Electronic Supplementary Information

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Methods

Photoirradiation

LEDs were used for AAP photoisomerization. *E*- to *Z*- isomerization was performed using a UV 1 W LED with an emission maximum at λ = 365 nm (*LedEngin*) and a green 3.8 W LED with an emission maximum at λ = 520 nm (*LedEngin*) was used for *Z*- to *E*- isomerization.

CD Spectroscopy

CD measurements were performed on a *J-815* circular dichroism spectrometer (*JASCO*) using a quartz glass cuvette (*Hellma*) with a light path of 2 mm. The device was operated using *Spectra Manager Version 2* (*JASCO*) and spectra were exported using *Spectra Analysis* version 2.15.09 (*JASCO*).

All samples and titrations were made from stock solutions of **bAAP** (1 mM), **Me-β-CD** (10 mM) and Fructose (100 mM) in phosphate buffer (pH 8.00, 100 mM). Duration of the photo irradiation was 5 min.

Isothermal Titration Calorimetry

ITC was performed on a *Nano ITC* low volume titration calorimeter (*TA Instruments*) with a cell volume of 170 µL. The program used 20 injections of 2.5 µL each in an interval of 2.5 min and a stirring rate of 350 rpm. The device was operated using ITCRun version 2.1.7.0 (*TA Instruments*). For each experiment a correction for the dilution was measured by titrating the titrant to pure solvent. For initial analysis of the heat rates *NanoAnalyze* version 3.8.0 (*TA Instruments*) was used. Data fits and thermodynamic data was obtained using a numerical approximation developed by JURRIAAN HUSKENS.

All ITC-measurements were done accordingly to the stock solutions given in the caption. Solutions containing **bAAP** were photo-irradiated for 10 min using UV or green light.

UV/Vis Spectroscopy

UV/Vis measurements were performed on a *V-770* or *V-650* double-beam photospectrometer (*JASCO*) at 25 °C using semi-micro PMMA (*BRAND*) with a light path of 10 mm. The device was operated using *Spectra Manager Version 2* (*JASCO*) and spectra were exported using *Spectragryph* version 1.2.13 (FRIEDRICH MENGES).

Photophysical Properties of bAAP

Photo Stationary State (PSS)

For determination of the PSS of **bAAP** a stock solution (500 µM) in pure D_2O was split into two samples. One sample was irradiated for 10 min with UV light. The sample was kept 5 min at room temperature and irradiated again for 3 min to compensate for photoinduced heating. The other sample was irradiated for 10 min with green light. Both samples were measured immediately after photo irradiation on a 500 MHz spectrometer.

Half-Life Time

For half-life time measurement, a UV/vis spectrum of a sample of **bAAP** (100 µM) in phosphate buffer (pH 8.00, 100 mM) was measured without irradiation, in order to get a baseline value for the thermal back isomerization. Afterwards the sample was irradiated with UV light and measured again. The sample was kept in the dark and was measured periodically until back isomerization was confirmed to be more than 50 %.

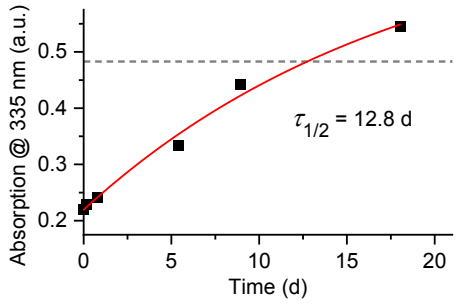


Fig. S1 Determination of the half-life time of *Z*-**bAAP** by UV/vis measurements.

Photoswitching

For photoswitching experiments, a spectrum of a dilute solution of **bAAP** in phosphate buffer (pH 8.00, 100 mM) was measured without initial irradiation. Then the same sample was irradiated for 10 min and subsequently measured alternating the photoirradiation between UV and green light.

Model Calculations

Concentrations were approximated in a numerical approach using the Solver Add-In in Microsoft Excel (as part of Office 365). The model was simplified by the assumption that the concentration of unbound **bAAP** is negligible in the presence of excess fructose and **Me-β-CD** (formular 1). Starting concentrations and equilibrium constants were known inputs, while concentrations after equilibration were calculated using formula 3 to 6. Formula 4 was derived from 2 and 3. **[F]** was varied by the Solver Add-In with the condition to minimize the error (formula 1).

Concentrations of **Me-ß-CD**, **bAAP**, D-fructose, the host guest complex and the boronic ester are **[CD]**, **[bAAP]**, **[F]**, **[bAAP-CD]** and **[bAAP-F]** respectively. $[X]_{total}$ is the total concentration of *X* including bound and species. K_{total} is the equilibrium constant of the reaction in formula 7. $K_{d.CD}$ is the dissociation constant of the host guest complex. $K_{a.CD}$ and $K_{a.fruc}$ are the association constants of the host guest complex and the boronic ester respectively.

$$[bAAP]_{total.} = [bAAP\text{-}F] + [bAAP\text{-}CD] \quad [1]$$

$$K_{total} = \frac{[CD][bAAP\text{-}F]}{[F][bAAP\text{-}CD]} = K_{d.CD} * K_{a.fruc} = \frac{K_{a.fruc}}{K_{a.CD}} \quad [2]$$

$$[CD] = [CD]_{total} - [bAAP\text{-}CD] \quad [3]$$

$$[bAAP\text{-}CD] = \frac{[CD]_{total}}{1 + (K_{total} * [F]/[bAAP\text{-}F])} \quad [4]$$

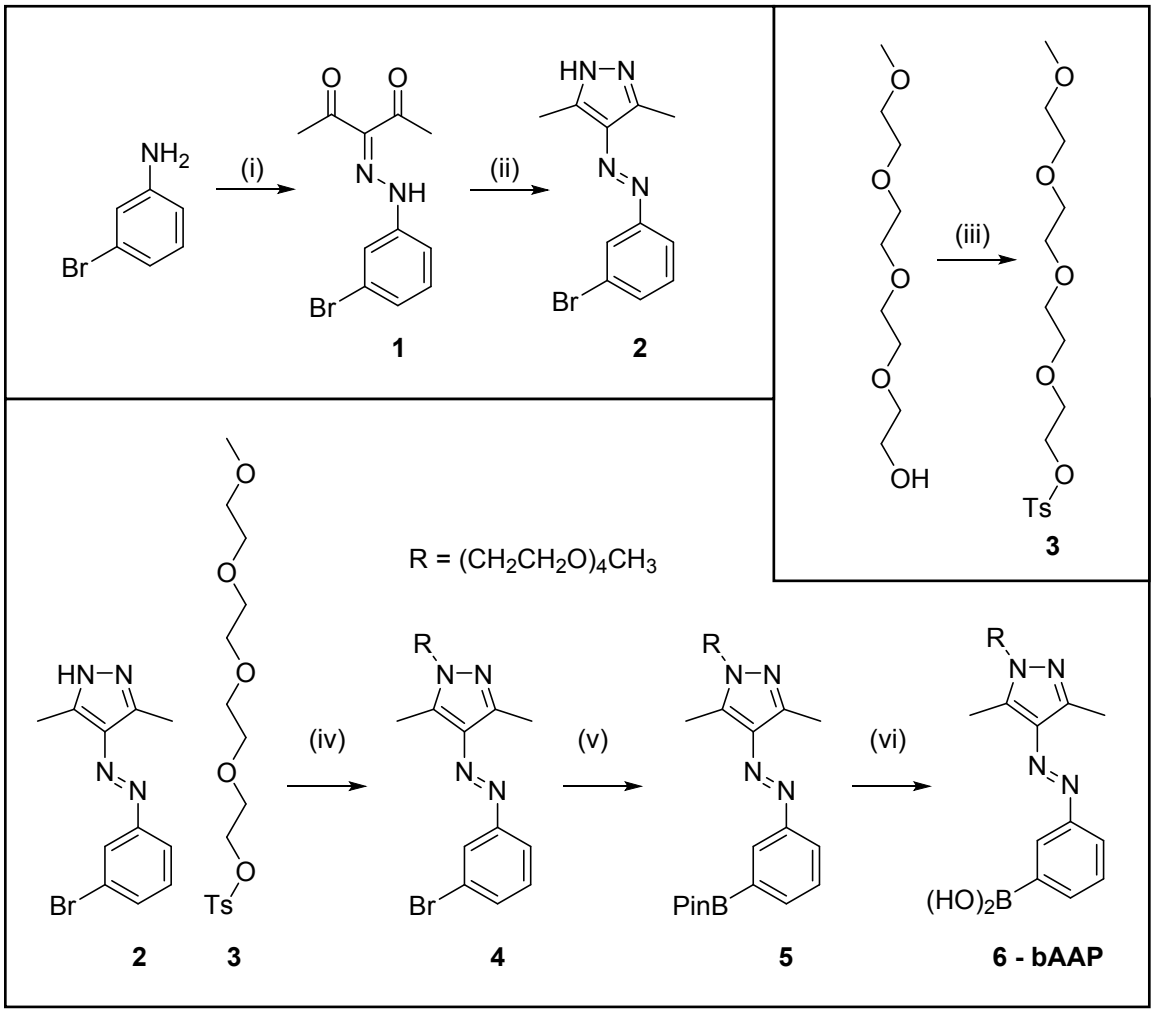
$$[bAAP\text{-}F] = [bAAP]_{total} - [bAAP\text{-}CD] \quad [5]$$

$$Error = [F]_{total} + [CD]_{total} - [bAAP\text{-}CD] - [F] - [bAAP\text{-}F] - [CD] \quad [6]$$

$$[bAAP\text{-}CD][F] \rightleftharpoons [bAAP\text{-}F][CD] \quad [7]$$

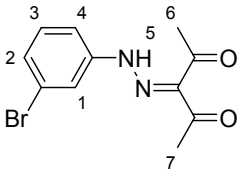
Synthesis

Overview of the Synthesis of bAAP



Scheme S1 (i) a) $NaNO_2$, H_2O, AcOH, HCl pentane-2,4-dione, 0 °C, 45 min, b) NaOAc, EtOH, 0 °C->r.t., 60 min **(ii)** N_2H_4 x $(H_2O)_x$, ErOH, reflux, 2 h **(iii)** TsCl, NaOH, THF, H_2O, 0 °C->r.t., 30 min **(iv)** K_2CO_3, LiBr, dry ACN, reflux, 2 d **(v)** B_2Pin_2, KAc, $[PdCl_2(dppf)]Cl_2$, dry dioxane, 90 °C, 18 h, **(vi)** H_2O/ACN (1:1), 2 h.

3-(2-(3-bromophenyl)hydrazineylidene)pentane-2,4-dione (1)



A concentrated solution of $NaNO_2$ (166 mg, 2.4 mmol. 1.2 eq.) in water was added dropwise to a solution of 3-bromoaniline (217 µL, 2 mmol, 1 eq.) in AcOH (3 mL) and conc. HCl (460 µL) at 0 °C and stirred for 45 min. The reaction mixture was transferred to a solution of pentane-2,4-dione (267 µL, 2.6 mmol, 1.3 eq.) and NaOAc (492 mg, 6 mmol, 3 eq.) in EtOH (2 mL) and water (1.2 mL) and was stirred for 1 h at room temperature. The yellow solid was collected by filtration and washed with EtOH/water (1:1). The crude product was filtered and dried *in vacuo*.

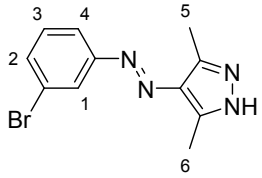
Yield: 530 mg (1.87 mmol, 94 %).

HR-MS: ESI-TOF: $[M+Na]^+$: *m*/z = 304.9897 (calc. *m*/*z* = 304.9902).

^{1}H-NMR: (400 MHz, $CDCl_3$) δ = 14.52 (s, 1H, 5-N*H*), 7.52 (t, *J* = 2.0 Hz, 1H, 1-C*H*), 7.27 – 7.18 (m, 3H, 2-/3-/4-C*H*), 2.53 (d, *J* = 1.7 Hz, 3H, 6-CH_3), 2.42 (d, *J* = 1.7 Hz, 3H, 7-CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$) δ = 198.4, 197.1, 143.0, 133.9, 131.1, 128.7, 123.7, 119.2, 115.1, 31.9, 26.8.

(*E*)-4-((3-bromophenyl)diazenyl)-3,5-dimethyl-1H-pyrazole (2)



A solution of 3-(2-(3-bromophenyl)hydrazineylidene)pentane-2,4-dione **1** (506 mg, 1.79 mmol, 1 eq.) and Hydrazine-x-hydrate (70 µL, 1.79 mmol, 1 eq.) in EtOH (100 mL) was refluxed for 3 h. Drying *in vacuo* gave the product **2** as an orange solid.

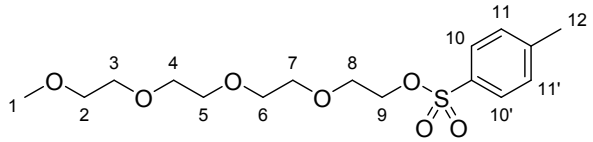
Yield: 485 mg (1.74 mmol, 97 %).

HR-MS: ESI-TOF: $[M+H]^+$: *m*/z = 279.0240 (calc. *m*/*z* = 279.0253).

^{1}H-NMR: (400 MHz, $CDCl_3$) δ = 7.92 (q, *J* = 1.8, 1H, 1-C*H*), 7.73 (ddd, *J* = 8.1 Hz, 2.1, 1.1, 1H, 4-C*H*), 7.50 (ddt, *J* = 7.9, 2.1, 1.1 Hz, 1H, 2-C*H*), 7.34 (td, *J* = 7.9, 1.4 Hz, 1H, 3-C*H*), 2.60 (2S, *J* = 1.3 Hz, 6H, 5-/6-CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$) δ = 154.5, 141.9, 134.7, 132.1, 130.3, 123.8, 123.0, 121.8, 12.2.

2,5,8,11-tetraoxatridecan-13-yl 4-methylbenzenesulfonate (3)



The procedure was adapted from literature.[1] Under argon, a solution of tetraethyleneglycol monomethylether (2.00 g, 9.6 mmol, 1 eq.) in THF (2.8 mL) was treated with a solution of NaOH (704 mg, 17.6 mmol, 1.83 eq.) in water (2.4 mL) at 0 °C. After stirring for 15 min, a solution of tosly chloride (1.83 g, 9.6 mmol, 1 eq.) in THF (4 mL) was added dropwise at 0 °C. Stirring was continued at room temperature for 30 min. The solvent was removed *in vacuo*. The crude product was dissolved in water and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and the solvent was removed *in vacuo* to yield the raw product **3** as pale yellow oil, which was used without further purification.

Yield: 3.08 g (8.49 mmol, 88 %).

HR-MS: ESI-TOF: $[M+Na]^+$: *m*/z = 385.1286 (calc. *m*/*z* = 385.1291).

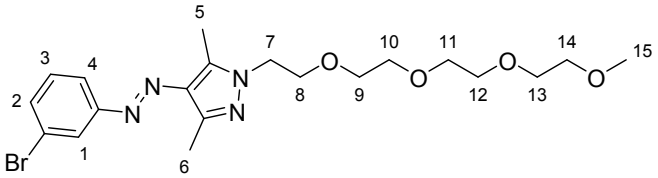
^{1}H-NMR: (400 MHz, $CDCl_3$) δ = 7.78 (dt, *J* = 8.5, 1.9 Hz, 2H, 11-/11'-C*H*), 7.33 (d, *J* = 8.0 Hz, 2H, 10-/11-C*H*), 4.16 – 4.11 (m, 2H, 9-CH_2), 3.69 – 3.64 (m, 2H, 2-CH_2), 3.63 –

[1] M. D. Tzirakis, M. N. Alberti, H. Weissman, B. Rybtchinski and F. Diederich, *Chem. Eur. J.*, **2014**, *20*, 16070–16073.

3.59 (m, 6H, 3- to 8-CH_2), 3.56 (d, *J* = 1.6 Hz, 4H, 3- to 8-CH_2), 3.54 – 3.50 (m, 2H, 3- to 8-CH_2), 3.35 (d, *J* = 1.6 Hz, 3H, 1-CH_3), 2.43 (s, 3H, 12-CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$) δ = 144.9, 133.1, 129.9, 128.1, 72.0, 70.8, 70.7, 70.7, 70.6, 69.3, 68.8, 59.1, 21.7.

4-((3-bromophenyl)diazenyl)-3,5-dimethyl-1-(2,5,8,11-tetraoxatridecan-13-yl)-1*H*-pyrazole (4)



(*E*)-4-((3-bromophenyl)diazenyl)-3,5-dimethyl-1H-pyrazole **VI-2** (297 mg, 1 mmol, 1 eq.) was dissolved in dry ACN (10 mL). K_2CO_3 (415 mg), LiBr (cat.) and 2,5,8,11-tetraoxatridecan-13-yl 4-methylbenzenesulfonate **3** were added. The heterogeneous mixture was refluxed for 2 d. Afterwards the solvent was removed under reduced pressure, the resulting residue was dissolved in EtOAc /H2O (1:1) and the layers were separated. The aqueous layer was extracted once with EtOAc, the combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The crude product **4** was purified by automated flash chromatography.

Time (min)	0	6	7	10	10.5	15.5
DCM (%)	99	96	94	94	90	90
MeOH (%)	1	4	6	6	10	10
Büchi Ecoflex 12 g silica column, 30 mL/min						

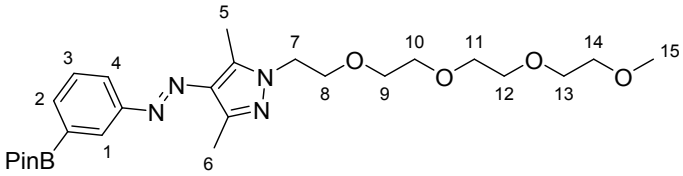
Yield: 484 mg (1.03 mmol, quant.).

HR-MS: ESI-TOF: $[M+Na]^+$: *m*/z = 491.1268 (calc. *m*/*z* = 491.1270).

^{1}H-NMR: (400 MHz, $CDCl_3$) *δ* =z 7.89 (q, *J* = 1.7 Hz, 1H, 1-C*H*), 7.71 (dd, *J* = 7.8, 1.8 Hz, 1H, 4-C*H*), 7.46 (dd, *J* = 8.1, 1.9 Hz, 1H, 2-C*H*), 7.35 – 7.28 (m, 1H, 3-C*H*), 4.21 (t, *J* = 5.3 Hz, 2H, 7-CH_2), 3.86 (d, *J* = 5.5 Hz, 2H, 8-CH_2), 3.70 – 3.47 (m, 12H, 9- to 14-CH_2), 3.34 (d, *J* = 1.3 Hz, 3H, 15-CH_3), 2.61 (d, *J* = 1.3 Hz, 3H, 5- or 6-CH_3), 2.47 (d, *J* = 1.2 Hz, 3H, 5- or 6-CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$) *δ* = 154.7, 142.7, 141.4, 135.1, 131.9, 130.4, 129.9, 128.1, 123.7, 123.1, 121.9, 72.0, 70.9, 70.7, 70.7, 70.6, 70.0, 59.1, 49.3, 14.3, 10.1.

3,5-dimethyl-4-((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)diazenyl)-1-(2,5,8,11-tetraoxatridecan-13-yl)-1H-pyrazole (5)



(*E*)-4-((3-bromophenyl)diazenyl)-3,5-dimethyl-1-(2,5,8,11-tetraoxatridecan-13-yl)-1H-pyrazole **4** (300 mg, 639 µmol, 1 eq.) and bis(pinacolato)diboron (244 mg, 959 µmol, 1.5 eq.) were dissolved in dry dioxane (10 mL) under argon. $[PdCl_2(dppf)]Cl_2$ (14 mg, 19 µmol, 3 mol%) and potassium acetate (118 mg, 1.92 mmol, 3 eq.) were added and the reaction mixture was stirred at 90 °C for 18 h. The

mixture was allowed to cool to room temperature, the volatiles were removed *in vacuo*, and the residue was purified by automated flash chromatography (DCM/MeOH – 100:4, R_f = 0.34) to obtain the boronic ester **5** as an orange solid.

Time (min)	0	1	16
DCM (%)	98	98	85
MeOH (%)	2	2	15
Büchi Ecoflex 12 g silica column, 30 mL/min			

Yield: 314 mg (609 µmol, 95 %).

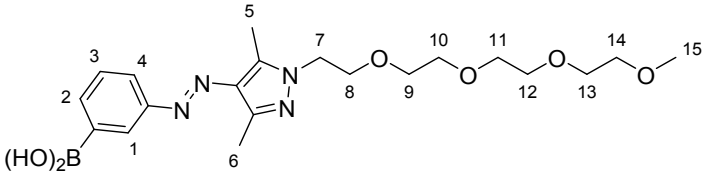
HR-MS: ESI-TOF: $[M+H]^+$: *m*/z = 517.3204 (calc. *m*/*z* = 517.3192).

$[M+Na]^+$: *m*/z = 539.3044 (calc. *m*/*z* = 539.3017).

^{1}H-NMR: (300 MHz, $CDCl_3$) δ = 8.20 (t, *J* = 1.6 Hz, 1H, 1-C*H*), 7.88 – 7.76 (m, 2H, 2-/4-C*H*), 7.44 (t, *J* = 7.6 Hz, 1H, 3-C*H*), 4.23 – 4.17 (m, 2H, 7-CH_2), 3.85 (t, *J* = 5.3 Hz, 2H, 8-CH_2), 3.68 – 3.48 (m, 12H, 9- to 14-CH_2), 3.34 (s, 3H, 15-CH_3), 2.62 (s, 3H, 5- or 6-CH_3), 2.49 (s, 3H, 5- or 6-CH_3), 1.37 (s, 12H, Pin-CH_3).

^{13}C-NMR**:** (75 MHz, $CDCl_3$) δ = 153.1, 142.6, 140.6, 135.8, 135.1, 129.8, 128.5, 122.9, 84.1, 72.0, 70.9, 70.7, 70.7, 70.6, 70.1, 59.1, 49.2, 25.1, 25.0, 24.7, 14.3, 10.1.

(3-((3,5-dimethyl-1-(2,5,8,11-tetraoxatridecan-13-yl)-1H-pyrazol-4-yl)diazenyl)phenyl)boronic acid (6 - bAAP)



AAP **5** (291 mg, 564 µmol) was dissolved in H_2O/ACN (1:1, 20 mL) and stirred at 40 °C for 2 h. The mixture was dried *in vacuo* at 60 °C. This procedure was repeated two times. The raw product was purified by reverse phase flash chromatography. The pure product **6** is obtained as an orange oil, that slowly transitions to an amorphous solid over several days.

Time (min)	0	15	17	21
Water (%)	60	40	20	20
ACN (%)	40	60	80	80
Büchi Select C18 12 g column, 30 mL/min				

Yield: 124 mg (284 µmol, 50 %).

HR-MS: ESI-TOF: $[M+H]^+$: *m*/z = 435.24000 (calc. *m*/*z* = 435.24131).

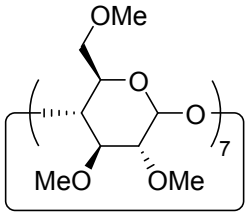
$[M+Na]^+$: *m*/z = 457.22196 (calc. *m*/*z* = 457.22326).

^{1}H-NMR: (300 MHz, $CDCl_3$) δ = 8.71 (s, 2H, B(O*H*)$_2$), 8.64 (s, 1H, 1-Ar*H**), 8.31 (d, *J* = 7.2 Hz, 1H, 4-Ar*H**), 8.18 (s, 1H, 1-Ar*H**), 8.00 (d, *J* = 7.9 Hz, 1H, 2-Ar*H**), 7.89 – 7.77 (m, 2H, 4-/2-Ar*H**), 7.63 (t, *J* = 7.6 Hz, 1H, 3-Ar*H**), 7.45 (t, *J* = 7.8 Hz, 1H, 1H, 3-Ar*H**), 4.32 (s, 2H, 7-CH_2), 3.85 (d, *J* = 11.6 Hz, 2H, 8-CH_2), 3.69 – 3.45 (m, 12H,

9- to 14-CH_2), 3.34 (d, *J* = 2.1 Hz, 3H, 15-CH_2), 2.73 – 2.50 (m, 6H, 5-/6-CH_3). *Two signal sets due to *E*-/*Z*-Isomerization. Integrals add up to 1 for each proton.

^{13}C-NMR: (101 MHz, $CDCl_3$) δ = 152.9, 142.5, 140.6, 135.5, 134.9, 128.7, 128.4, 122.8, 71.8, 70.7, 70.5, 70.4, 70.4, 70.3, 69.8, 58.9, 48.9, 13.8, 10.0.

Permethylated β-cyclodextrin (7 – Me-β-CD)



Sodium hydride (60 %, 2.00 g, 50.0 mmol, 50 eq.) was slowly added to a solution of β-cyclodextrin (1.14 g, 1.0 mmol, 1 eq.) in DMSO (35 mL) and the solution was stirred for 1 h at room temperature. The mixture was cooled down to 0 °C, methyl iodide (3.1 mL, 50 mmol, 50 eq.) was added dropwise, and the solution was stirred overnight at room temperature. The reaction was quenched by addition of water (140 mL) at 0 °C. After extracting with diethyl ether, the combined organic phase was washed with brine. The solution was dried over $MgSO_4$ and the solvent was removed. The residue was purified by automated column chromatography. Residual DMSO was removed by freeze drying. **7** was obtained as a white solid. NMR spectra agree with literature data.[2]

Time (min)	0	3	13	16
DCM (%)	100	100	90	90
MeOH (%)	0	0	10	10
Büchi Ecoflex 40 g silica column, 30 mL/min				

Yield: 1.12 g (786 µmol, 79 %).

HR-MS: MALDI-TOF: $[M+Na]^+$: *m*/z = 1451.81 (calc. *m*/*z* = 1451.69).

$[M+K]^+$: *m*/z = 1467.80 (calc. *m*/*z* = 1467.66).

^{1}H-NMR: (300 MHz, $CDCl_3$) δ = 5.12 (d, *J* = 3.6 Hz, 7H, C*H*), 3.90 – 3.74 (m, 14H, C*H*), 3.64 (s, 21H, CH_3), 3.61 – 3.46 (m, 42H, C$H_{1/2/3}$), 3.37 (s, 21H, CH_3), 3.18 (dd, *J* = 9.6, 3.5 Hz, 7H, C*H*).

^{13}C-NMR: (75 MHz, $CDCl_3$) δ = 99.10, 82.19, 81.89, 80.43, 71.54, 71.06, 61.59, 59.10, 58.65.

[2] W. Keim, A. Köhnes, W. Meltzow and H. Römer, *J. High Resolut. Chromatogr.* **1991**, *14*, 507–529.

Additional Data

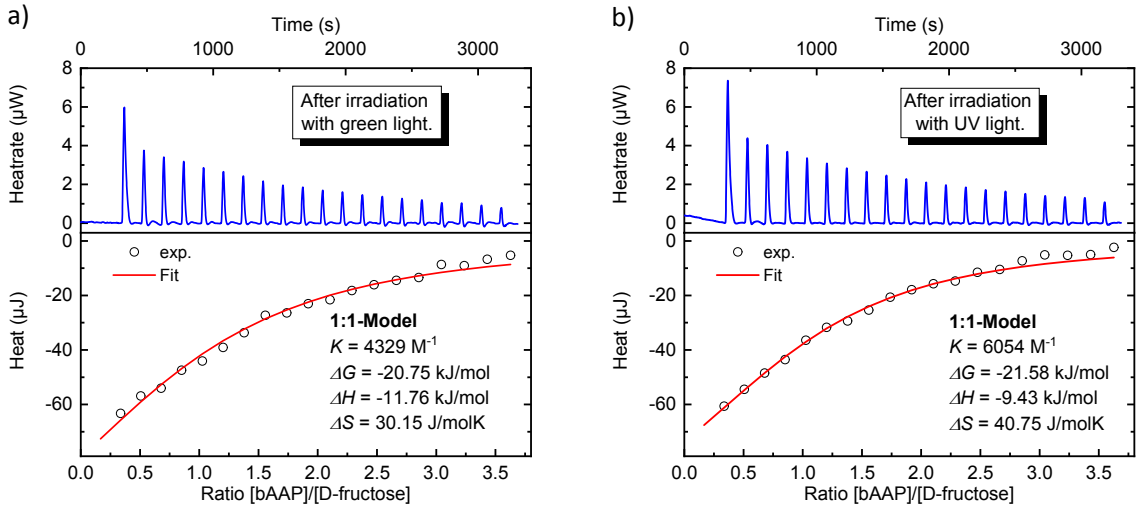


Fig. S2: ITC of bAAP (5 mM) to D-fructose (250 µM) in phosphate buffer (pH 8.00, 100 mM). a) After irradiation with green light and b) UV light at the respective PSS.

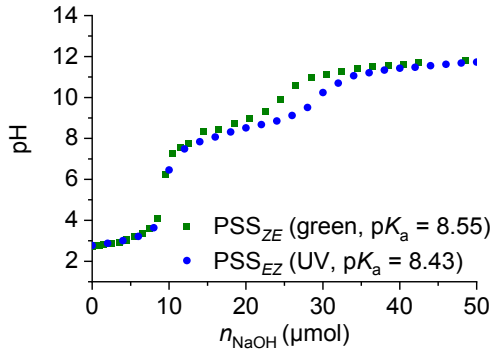


Fig. S3: pH-titration of NaOH (2 M) to **bAAP** (4 mM).

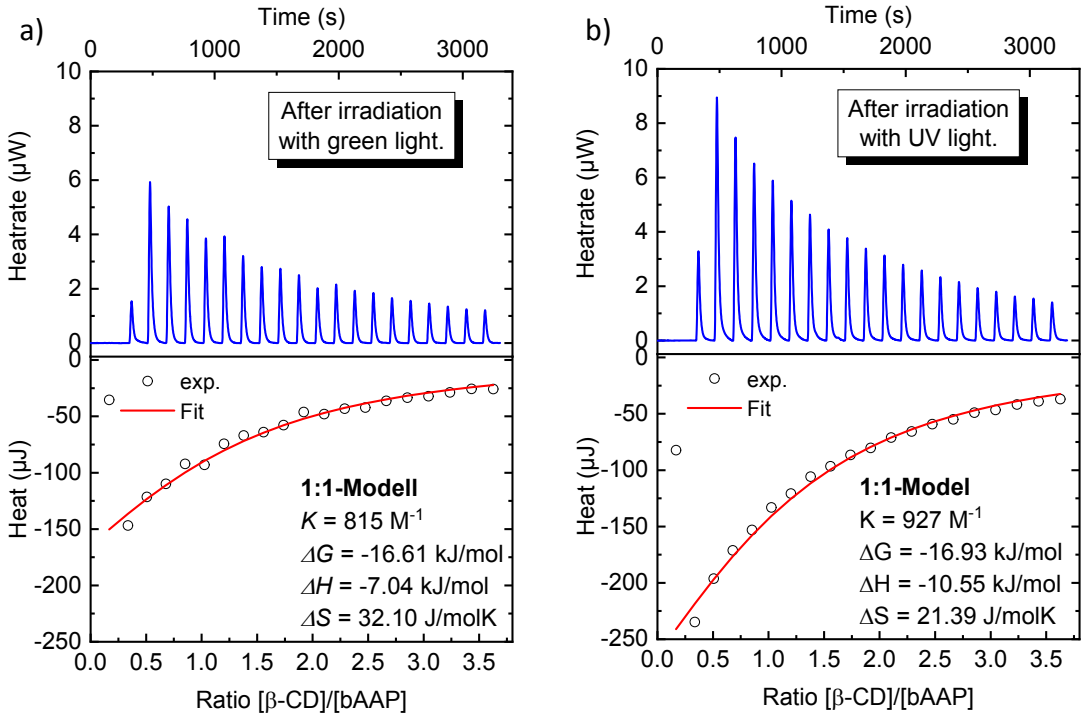


Fig. S4 ITC of β-CD (20 mM) to **bAAP** (1 µM) in phosphate buffer (pH 8.00, 100 mM). a) After irradiation with green light and b) UV light at the respective PSS.

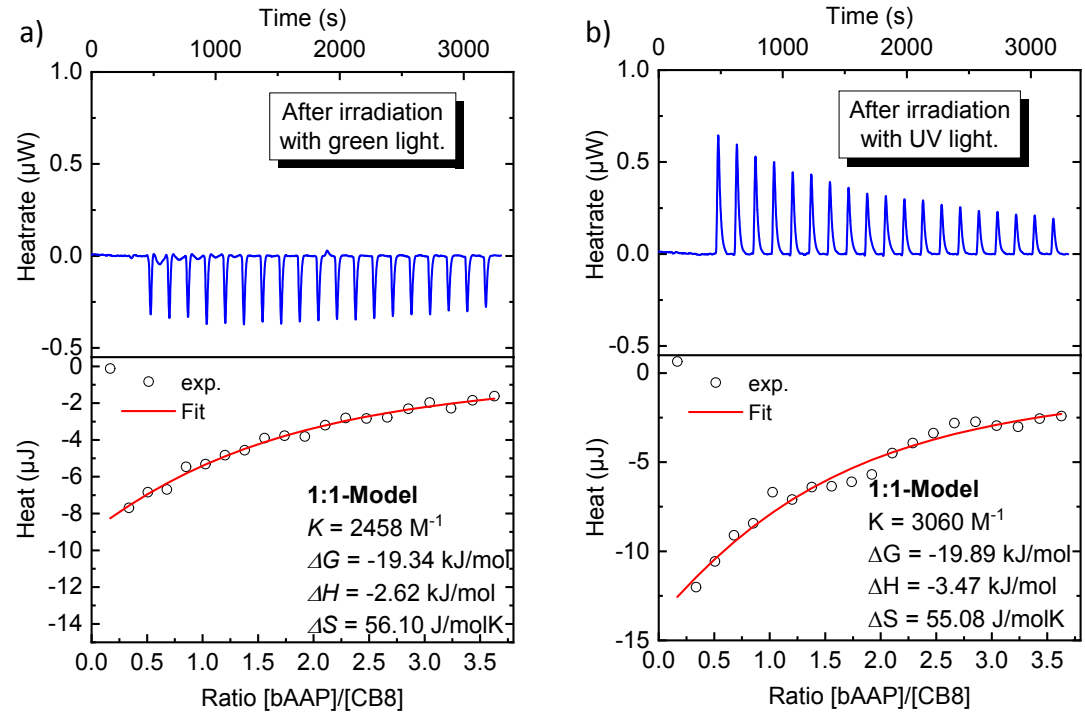


Fig. S5 ITC of **bAAP** (2 mM) to **CB[8]** (1 µM) in phosphate buffer (pH 8.00, 100 mM). a) After irradiation with green light and b) UV light at the respective PSS.

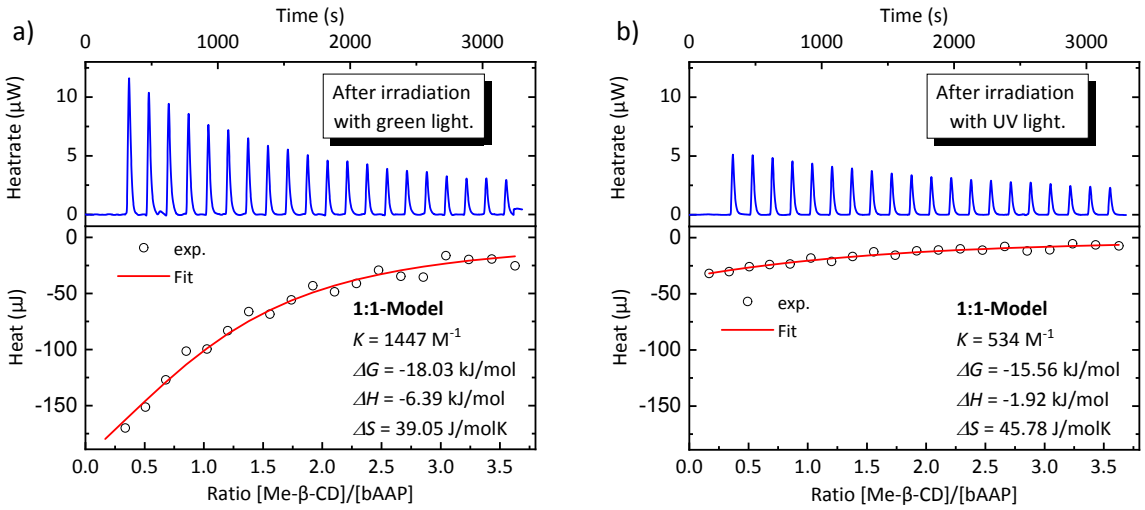


Fig. S6: ITC of Me-β-CD (20 mM) to bAAP (1 µM) in phosphate buffer (pH 8.00, 100 mM). a) After irradiation with green light and b) UV light at the respective PSS.

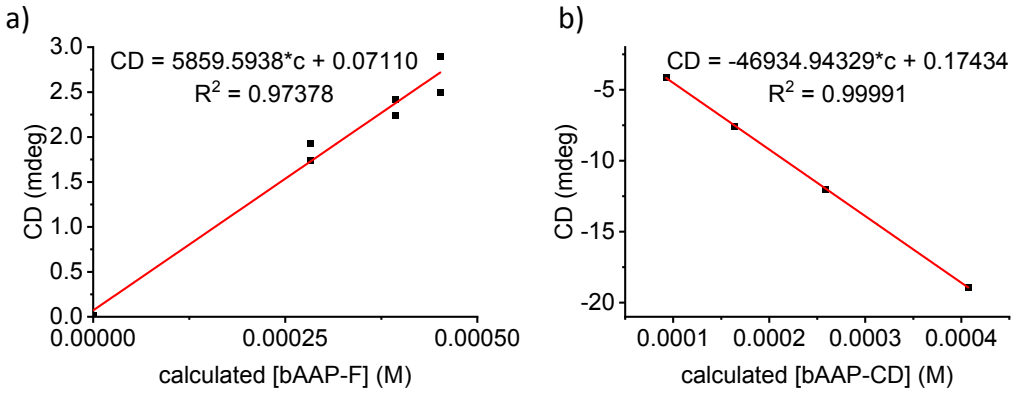


Fig. S7 Calibration for quantification of a) [bAAP-F] after UV irradiation and b) [bAAP-CD] after irradiation with green light.

NMR Spectra

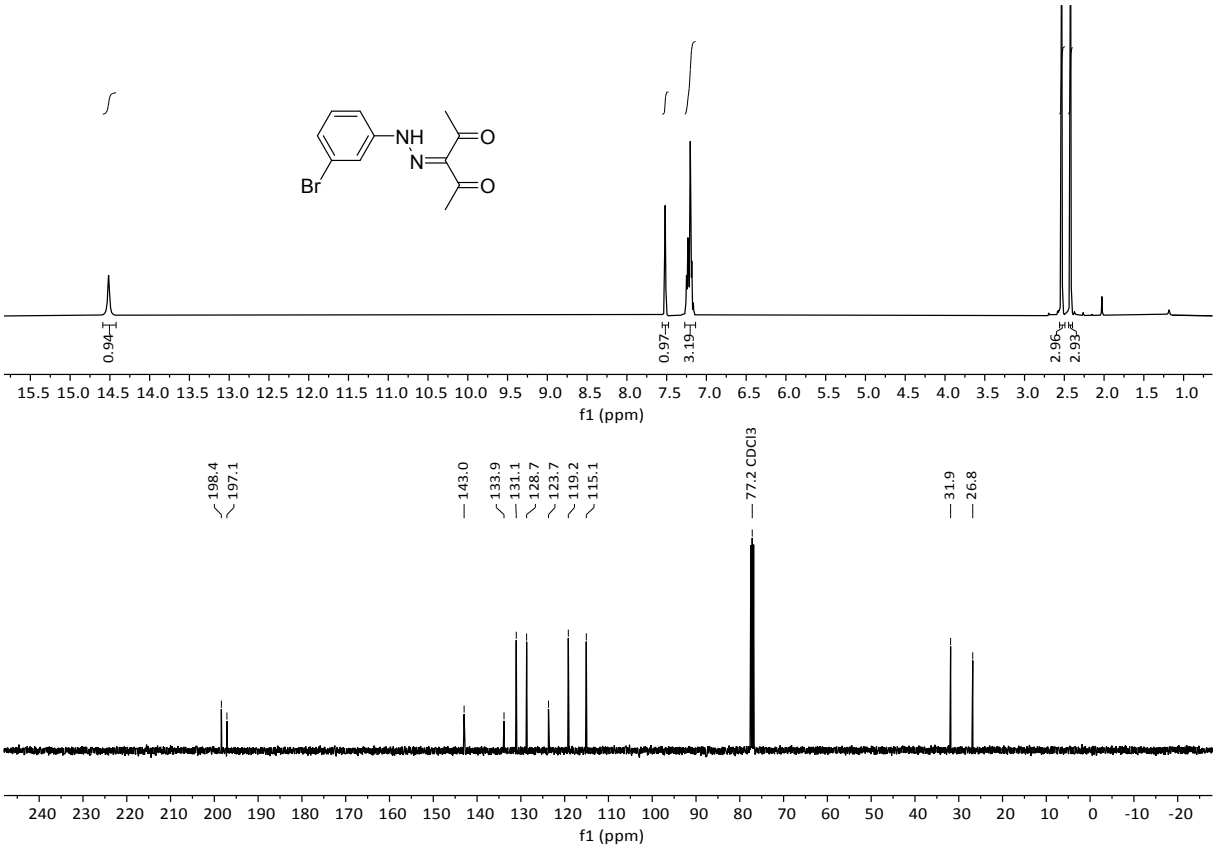


Fig. S8 - Top: ^{1}H-NMR, **Bottom:** ^{13}C-NMR of 3-(2-(3-bromophenyl)hydrazineylidene)pentane-2,4-dione (**1**).

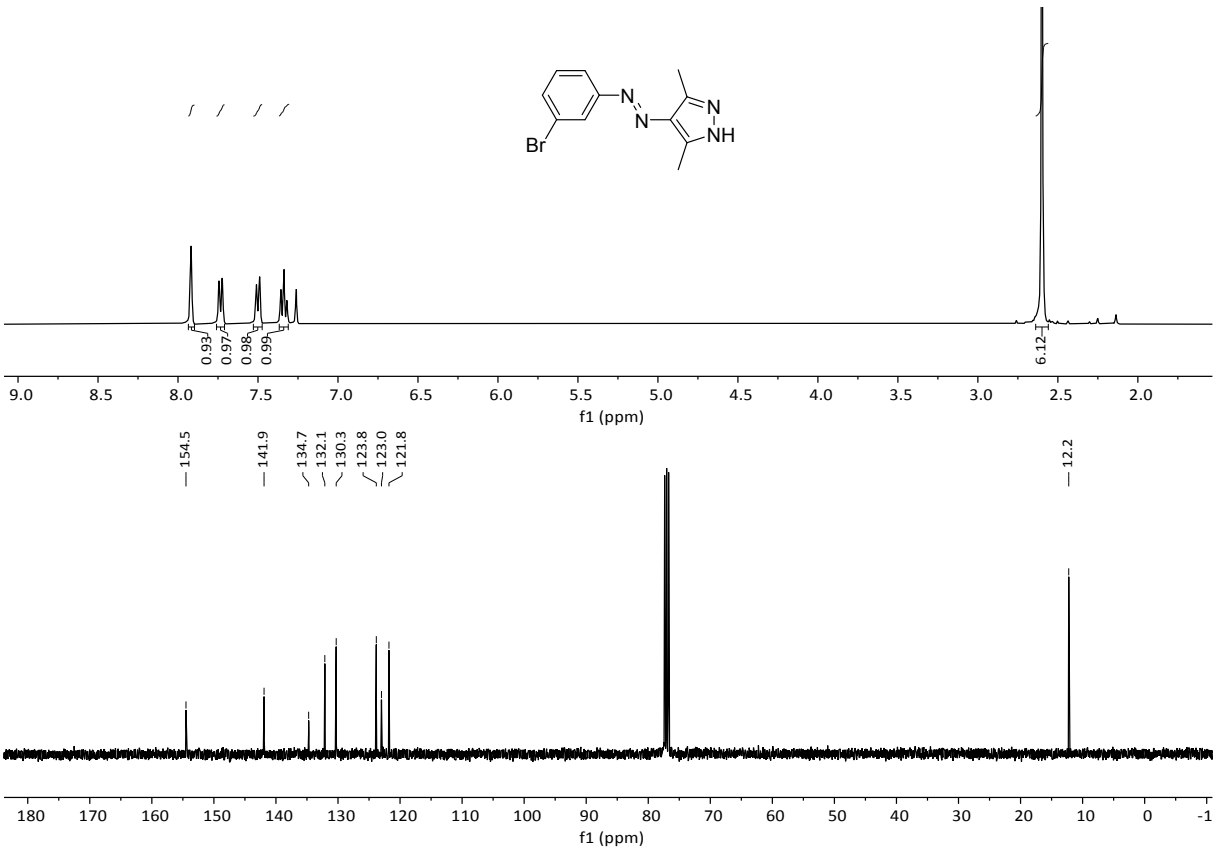


Fig. S9 -: ^{1}H-NMR, **Bottom:** ^{13}C-NMR of 4-((3-bromophenyl)diazenyl)-3,5-dimethyl-1H-pyrazole (**2**).

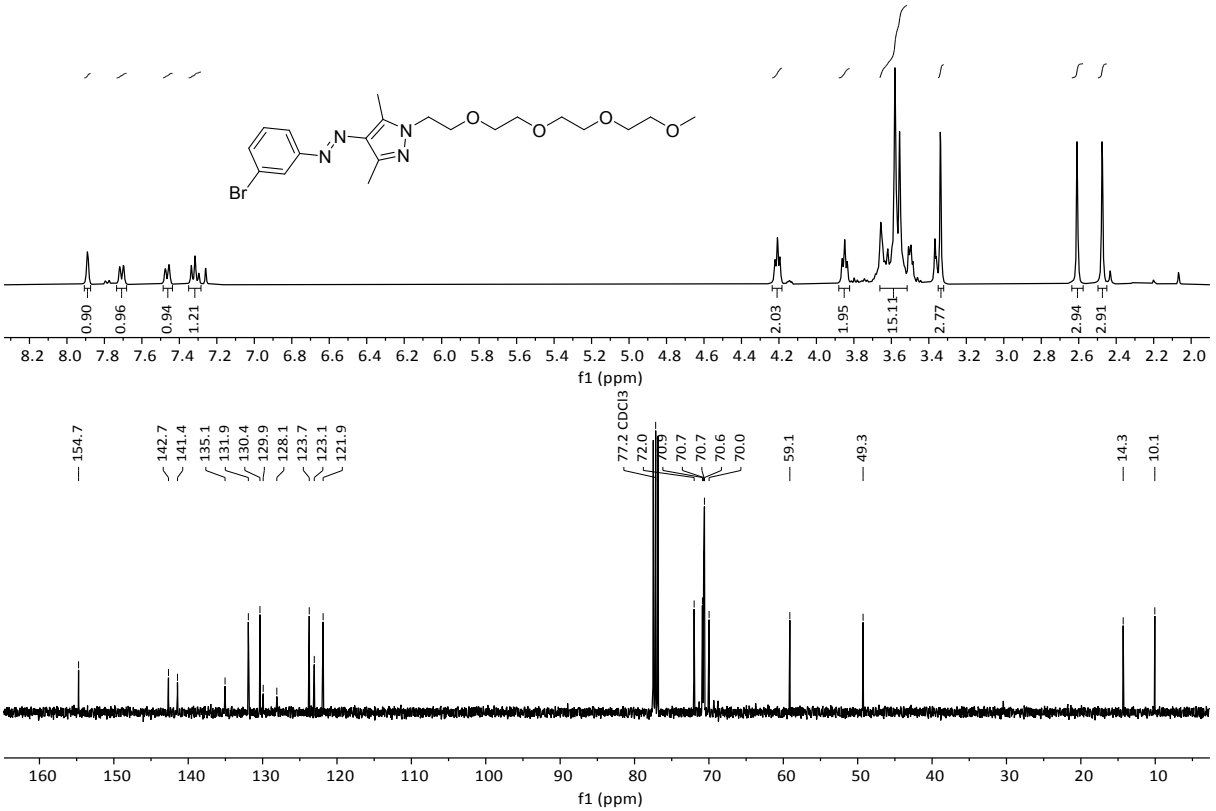


Fig. S10 – Top: ^{1}H-NMR, **Bottom:** ^{13}C-NMR of 4-((3-bromophenyl)diazenyl)-3,5-dimethyl-1-(2,5,8,11-tetraoxatridecan-13-yl)-1*H*-pyrazole (**4**).

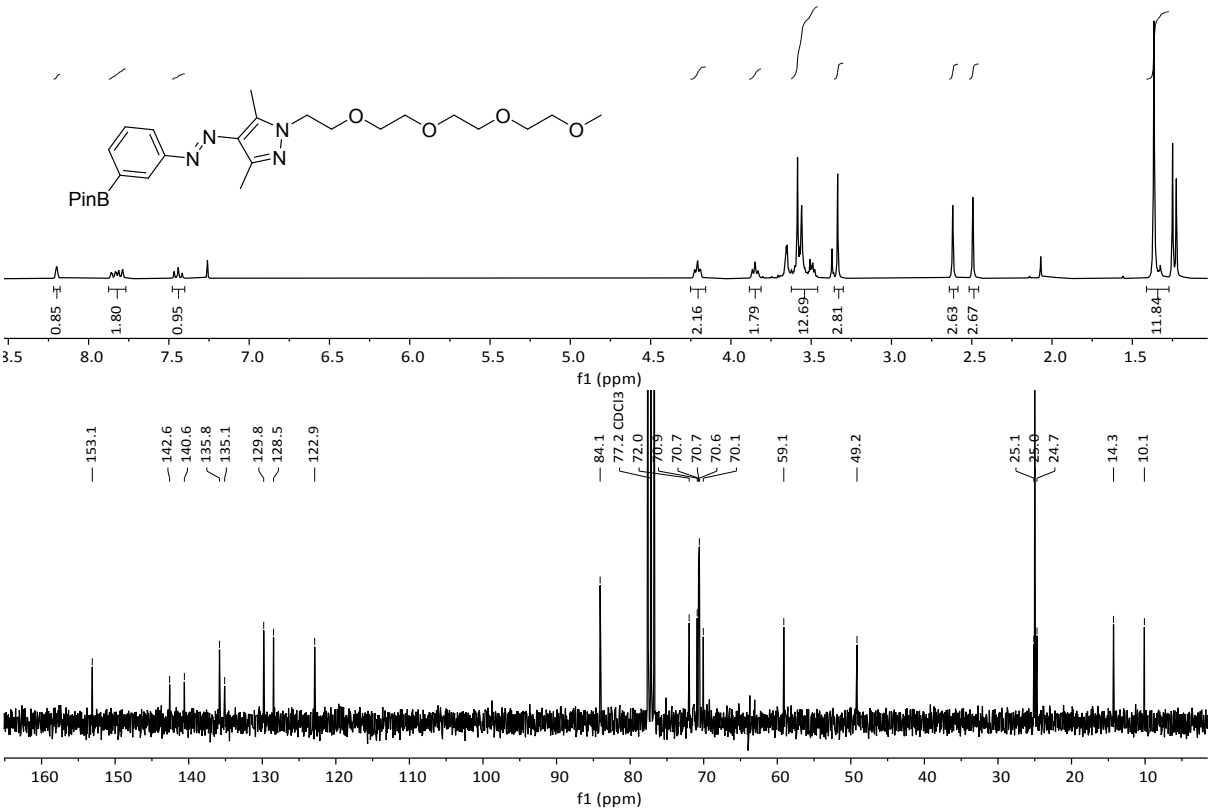


Fig. S11 - Top: ^{1}H-NMR, **Bottom:** ^{13}C-NMR of 3,5-dimethyl-4-((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)diazenyl)-1-(2,5,8,11-tetraoxatridecan-13-yl)-1H-pyrazole (**5**).

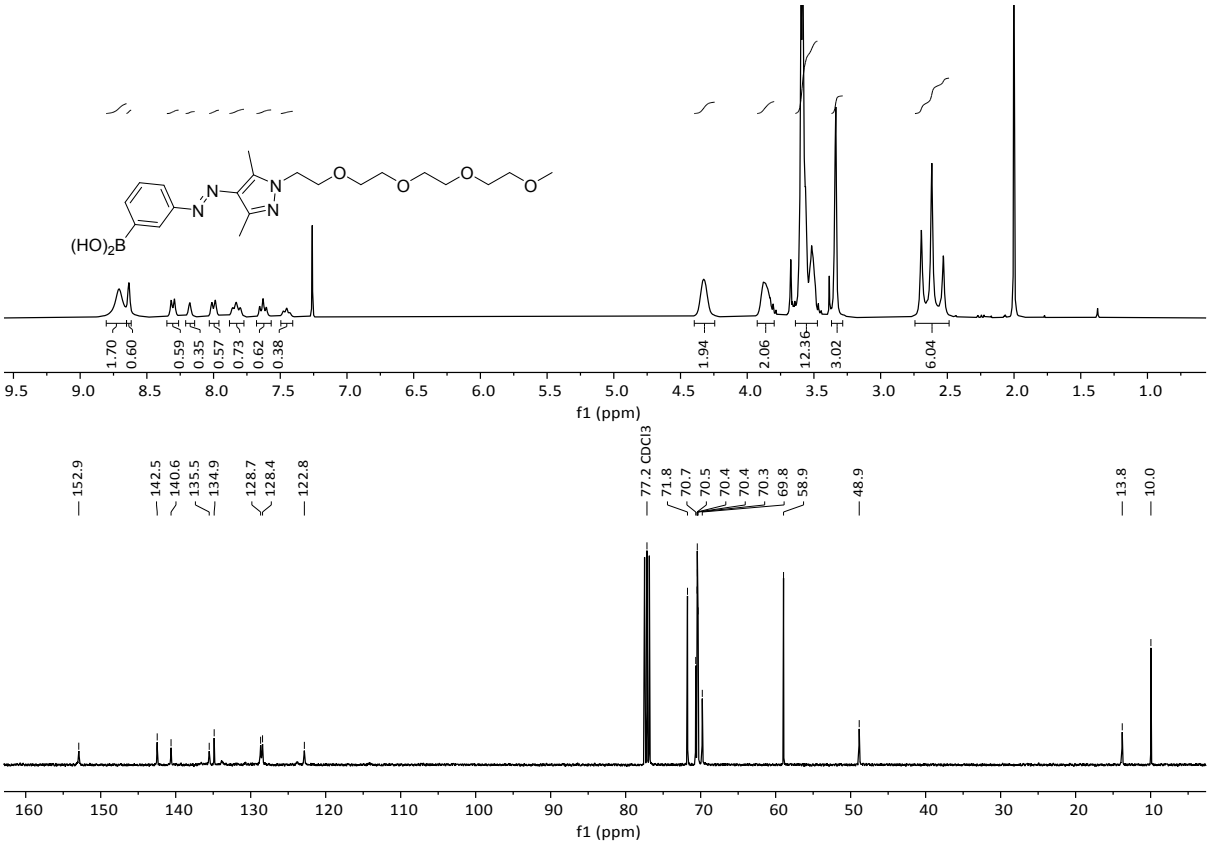


Fig. S12 - Top: ^{1}H-NMR, **Bottom:** ^{13}C-NMR of (3-((3,5-dimethyl-1-(2,5,8,11-tetraoxatridecan-13-yl)-1H-pyrazol-4-yl)diazenyl)phenyl)boronic acid (**6** – **bAAP**).

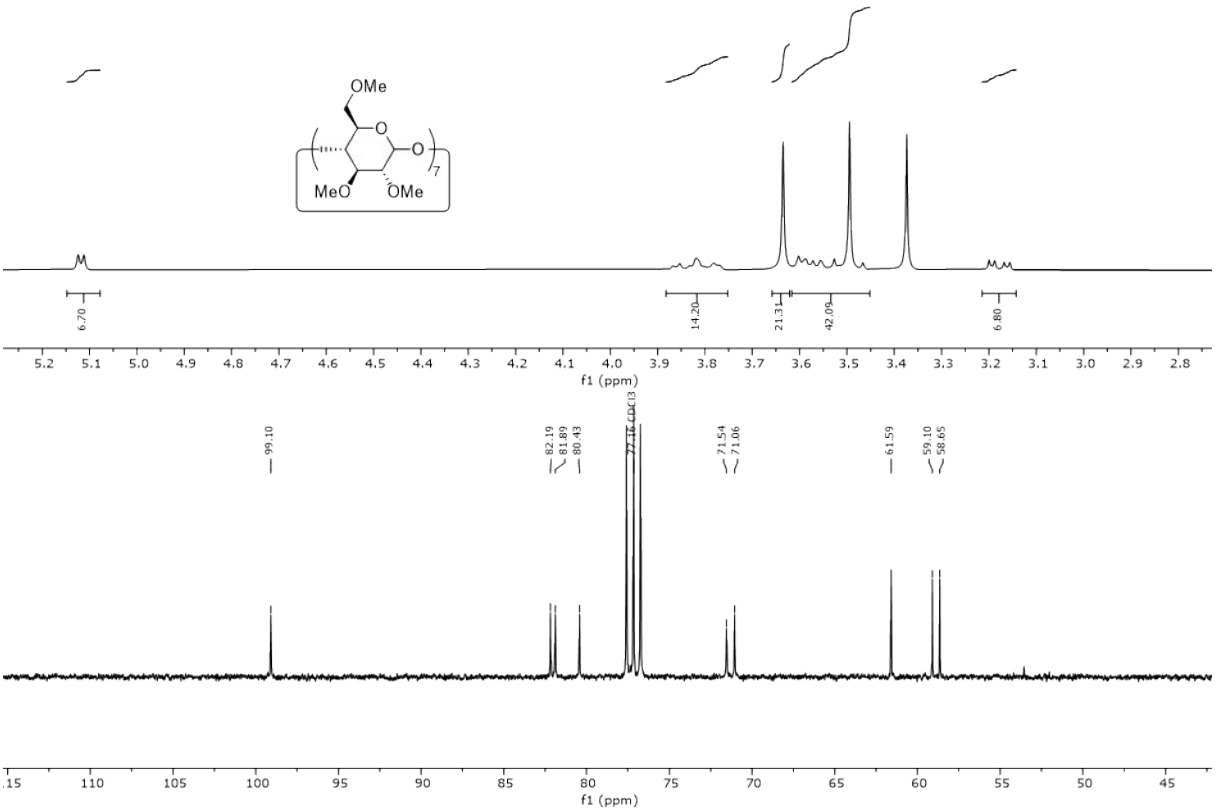


Fig. S13 - Top: ^{1}H-NMR, **Bottom:** ^{13}C-NMR of permethylated β-cyclodextrin (**7** – **Me-β-CD**).