 ppm.

- To ensure the volume in the NMR tube was maintained at 0.50 mL throughout these experiments (and hence a constant 2.0 mM concentration of Bu₃PO), a ‘reference NMR sample’ was prepared containing 0.50 mL of CH₂Cl₂ and an empty capillary tube (the same size as used for the external standard); a line was marked on this tube at the solvent level as a reference.

- The total time between each deprotonation / re-protonation cycle – from adding t-BuN=P(NMe₂)₃ to form 7⁺, recording the ¹H and ³¹P NMR spectra, and re-protonating with [4-Cl-pyH]⁺·[BArF₄]⁻ – was no
longer than 30–45 minutes each time; this prevents alkylation of 7− by CD2Cl2 as discussed previously. After re-protonation to re-form 7, the time before the next addition of t-BuN=P(NMe2)3 (usually 0.5–2 h) is less important, because 7 itself, Bu3PO and the by-products [t-BuHN−P(NMe2)3]+[BARF4]− and 4-Cl-py appear to be stable under these conditions, at least over the time course of these experiments (~8–12 h).

Procedure for 31P NMR capture-and-release cycles with compound 7: A 1.7 mL vial was charged with 7 (9.24 mg, 5.0 μmol, 5.0 equiv) and a solution of Bu3PO (2.0 mM in CD2Cl2, 0.50 mL, 1.0 μmol, 1.0 equiv) was added. The resulting solution was transferred via pipette to an NMR tube. Additional CD2Cl2 (~0.15 mL) was added to the vial and the solution was again transferred to the NMR tube to ensure quantitative transfer of 7 and Bu3PO. A sealed capillary tube containing Ph3PO (150 mM in CD2Cl2) was added to the NMR tube as an external standard. The volume in the NMR tube was then re-adjusted to the reference 0.50 mL mark (see second point above) by blowing N2 into the tube using a 120 mm length, 21-gauge needle attached to a N2-filled balloon. During this process, the moisture building up on the exterior of the NMR tube (due to endothermic evaporation) was removed with paper towel. 1H and 31P{1H} NMR spectra were acquired. Next, under air, a solution of t-BuN=P(NMe2)3 (50 mM in CD2Cl2, 100 μL, 5.0 μmol, 5.0 equiv) was added via a Gilson pipette and additional CD2Cl2 (~0.05 mL) was added to rinse the upper interior of the NMR tube. The volume in the NMR tube was re-adjusted to the reference 0.50 mL mark as described. 1H and 31P{1H} NMR spectra were then acquired. A solution of [4-Cl-pyH]+[BARF4]− (4.89 mg, 5.0 μmol, 5.0 equiv) in CD2Cl2 (~0.5 mL) was then added from a 1.7 mL vial. Further CD2Cl2 (~0.15 mL) was added to the vial and this solution was again added to the NMR tube to ensure complete transfer of [4-Cl-pyH]+[BARF4]−. A small amount of additional CD2Cl2 (~0.05 mL) was then used to rinse the upper interior of the NMR tube. The volume in the NMR tube was again re-adjusted to the reference 0.50 mL mark as described, and the 1H and 31P{1H} NMR spectra were acquired. The process of sequentially adding t-BuN=P(NMe2)3 and [4-Cl-pyH]+[BARF4]− (and each time recording the 1H and 31P{1H} NMR spectra) was repeated three more times as described.
Figure S40 – (a) $^{31}$P{¹H} NMR spectrum of ‘free’ Bu₃PO (162 MHz, 2.0 mM, CD₂Cl₂). (b) $^{31}$P{¹H} NMR spectrum of a mixture of Bu₃PO (2.0 mM) and 7 (5 equiv, 10 mM) (162 MHz, CD₂Cl₂) and (c) after addition of $t$-BuN=P(NMe₂)₃ (5 equiv) to the same sample, generating a mixture of Bu₃PO (2.0 mM) and $[t$-BuHN=P(NMe₂)₃]+·7⁻ (10 mM) and (d) after addition of [4-Cl-pyH⁺]⁺·[BArF₄]⁻ (5 equiv) to the same sample, generating a mixture of Bu₃PO (2.0 mM), 7 (10 mM), $[t$-BuHN=P(NMe₂)₃]+·[BArF₄]⁻ (10 mM) and 4-Cl-py (10 mM). (e)–(j) $^{31}$P{¹H} NMR spectra from further cycles of deprotonation (of 7) with $t$-BuN=P(NMe₂)₃ and re-protonation (of 7) with [4-Cl-pyH⁺]⁺·[BArF₄]⁻. Where both $[t$-BuHN=P(NMe₂)₃]+·7⁻ and $[t$-BuHN=P(NMe₂)₃]+·[BArF₄]⁻ are present in (e), only a single signal is observed for $[t$-BuHN=P(NMe₂)₃]+. Note that this Figure is an expansion of Figure 5 in the manuscript.
Figure S41 – (a) Accompanying $^1$H NMR spectrum of a mixture of Bu$_3$PO (2.0 mM) and 7 (5 equiv, 10 mM) (400 MHz, CD$_2$Cl$_2$) and (b) after addition of $t$-BuN=P(NMe$_2$)$_3$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (2.0 mM) and $[t$-BuHN$=P$(NMe$_2$)$_3]$∙7$^-$ (10 mM) and (c) after addition of [4-Cl-pyH]$^+$$[\text{BArF}_4]^-$ (5 equiv) to the same sample, generating a mixture of Bu$_3$PO (2.0 mM), 7 (10 mM), $[t$-BuHN$=P$(NMe$_2$)$_3]$∙$[\text{BArF}_4]^-$ (10 mM) and 4-Cl-py (10 mM). (d)–(i) $^1$H NMR spectra from further cycles of deprotonation (of 7) with $t$-BuN=P(NMe$_2$)$_3$ and re-protonation (of 7) with [4-Cl-pyH]$^+$$[\text{BArF}_4]^-$]. The formation of 7$^-$ in (b),(d),(f),(h) is indicated by the loss of the thiourea proton signal at $\delta_H = 10.77$ ppm. The formation of 7 in (c),(e),(g),(i) is indicated by the reappearance of the thiourea proton signal. (All spectra also contain signals in the aromatic region arising from the Ph$_3$PO external standard.)
NMR Spectra of Novel Compounds

Figure S42 – $^1$H NMR spectrum of 1-1 (500 MHz, CDCl$_3$).

Figure S43 – $^{13}$C NMR spectrum of 1-1 (126 MHz, CDCl$_3$).
Figure S44 – $^1$H NMR spectrum of 1-2 (500 MHz, CDCl$_3$).

Figure S45 – $^{13}$C NMR spectrum of 1-2 (126 MHz, CDCl$_3$).
Figure S46 – $^1$H NMR spectrum of 1-3 (500 MHz, CDCl$_3$).

Figure S47 – $^{13}$C NMR spectrum of 1-3 (126 MHz, CDCl$_3$).
Figure S48 – $^1$H NMR spectrum of 1 (500 MHz, CD$_2$Cl$_2$).

Figure S49 – $^{13}$C NMR spectrum of 1 (126 MHz, CD$_2$Cl$_2$).
Figure S50 – $^1$H NMR spectrum of 2 (500 MHz, CD$_2$Cl$_2$).

Figure S51 – $^{13}$C NMR spectrum of 2 (126 MHz, CD$_2$Cl$_2$).
Figure S52 – $^1$H NMR spectrum of 4-1 (400 MHz, CDCl$_3$).

Figure S53 – $^{13}$C NMR spectrum of 4-1 (101 MHz, CDCl$_3$).
Figure S54 – $^1$H NMR spectrum of 4 (500 MHz, CD$_2$Cl$_2$).

Figure S55 – $^{13}$C NMR spectrum of 4 (126 MHz, CD$_2$Cl$_2$).
Figure S56 – $^1$H NMR spectrum of 5-1 (500 MHz, CDCl$_3$).

Figure S57 – $^{13}$C NMR spectrum of 5-1 (126 MHz, CDCl$_3$).
Figure S58 – $^1$H NMR spectrum of 5 (500 MHz, CD$_2$Cl$_2$).

Figure S59 – $^{13}$C NMR spectrum of 5 (126 MHz, CD$_2$Cl$_2$).
Figure S60 – $^1$H NMR spectrum of 6-1 (500 MHz, CDCl$_3$).

Figure S61 – $^{13}$C NMR spectrum of 6-1 (126 MHz, CDCl$_3$).
Figure S62 – $^1$H NMR spectrum of 6-2 (500 MHz, CDCl$_3$).

Figure S63 – $^{13}$C NMR spectrum of 6-2 (126 MHz, CDCl$_3$).
Figure S64 – $^1$H NMR spectrum of 6 (500 MHz, CD$_2$Cl$_2$).

Figure S65 – $^{13}$C NMR spectrum of 6 (126 MHz, CD$_2$Cl$_2$).
Figure S66 – $^1$H NMR spectrum of 7-2 (500 MHz, CDCl$_3$).

Figure S67 – $^{13}$C NMR spectrum of 7-2 (126 MHz, CDCl$_3$).
Figure S68 – $^1$H NMR spectrum of 7-3 (500 MHz, CDCl$_3$).

Figure S69 – $^{13}$C NMR spectrum of 7-3 (126 MHz, CDCl$_3$).
Figure S70 – $^1$H NMR spectrum of 7-4 (500 MHz, CD$_2$Cl$_2$).
Figure S72 – $^1$H NMR spectrum of 7 (500 MHz, CD$_2$Cl$_2$).

Figure S73 – $^{13}$C NMR spectrum of 7 (126 MHz, CD$_2$Cl$_2$).
Figure S74 – $^1$H NMR spectrum of S8 (500 MHz, CD$_2$Cl$_2$).

Figure S75 – $^{13}$C NMR spectrum of S8 (126 MHz, CD$_2$Cl$_2$).
Figure S76 – $^1$H NMR spectrum of S9 (500 MHz, CD$_2$Cl$_2$).
Figure S78 – $^1$H NMR spectrum of S10 (500 MHz, CD$_2$Cl$_2$).

Figure S79 – $^{13}$C NMR spectrum of S10 (126 MHz, CD$_2$Cl$_2$).
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