Supplementary Material (ESI) for Chemical Communications

A rotaxane mimic of the photoactive yellow protein chromophore environment: Effects of hydrogen bonding and mechanical interlocking on a coumaric amide derivative

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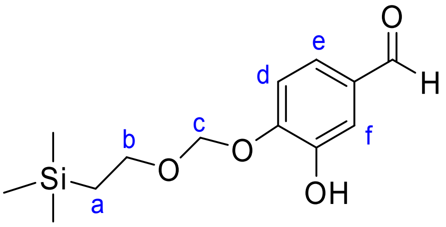
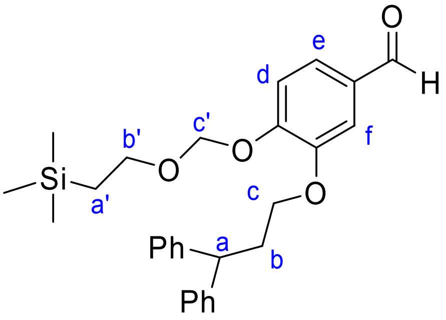
Synthesis

3-Hydroxy-4-(2-trimethylsilylethoxymethoxy)benzaldehyde (S1)



This compound was prepared as described by, S. Shizuri, H. Shigemori, Y. Okuno and S. Yamaura, *Chemistry Letters*, **1986**, 2097-2100, and showed identical spectroscopic data to therein. The relative position of alkylation was also confirmed by NOESY correlation.

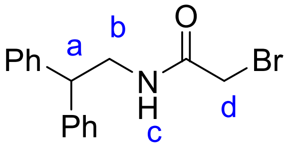
3-(3,3-diphenylpropyloxy)-4-(2-trimethylsilylethoxymethoxy)benzaldehyde (S2)



A solution of the mono-protected aldehyde S1 (1 g, 3.73 mmol), 3,3-diphenylpropyl alcohol (0.74 mL, 3.73 mmol) and triphenylphosphine (0.98 g, 3.73 mmol) in CH_2Cl_2 (37 mL) was stirred at 0 °C while diisopropylazodicarboxylate (0.73 mL, 3.73 mmol) was added drop-wise. The resultant solution was warmed to room temperature and stirred for 18 hours before being concentrated to dryness on the rotary evaporator. The crude was subjected to flash column chromatography on silica using a mixture of ethyl acetate: petrol 40-60 °C (30:70) to yield the title compound as a light yellow solid mp 58-59 °C (1.49 g, 3.22 mmol, 86%).

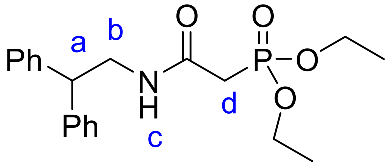
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.80 (br, 1H, CO*H*), 7.41 (dd, 1H, *J*= 8.3, 2.0 Hz CH_e), 7.39-7.25 (m, 10H, ArC*H*), 7.21-7.17 (m, 2H, ArC*H*), 5.36 (s, 2H, $CH_{c'}$), 4.23 (t, *J*= 7.8 Hz, 1H, CH_a), 4.01 (m, 2H, CH_c), 3.81 (t, *J*= 8.1 Hz, 1H, $CH_{b'}$), 2.58-2.63 (m, 2H, CH_b), 0.97 (t, *J*= 8.1 Hz, 1H, $CH_{a'}$) and 0.00 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 192.48 (*C*O), 153.97 (Ar*C* (ipso)), 150.80 (Ar*C* (ipso)), 145.47 (Ar*C* (ipso)) 132.23(Ar*C* (ipso)), 130.01 (Ar*C*H (meta)), 129.23, (Ar*C*H (ortho)), 127.83 (Ar*C*H (para)), 127.59 (Ar*C*H), 116.53 (Ar*C*H), 112.62 (Ar*C*H), 94.83 ($CH_{c'}$), 68.77, 68.27 ($CH_{b'}$, CH_c), 48.67 (CH_a), 36.01 (CH_b), 19.47 ($CH_{a'}$), 0.0 $Si(CH_3)_3$). HRMS (EI) Calcd. for $C_{28}H_{34}O_4Si$ $[M]^+$ 462.22264. Found 422.22195.

2-Bromo- *N*-(2,2-diphenylethyl)acetamide (S3)



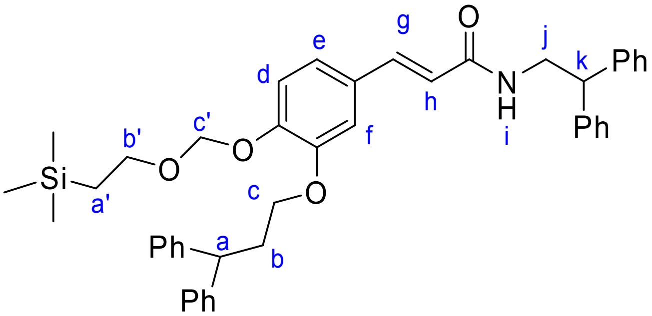
A solution of 2,2-diphenylethyl amine (2.01 g, 10.2 mmol), Et_3N (1.7 mL, 12.4 mmol) and DMAP (0.06 g, 0.49 mmol) in CH_2Cl_2 (10 mL) was stirred at 0 °C while a solution of bromacetyl bromide (0.86 mL, 9.91 mmol) in CH_2Cl_2 (5 mL) was added dropwise. The resultant solution was allowed to warm to room temperature and stirred for 18 hours before being cooled to 0 °C and quenched with 2N HCl. The organic layer was collected and concentrated *in vacuo*. The resultant oil was re-dissolved in Et_2O, washed with H_2O, and saturated NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The title product was obtained after flash column chromatography on silica (3:1 Et_+O: hexane) as an off white solid mp 74-75 °C, (3.36 g, 9.9 mmol, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28-7.15 (m, 10H, ArC*H*), 6.32 (br, 1H, NH_c), 4.13 (t, *J*= 7.8 Hz, 1H, CH_a) 3.86 (dd, *J*= 5.8, 7.8 Hz, 2H, CH_b), 3.72 (b, 2H, CH_d); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 158.01 (*C*O), 141.36 (Ar*C* (ipso)), 128.83 (Ar*C*H (meta)), 128.00 (Ar*C*H (ortho)), 127.03 (Ar*C*H (para)), 50.27 (CH_a), 44.33 (CH_b), 29.19 (CH_d); HRMS (EI) Calcd. for $C_{16}H_{16}N_1O_1Br$ $[M]^+$ 317.04153. Found 317.04163.

Diethyl (2,2-diphenylethylcarbamoyl)-methyl phosphonate (S4)



A slurry of the bromoamide S3 (0.64 g, 2.01 mmol) in neat triethylphosphite (0.36 mL, 2.08 mmol), was heated in a flask fitted with a reflux condenser under a steady stream of nitrogen, until all the solids went into solution and gentle reflux commenced (ca. 80 °C). Heating was finished when reflux had stopped (2h) after which time the product phosphonate had solidified. The solid was dried under vacuum to remove any excess triethyl phosphite and the title compound obtained as an off white solid mp 121-122 °C, which was not purified before further use (0.75g, 1.99 mmol, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25-7.12 (m, 10H, ArC*H*), 6.68 (br, 1H, NH_c), 4.17 (t, *J*= 7.8 Hz, 1H, CH_a) 3.91-3.83 (m, 6H, CH_b, OCH_2CH$_3$) 2.68 (d, *J*(H,P) = 20.5 Hz, 2H, CH_d), 1.16 (t, *J*= 7.1 Hz, 6H, OCH$_2$CH_3); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 158.00 (*C*O), 141.75 (Ar*C* (ipso)), 128.82 (Ar*C*H (meta)), 128.71 (Ar*C*H (meta)), 128.01(Ar*C*H (ortho)), 128.02 (Ar*C*H (ortho)), 127.02(Ar*C*H (para)), 126.81 (Ar*C*H (para)), 62.61 (O*C*H$_2$CH$_3$), 62.58 (O*C*H$_2$CH$_3$), 50.52 (*C*H$_a$), 44.19 (*C*H$_b$), 34.98 (d, *J*(C,P) = 130.99 Hz, *C*H$_d$), 16.32 (OCH$_2$*C*H$_3$), 16.28 (OCH$_2$*C*H$_3$). HRMS (FAB) Calcd. for $C_{12}H_{27}N_1O_4P$ $[M+1]^+$ 376.16777. Found 376.16818.

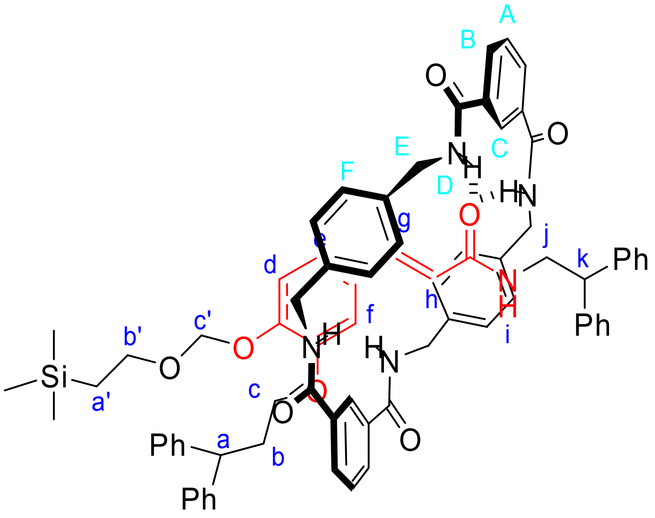
SEM protected thread (2)



The phosphonate ester S4 (0.71 g, 1.62 mmol) was dissolved in dry THF (10 mL) under N_2 and cooled to 0 °C. NaH (60% dispersion in oil, 0.08 g, 1.94 mmol) was added in one portion and after effervescence had subsided a solution of the aldehyde (0.75 g, 1.62 mmol) in dry THF (5 mL) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 2 hours before being poured onto H_2O, and extracted with CH_2Cl_2. The organic layer was collected washed with H_2O, dried over $MgSO_4$ and evaporated to dryness on the rotary evaporator. The crude mixture was purified by silica gel chromatography (25:75 EtOAc: petrol) to yield the title compound as a white solid mp 58-59 °C (0.74 g, 1.08 mmol, 74%).

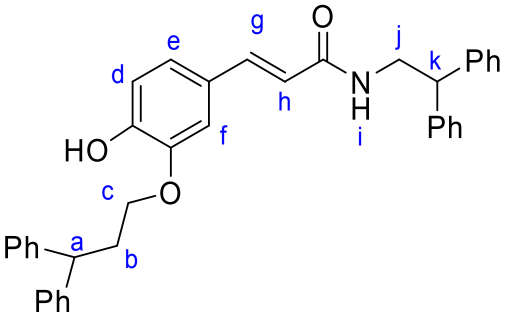
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, 1H, *J*= 15.4 Hz CH_g), 7.36-7.23 (m, 18H, ArC*H*), 7.18-7.14 (m, 2H, ArC*H*), 7.10 (d, 1H, *J*= 8.3 Hz CH_d), 6.98(dd, 1H, *J*= 8.3, 2.0 Hz CH_e), 6.80 (d, 1H, *J*= 2.02 Hz CH_f), 5.99 (d, 1H, *J*= 15.4 Hz CH_h), 5.47 (t, 1H, *J*= 5.81 Hz NH_i), 5.26 (s, 2H, C$H_{c'}$), 4.20-4.28 (m, 2H, C$H_{a,\,k}$), 4.01 (dd, *J*= 7.8, 5.8, 2H CH_j), 3.96 (m, 2H, CH_c), 3.79 (t, *J*= 8.6 Hz, 1H, C$H_{b'}$), 2.59-2.54 (m, 2H, CH_b), 0.96 (t, *J*= 8.6 Hz, 1H, C$H_{a'}$) and 0.00 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.37 (NH-*C*O), 150.47 (Ar*C* (ipso)), 150.05 (Ar*C* (ipso)), 145.59 (Ar*C* (ipso)), 143.24 (Ar*C* (ipso)), 142.38 (*C*H_g), 130.33(Ar*C* (ipso)), 130.21 (Ar*C*H (meta)), 130.12 (Ar*C*H (meta)) 129.99 (Ar*C*H (ortho)), 129.49 (Ar*C*H (ortho)), 129.27 (Ar*C*H (ortho)), 128.33 (Ar*C*H (para)), 127.77 (Ar*C*H (para)), 123.29 (*C*H_e), 119.98(*C*H_h), 117.92 (*C*H_d), 113.59 (*C*H_f), 95.11 (*C*$H_{c'}$), 68.47 (*C*H_c), 67.89 (*C*$H_{b'}$), 52.04 (*C*H_k) , 48.61 (*C*H_a),45.33 (*C*H_j) 36.12 (*C*H_b), 19.47 (*C*$H_{a'}$), 0.0 Si(*C*H_3)$_3$). HRMS (FAB) Calcd. for $C_{44}H_{50}NO_4Si$ $[M+1]^+$ 684.35091. Found 684.35072.

Rotaxane (1)



To a stirred solution of thread **2** (0.4 g, 0.59 mmol) in anhydrous $CHCl_3$ (50 mL) with Et_3N (0.95 g, 9.44 mmol) were added simultaneously solutions of *para*-xylylenediamine (0.64 g, 4.72 mmol) in $CHCl_3$ (25 mL), and isophthaloyl dichloride (0.96 g, 4.72 mmol) in $CHCl_3$ (25 mL) over a period of 3 h using motor-driven syringe pumps. After a further 16 h the resulting suspension was filtered and the filtrate washed with 1N HCl (150 ml), saturated $NaHCO_3$ (150 mL) and saturated aqueous NaCl solution (150 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to afford the crude product that was purified by column chromatography on silica gel using an ethyl acetate/petroleum spirit (40-60 °C) (50:50) mixture initially as eluent to remove unreacted thread, followed by neat ethyl acetate to give the title compound as a colourless foam (0.1 g, 0.08 mmol, 14%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.14 (s, 2H, ArC*H*$_{C}$), 8.06 (d, *J* = 7.8 Hz, 4H, ArC*H*$_{B}$), 7.58 (t, *J* = 7.8 Hz, 2H, ArC*H*$_{A,}$), 7.34 – 7.12 (m, 16H, ArC*H*), 7.10 (m, 1H, N*H*$_{i}$), 7.01 – 6.97 (m, 4H, ArC*H*), 6.85- 6.84 (m, 11 H, ArC*H*$_{F,}$ N*H*$_{D,}$ C*H*$_{d}$), 6.41 (d, 1H, *J*= 15.4 Hz C*H*$_{g}$), 6.25 (d, 1H, *J*= 8.3 C*H*$_{e}$), 6.96 (s, 1H, C*H*$_{f}$), 5.18 (s, 2H, C*H*$_{c'}$), 4.78 (d, 1H, *J*= 15.4 Hz C*H*$_{h}$), 4.54 (dd, 4H, *J* = 14.4, 5.5 Hz, C*H*$_{E}$), 4.54 (m, 5H, C*H*$_{E'}$, C*H*$_{a}$), 3.89 (t, 1H, *J* = 8.3 Hz C*H*$_{j}$), 3.75 (t, *J*= 8.3 Hz, 2H, C*H*$_{b'}$) 3.37 (m, 2H, C*H*$_{k}$), 3.19-3.17 (m, 2H, C*H*$_{c}$), 2.46-2.40 (m, 2H, C*H*$_{b}$), 0.95 (t, *J*= 8.3 Hz, 2H, C*H*$_{a'}$) and 0.00 (s, 9H, Si(C*H*$_{3}$)$_{3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.8 (NH-*C*O$_{i}$), 166.5 (NH*C*O macrocycle), 149.2 (Ar*C* (ipso)), 148.7 (Ar*C* (ipso)), 144.3 (Ar*C* (ipso)), 142.1 (Ar*C* (ipso)),138.8 (*C*H$_{g}$), 137.0 (Ar*C*-CH$_{E}$ (ipso)), 134.2 (Ar*C*-CO-NH$_{D}$ (ipso)), 130.8 (Ar*C*H$_{B}$), 129.2, (Ar*C*H (meta)), 128.7 (Ar*C*H (meta)), 128.5 (Ar*C*H (ortho)), 128.2 (Ar*C*H (ortho)), 128.0 (Ar*C* (ipso)), 127.6 (Ar*C*H (para)), 126.6 (Ar*C*H (para)), 125.0 (Ar*C*H_C), 121.9 (*C*H_e) 118.3 (*C*H_h), 116.1 (*C*H_d), 110.0 (*C*H_f), 93.6 (*C*$H_{c'}$), 66.6(*C*$H_{b'}$), 66.1 ((*C*H_c), 49.7 (*C*H_k), 47.1 (*C*H_a) , 44.7 (*C*H_j), 44.3 (*C*H_E), 34.7 (*C*H_g), 18.0 (*C*$H_{a'}$ **,** -1.4 (Si*C*H_3) ; HRMS (FAB) Calcd. for $C_{76}H_{78}N_5O_8Si$ $[M+1]^+$ 1216.56197. Found 1216.55977

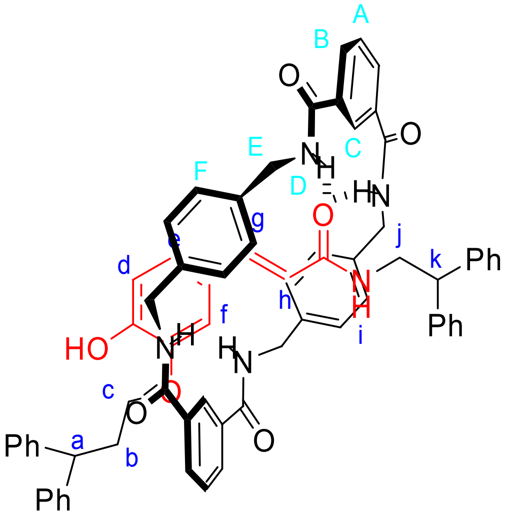
Thread (4)



A solution of tetrabutylammonium fluoride in THF (1M cont 5% H_2O) (0.92 mL, 0.92 mmol) was added to the SEM protected thread **2** (125 mg, 0.18 mmol) and the solution concentrated in vacuo. The resulting oil was dissolved in anhydrous DMPU (0.5 mL) and powdered activated 4Å molecular sieves were added (ca 0.06g). The resultant suspension was heated to 45 °C for 9 hours, protected from UV light, before being cooled diluted with $CHCl_3$ (15 mL) and poured onto H_2O (15 mL). The solution was extracted with $CHCl_3$ (3 x 20 mL) and the combined organic layers dried over $MgSO_4$ and concentrated in vacuo. The resulting oil was washed with hexane to remove residual DMPU and subjected to flash column chromatography on silica using a mixture of ethyl acetate/petroleum spirit 40-60 °C (80/20) as eluent to give the title compound as light yellow foam (87 mg, 0.14 mmol, 78%) along with 3% *Z* isomer.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, 1H, *J*= 15.4 Hz CH_g), 7.30-7.07 (m, 20H, ArCH), 6.89 (dd, 1H, *J*= 8.1, 1.7 Hz CH_e), 6.77 (d, 1H, *J*= 8.1 Hz CH_d), 6.69 (d, 1H, *J*= 1.7 Hz CH_f), 5.90 (d, 1H, *J*= 15.4 Hz CH_h), 5.44(1H, s, O*H*), 5.37 (t, 1H, *J*= 5.05 Hz NH_i), 4.18 (t, *J*= 7.8 Hz, 1H, CH_k), 4.10 (t, *J*= 7.6 Hz, 1H, CH_a), 3.98 – 3.93 (m, 4H $CH_{c,\,j}$), 2.54-2.49 (m, 2H, CH_b); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1 (NH-*C*O), 147.5 (Ar*C* (ipso)), 145.9 (Ar*C* (ipso)), 144.1 (Ar*C* (ipso)), 141.89 (Ar*C* (ipso)), 141.20 (CH_g), 128.8 (Ar*C*H (meta)), 128.1 (Ar*C*H (meta)) 127.7 (Ar*C*H (ortho)), 129.27 (Ar*C*H (ortho)), 126.8 (Ar*C*H (para)), 126.5 (Ar*C*H (para)), 122.4 (CH_e), 117.9(CH_h), 114.7 (CH_d), 110.3 (CH_f), 67.4 (CH_c), 50.7 (CH_k) , 48.0 (CH_a),43.9 (CH_j) 34.8 (CH_b). HRMS (FAB) Calcd. for $C_{38}H_{36}NO_3$ $[M+1]^+$ 554.26952. Found 554.26984.

Rotaxane (5)



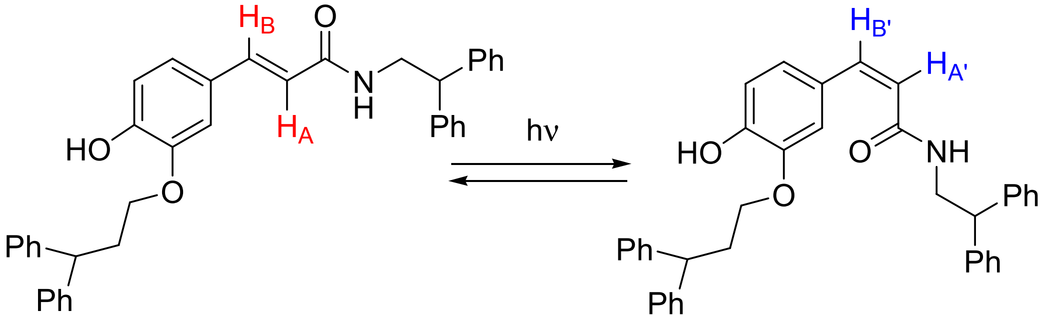
A solution of tetrabutylammonium fluoride in THF (1M cont 5% H_2O) (0.41 mL, 0.41 mmol) was added to the SEM protected rotaxane (100 mg, 0.08 mmol) and the solution concentrated in vacuo. The resulting oil was dissolved in anhydrous DMPU (0.3 mL) and powdered activated 4Å molecular sieves were added (ca 0.04g). The resultant suspension was heated to 45 °C for 16 hours, protected from UV light, before being cooled diluted with $CHCl_3$ (15 mL) and poured onto H_2O (20 mL). The solution was extracted with $CHCl_3$ (3 x 20 mL) and the combined organic layers dried over $MgSO_4$ and concentrated in vacuo. The resulting oil was washed with hexane to remove residual DMPU and subjected to flash column chromatography on silica using ethyl acetate as eluent to give the title compound as light yellow foam (60 mg, 0.55 mmol, 67%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 (s, 2H, ArCH_C), 8.00 (d, *J* = 7.8 Hz, 4H, ArCH_B), 7.55 (t, *J* = 7.8 Hz, 2H, ArC$H_{A,}$), 7.32 – 6.93 (m, 21H, ArC*H*, NH_i)), 6.81 (b, 4 H, NH_D), 6.77 (s, 8 H, ArCH_F)$_,$ 6.45 (d, 1H, *J*= 8.1 Hz CH_d), 6.32 (d, 1H, *J*= 15.6 Hz CH_g), 6.08 (d, 1H, *J*= 8.1 Hz CH_e), 5.89 (s, 1H, CH_f), 5.53 (1H, s, O*H*), 4.71 (d, 1H, *J*= 15.6 Hz CH_h), 4.46 (dd, 4H, *J* = 14.4, 5.5 Hz, CH_E), 4.18 (dd, 4H, *J* = 14.4, 5.5 Hz, C$H_{E'}$), 4.08 (t, 1H, *J* = 8.1 Hz CH_a), 3.81 (t, 1H, *J* = 7.07 Hz CH_j), 3.32-3.23 (m, 4H, CH_k, CH_c), 2.42-2.37 (m, 2H, CH_b); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.8 (NH-*C*O_i), 166.4 (NH*C*O macrocycle), 147.4 (Ar*C* (ipso)), 145.8 (Ar*C* (ipso)), 144.1 (Ar*C* (ipso)), 142.2 (Ar*C* (ipso)), 139.0 (*C*H_g), 137.1 (Ar*C*-CH_E (ipso)), 134.24 (Ar*C*-CO-NH_D (ipso)), 130.86 (Ar*C*H$_B$), 129.28, 128.5 (Ar*C*H (meta)), 128.2 (Ar*C*H (meta)), 128.1 (Ar*C*H (ortho)),127.8 (Ar*C*H (ortho)), 126.8 (Ar*C*H (para)), 126.7 (Ar*C* (ipso)), 126.6 (Ar*C*H (para)), 125.0 (Ar*C*H$_C$), 122.9 (*C*H$_e$) 117.7 (*C*H$_h$), 114.6 (*C*H$_d$), 109.1 (*C*H$_f$), 66.5(*C*H$_c$), 49.82 (*C*H$_k$), 47.8 (*C*H$_a$) , 44.7 (*C*H$_j$), 44.3 (*C*H$_E$), 34.7 (*C*H$_g$); HRMS (FAB) Calcd. for $C_{70}H_{64}N_5O_7Si$ $[M+1]^+$1086.48058 Found 1086.48063.

Photostationary States

The isomerization experiments at 313 nm of solutions placed in standard 5 mm ^{1}H NMR glass tubes or in quartz cuvettes was performed using an Oriel 200 W high pressure Hg lamp, in combination with a monochromator (Oriel 7240). The concentration of the samples for NMR experiments was ca. 1 mM. Solutions were purged with Ar for 15 min before the irradiation.

The ^{1}H-NMR spectra (400 MHz, $CDCl_3$) of thread *E*-**4** and the photostationary mixture of *E*-**4** and *Z*-**4** are shown in Figure S1. In the photostationary state the predominant isomer is *Z*-**4**, characterized by the signals of the olefinic protons $H_{B'}$ and $H_{A'}$.



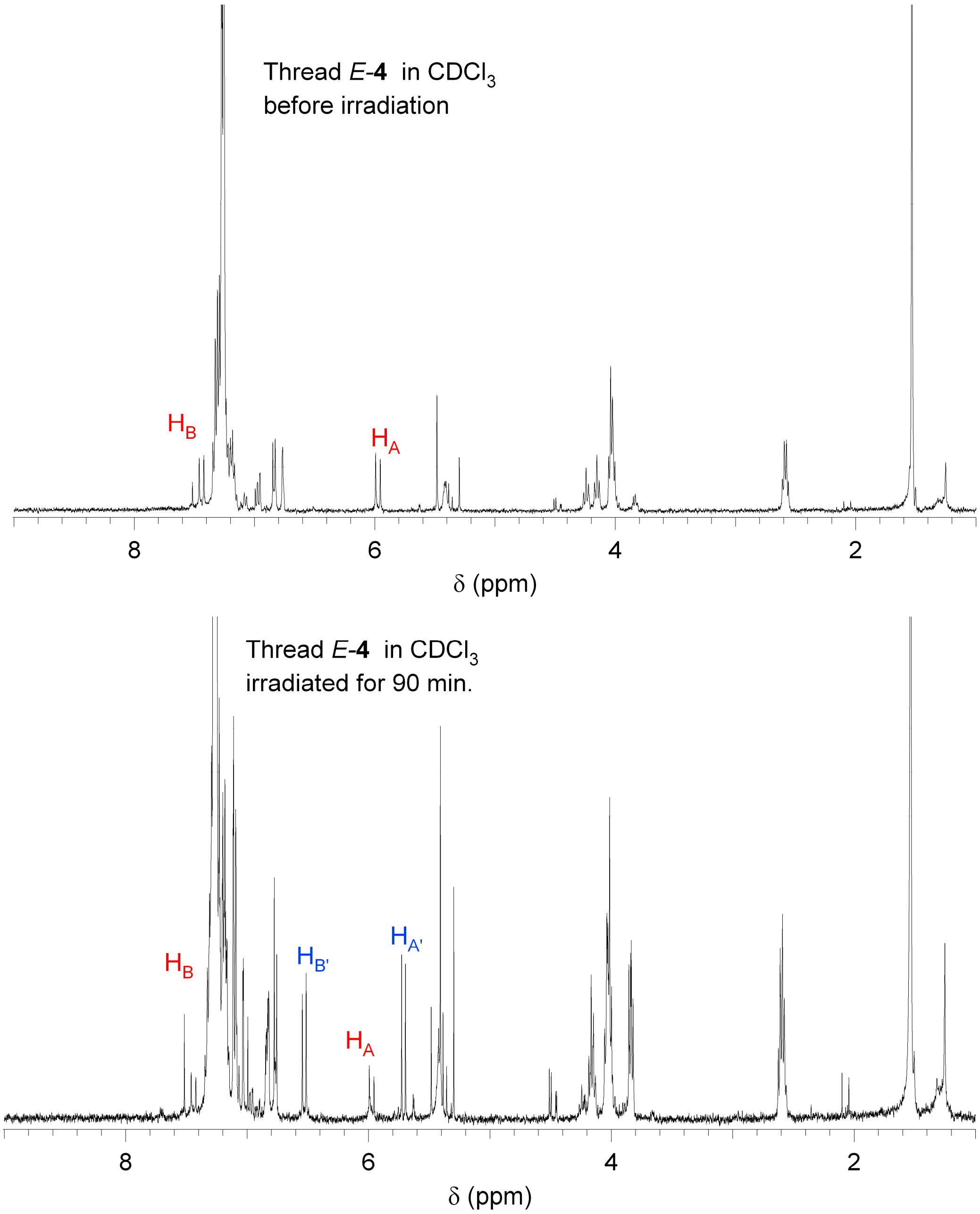


Figure S1. ^{1}H NMR spectra of **4** and the photostationary state produced upon irradiation at 313 nm.

Determination of pK_a values

The pK_a values were obtained form an analysis of the UV-Vis absorption spectra at different pH values (Figure S2).

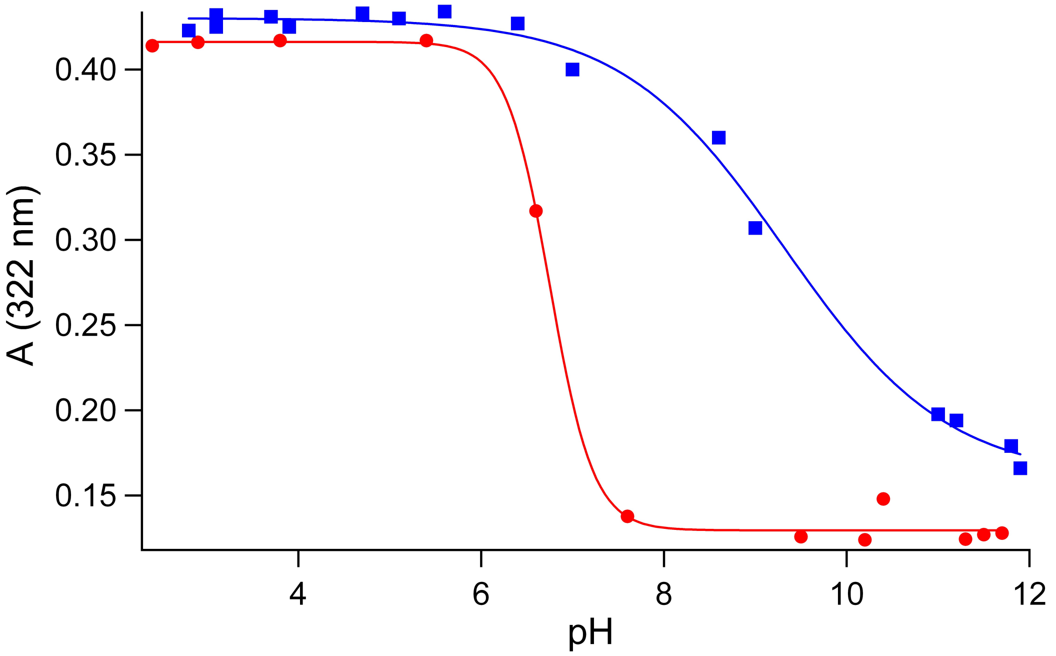


Figure S2. Absorption at 322 nm as a function of pH and fitted sigmoidal curves for thread **4** (blue, squares) and rotaxane **5** (red, filled circles) in methanol:water 3:2.