

Supplementary Information

Reversible photocontrolled disintegration of a dimeric tetraurea-calix[4]pyrrole capsule with *all-trans* appended azobenzene units

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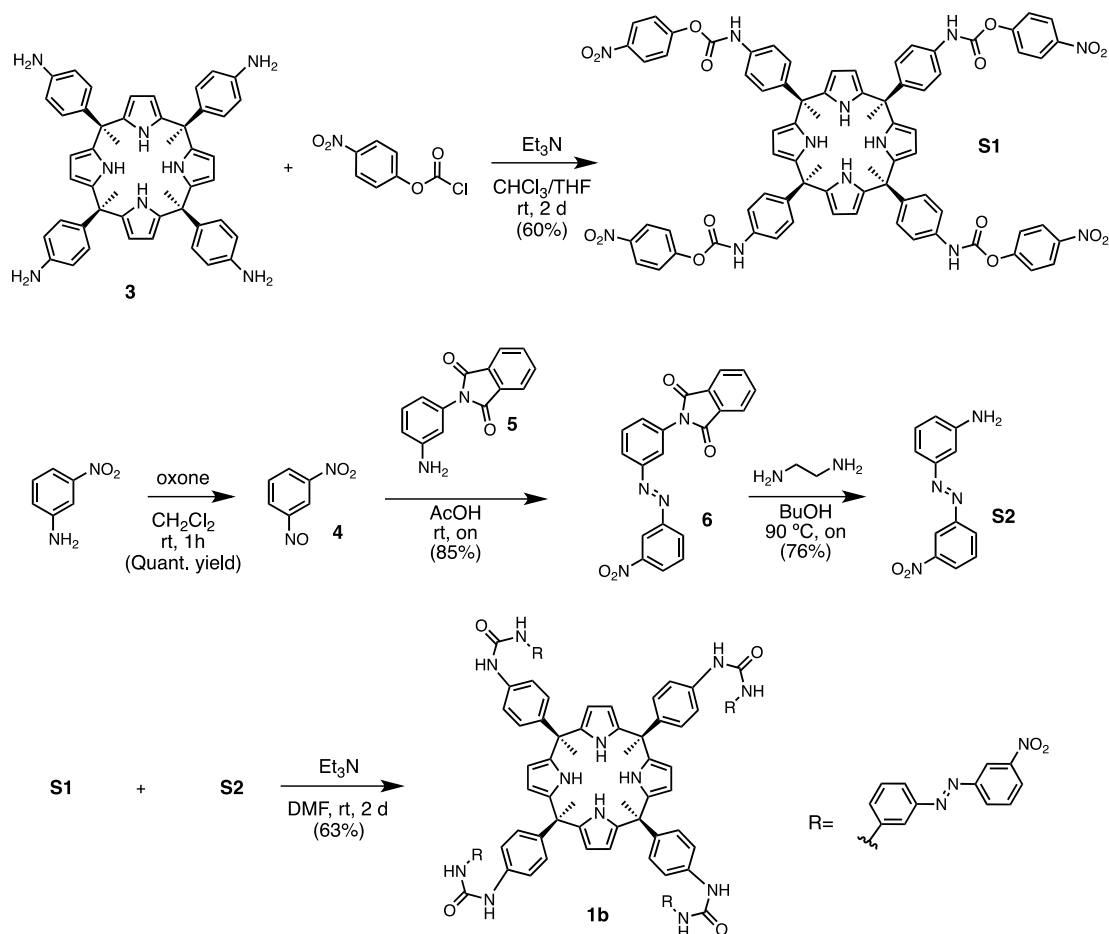
1. General Information

All reagents were obtained from commercial suppliers and used without further purification. All solvents were of HPLC grade quality, obtained commercially and used without further purification.

^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded on a Bruker Avance 400 (400.1 MHz for ^1H -NMR and 100.6 MHz for $^{13}\text{C}\{^1\text{H}\}$) and Bruker Avance 500 (500 MHz for ^1H -NMR and 126 MHz for $^{13}\text{C}\{^1\text{H}\}$) ultrashield spectrometer. The deuterated solvents used are indicated in between brackets; chemical shifts, δ , are given in ppm, referenced to the solvent residual signal (^1H , ^{13}C). Coupling constants, J , are given in Hz. Both low and high resolution mass spectrometry analyses were performed either in a Waters LCD PremierTM instrument, operating in ESI (Electro-Spray Ionization) mode or APCI (Atmospheric Pressure Chemical Ionization) mode, or in an AutoFlex (Bruker Daltonics) instrument for MALDI (Matrix-assisted laser desorption/ionization) analyses. UV/Vis spectra were obtained using a Varian Cary 50 Scan UV/Vis spectrometer and Helma SUPRASIL precision cuvettes (10 mm light path). Photoisomerization of UV/Vis and NMR samples was accomplished by irradiation with a Polychrome V system monochromator (Till Photonics) containing a 150 W Xenon short arc lamp with an output range of 320–680 nm. The output of the monochromator was coupled to a fiber optic cable (4 m length, FT-600-UMT, NA 0.39: LEONI Fiber Optics GmbH). The end section of the fiber was inserted into either the NMR tube or the UV/Vis cuvette, to a point directly above the volume of the solution. The output from the fiber optic cable between 340–480 nm ranged from 0.3–9.0 $\mu\text{W}/\text{cm}^2$.

2. Synthesis of the azobenzene-functionalized tetraurea calix[4]pyrrole **1b**

Synthetic strategy:



Activated urethane calix[4]pyrrole (**S1**)

Tetraaminocalix[4]pyrrole¹ (**3**) (129 mg, 0.175 mmol) was dissolved in 20 mL of a solvents mixture CHCl_3/THF (3:2). Nitrophenylchloroformate (159 mg, 0.788 mmol) was slowly added to this solution under argon atmosphere. Then, triethylamine (73 μL , 0.525 mmol) was added and the resulting solution was stirred under argon for 2 days. The reaction mixture was filtered and washed with water (150 mL) to yield a brownish solid (60%). It was used in the next reaction without further purification.

¹**H NMR** (400 MHz, $\text{DMSO}-d_6$): δ 10.33 (s, 4H), 9.60 (s, 4H), 8.18 (d, $J = 9.2$ Hz, 8H), 7.43 (d, $J = 9.2$ Hz, 8H), 7.38 (d, $J = 8.5$ Hz, 8H), 6.93 (d, $J = 8.5$ Hz, 8H), 5.90 (s, 8H), 1.82 (s, 12H).

MS (MALDI-TOF): m/z calculated for $\text{C}_{76}\text{H}_{61}\text{N}_{12}\text{O}_{16}$ $[\text{M}+\text{H}]^+$: 1397.4, found 1397.6.

¹ Gil-Ramirez, G.; Ballester, P. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 10455.

1-Nitro-3-nitrosobenzene (4)

3-Nitroaniline (2.36 g, 17.10 mmol) was dissolved in 52 ml of CH₂Cl₂. To this solution, oxone (21.02 g, 34.20 mmol) dissolved in 207 ml of water was added. The mixture was stirred vigorously at rt until TLC monitoring indicated complete consumption of the starting material (1 h). After separation of the layers, the aqueous phase was extracted with CH₂Cl₂ (2 × 50 mL). The combined organic layers were washed with 1 N HCl (100 mL), saturated sodium bicarbonate solution (100 mL), water (100 mL) and brine (100 mL) and dried over MgSO₄. Then, the solution was filtered and evaporated under reduced pressure. The target compound was obtained in quantitative yield (2.60, 17.10 mmol) as a pale green solid and was used in the next step without further purification.

¹H NMR (400 MHz, CDCl₃): δ 8.64–8.57 (m, 2H), 8.34 (d, *J* = 7.8 Hz, 1H), 7.90 (t, *J* = 7.8 Hz, 1H).

¹³C NMR (100.6 MHz, CDCl₃): δ 163.4, 149.2, 130.9, 128.8, 126.6, 114.7.

IR (ATR): 3095, 3066, 3041, 1530, 1414, 1390, 1352 cm⁻¹.

m.p.: 86–88 °C.

HRMS (APCI–): *m/z* calculated for C₆H₄N₂O₃ [M–H][–]: 152.0222, found 152.0224.

(*E*)-2-(3-((3-Nitrophenyl)diazenyl)phenyl)isoindoline-1,3-dione (6)

Nitroso derivative **4** (1.92 g, 12.63 mmol) was dissolved in 87 ml of AcOH. Then, 2-(3-aminophenyl)isoindoline-1,3-dione² (**5**, 2.50 g, 10.50 mmol) was added to this solution and the mixture stirred overnight at rt. The brown precipitate formed was filtered and the filter cake was washed first with water (100 ml) and saturated bicarbonate solution (100 ml). These aqueous extracts were discarded and subsequently the solid was washed with CH₂Cl₂ (6 × 100 ml). The organic extract was collected, dried over MgSO₄ and evaporated under reduced pressure to obtain the title compound in 85% yield as a brown solid (3.99 g, 10.73 mmol). The product was used in the next step without further purification.

¹H NMR (500 MHz, CDCl₃): δ 8.77 (t, *J* = 2.1 Hz, 1H), 8.35 (ddd, *J* = 8.2, 2.1, 1.0 Hz, 1H), 8.28 (ddd, *J* = 7.9, 2.1, 1.0 Hz, 1H), 8.12 (t, *J* = 1.8 Hz, 1H), 8.05 (dt, *J* = 7.7, 1.8 Hz, 1H), 8.01 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (t, *J* = 8.2, 1H), 7.71 (t, *J* = 7.7, 1H), 7.67 (dt, *J* = 7.7, 1.8 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃): δ 167.1 (×2), 152.9, 152.7, 149.2, 134.7 (×2), 133.0, 131.8 (×2), 130.2, 130.0, 129.8, 129.4, 125.4, 124.1 (×2), 123.8, 120.7, 117.5.

IR (ATR): 3100, 2922, 2850, 1723, 1530, 1381, 1353 cm⁻¹.

m.p.: 260–262 °C.

HRMS (ESI⁺): *m/z* calculated for C₂₀H₁₂N₄NaO₄ [M+Na]⁺: 395.0756, found 395.0757.

² Tie, C.; Gallucci, J. C.; Parquette, J. R. *J. Am. Chem. Soc.* **2006**, *128*, 1162.

(*E*)-3-((3-Nitrophenyl)diazenyl)aniline (S2)

Compound **6** (1.60 g, 4.30 mmol) was dissolved in 86 ml of *n*-butanol in a 250 ml two neck round-bottom flask equipped with a condenser. Then, ethylenediamine (2.87 ml, 43.0 mmol) was added and the reaction mixture was stirred at 90 °C overnight. The solvent was evaporated under reduced pressure and then water was added (100 mL) and it was extracted with CH₂Cl₂ (3× 60 mL). The combined organic layers were washed with brine (100 mL), dried over MgSO₄ and the solvent was evaporated under reduced pressure. The crude was purified by flash column chromatography on silica gel with 2.5% of Et₃N (from hexane/EtOAc 85:15 to hexane/EtOAc 50:50) to afford an orange solid in 76% yield (0.79 g, 3.27 mmol).

¹H NMR (400 MHz, CDCl₃): δ 8.72 (t, *J* = 2.0 Hz, 1H), 8.32 (dd, *J* = 8.0, 2.0 Hz, 1H), 8.23 (ds, *J* = 8.0, 2.0 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.41 (dd, *J* = 7.8, 2.3 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.26 (t, *J* = 2.3 Hz 1H), 6.86 (dd, *J* = 7.8, 2.3 Hz, 1H), 3.87 (s, 2H). The minor signals in the spectrum correspond to the *cis* isomer (≈ 4%).

¹³C NMR (101.6 MHz, CDCl₃): δ 153.4, 153.2, 149.2, 147.5, 130.2, 130.1, 129.3, 124.9, 119.2, 117.2, 115.7, 107.7.

IR (ATR): 3464, 3369, 3200, 3100, 2920, 2822, 1624, 1600, 1527, 1484, 1350 cm⁻¹.

m.p.: 116–118 °C.

HRMS (ESI⁻): *m/z* calculated for C₁₂H₉N₄O₂ [M-H]⁻: 241.0726, found 241.0731.

Tetraurea azo-calix[4]pyrrole (1b)

Compound **S2** (236 mg, 0.973 mmol) was dissolved in 1 mL of dry DMF and then the activated calix[4]pyrrole urethane **S1** (136 mg, 0.097 mmol) was added, previously dissolved in dry DMF (10 mL). Finally, triethylamine (136 μL, 0.973 mmol) was added. The reaction mixture was stirred under argon atmosphere at room temperature for 2 days. Then, it was diluted with CH₂Cl₂ (100 mL) and 1 M K₂CO₃ aq. sol. (100 mL). It was stirred for 30 min and the phases were separated. The organic phase was washed with 0.3 M K₂CO₃ aq. sol. until the aqueous phase was colorless (yellow color due to the by-product *p*-nitrophenol). It was dried over anhydrous MgSO₄ and the solvent was evaporated under reduced pressure. The crude was purified by flash column chromatography on silica gel (from CH₂Cl₂ to CH₂Cl₂/THF 50:50) to afford an orange solid in 63% yield (111 mg, 0.061 mmol).

The ¹H NMR spectrum in THF-*d*₈ of this compound was complex (see section 3 and 6). Most likely, it is due to the existence of the azo-calix[4]pyrrole as an averaged mixture of the different *cis/trans* isomers of the four azobenzene side chains.

HRMS (ESI⁻): *m/z* calculated for C₁₀₀H₇₉N₂₄O₁₂ [M-H]⁻: 1807.6315, found 1807.6322.

3. Study of the photoisomerization of **1b** by ^1H NMR spectroscopy

A 1 mM solution of **1b** (0.9 mg) in THF- d_8 (0.5 mL) was irradiated *in situ* in the NMR spectrometer as described in Section 1. Although initially there is a mixture of the different stereoisomers in different ratio, one of them is clearly in major proportion, most likely the one with the four azobenzene groups in *trans* form, the “*all-trans-1b*”. (Figure S1, red). Upon irradiation at 380 nm, some signals grew in intensity at the expenses of those assigned to *all-trans-1b* and new proton signals emerge (see region 7.0 – 7.2 ppm of the green spectra, Figure S1). Probably, the signals increasing in intensity and the new ones correspond to *cis-enriched* stereoisomers of **1b**. Subsequent irradiation for 1 h at 480 nm, produces a moderate increase in the intensity of the original major signals. (Figure S1, blue). Leaving the sample in the dark for two weeks generates a mixture of stereoisomers quite similar to the original state (Figure S1, purple).

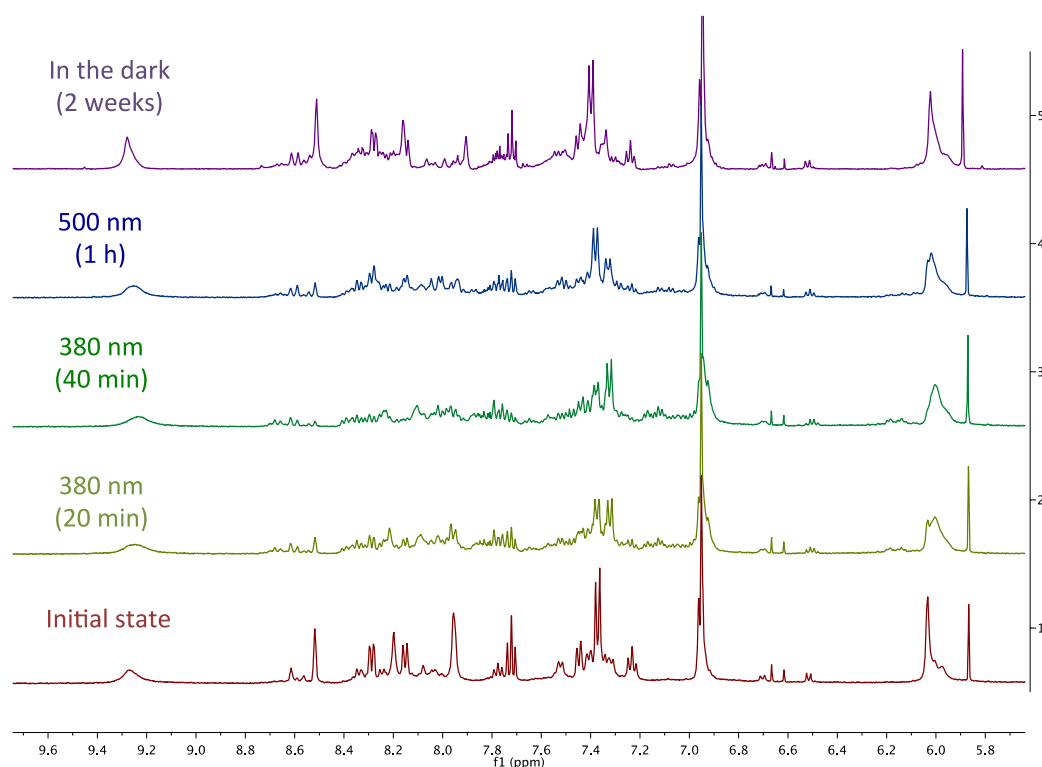


Figure S1. Photoisomerization experiments of **1b** analyzed by ^1H NMR spectroscopy.

4. Experimental procedure for the self-assembly of **2**⊂**1b**•**1b**

Capsule **2**⊂**1b**•**1b** was self-assembled by adding 0.6 equivalents of a stock solution of guest **2** in $\text{CH}_2\text{Cl}_2-d_2$ to a NMR tube containing a 0.8 mM suspension of tetraurea **1b** in $\text{CH}_2\text{Cl}_2-d_2$. The sample was left standing in the dark overnight and the resulting solution was filtered and analyzed by ^1H NMR spectroscopy.

5. ^1H NMR irradiation experiments of $2\subset 1\text{b}\cdot 1\text{b}$ at 380 nm

The capsule was self-assembled following the procedure described in Section 3. The *in situ* photoisomerization experiments were performed in the NMR spectrometer as described in Section 1.

As mentioned in the main text, when the capsule was irradiated at 380 nm for 2 h in the presence of excess **2** no changes are observed in the ^1H NMR (*Figure S2*). Conversely, when the dimerization process was templated by addition of 0.25 equivalents of **2** (excess host) the irradiation at the same wavelength led to the gradual disappearance of the ternary inclusion complex $2\subset 1\text{b}\cdot 1\text{b}$ (*Figure S3*).

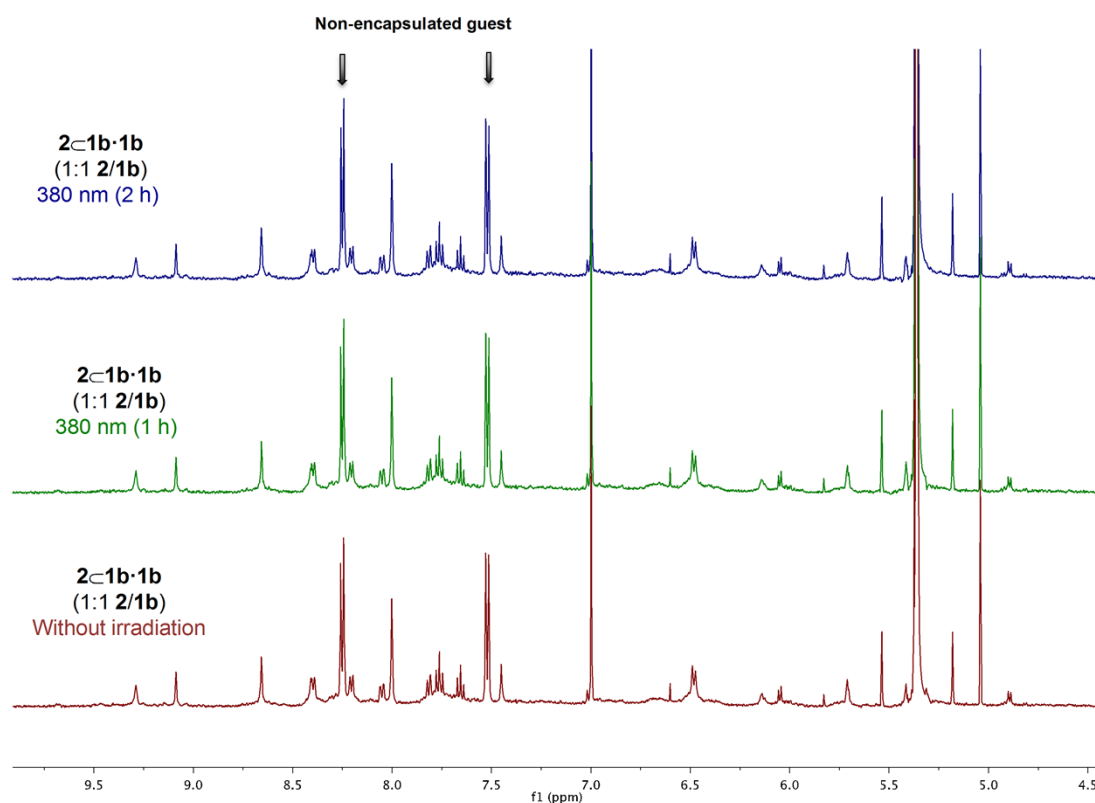


Figure S2. Selected region of the ^1H NMR spectra of a $\text{CH}_2\text{Cl}_2\text{-}d_2$ solution of $2\subset 1\text{b}\cdot 1\text{b}$ self-assembled in the presence of 1 equivalent of **2** before irradiation (red), after 1 h irradiation at 380 nm (green) and after 2 h irradiation at 380 nm (blue).

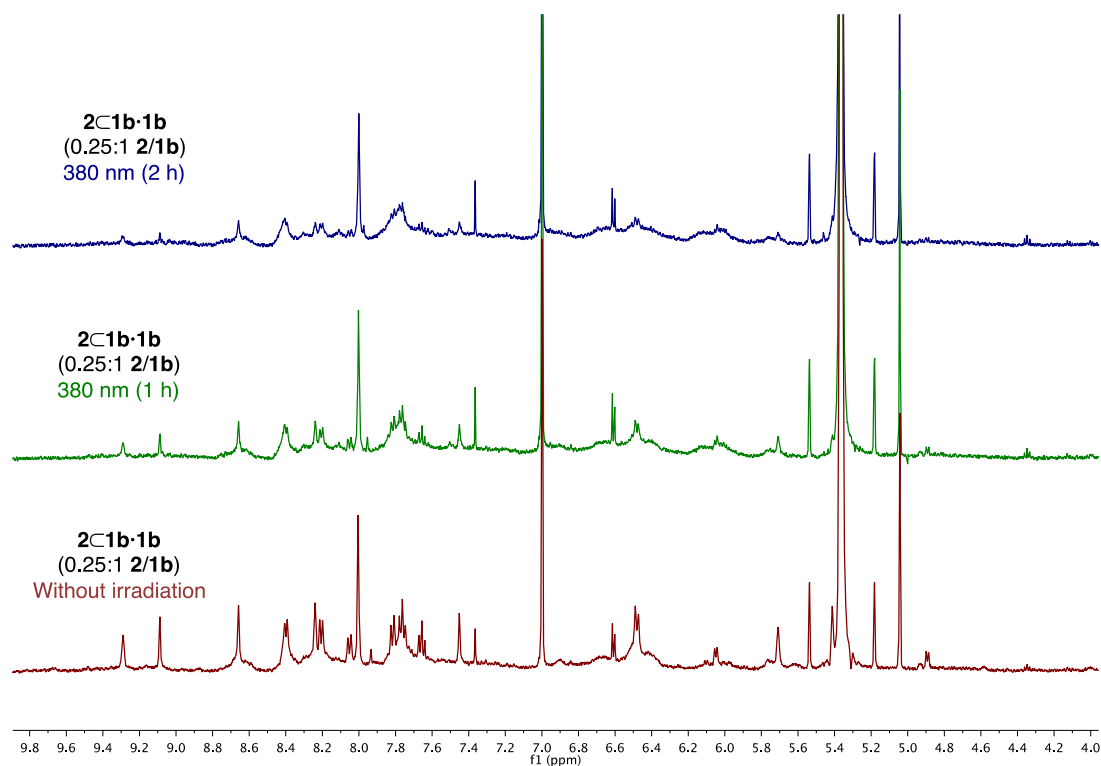
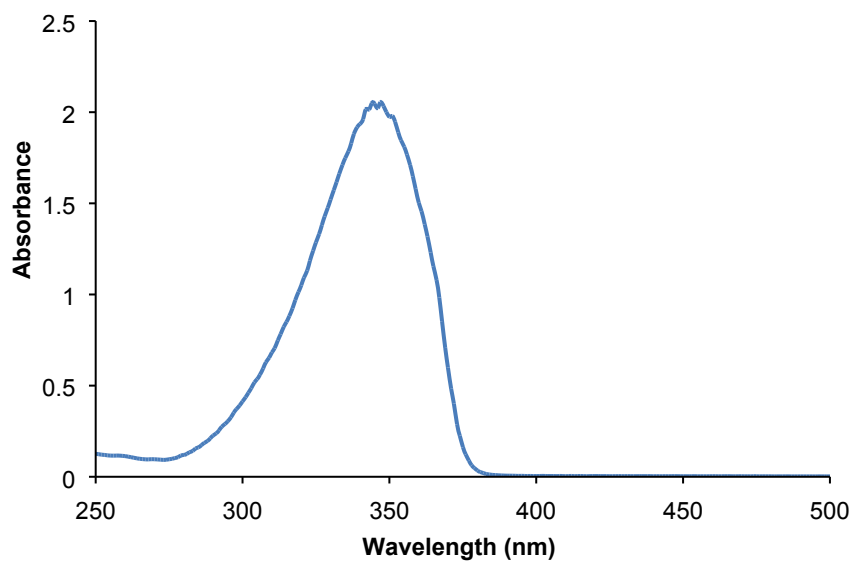
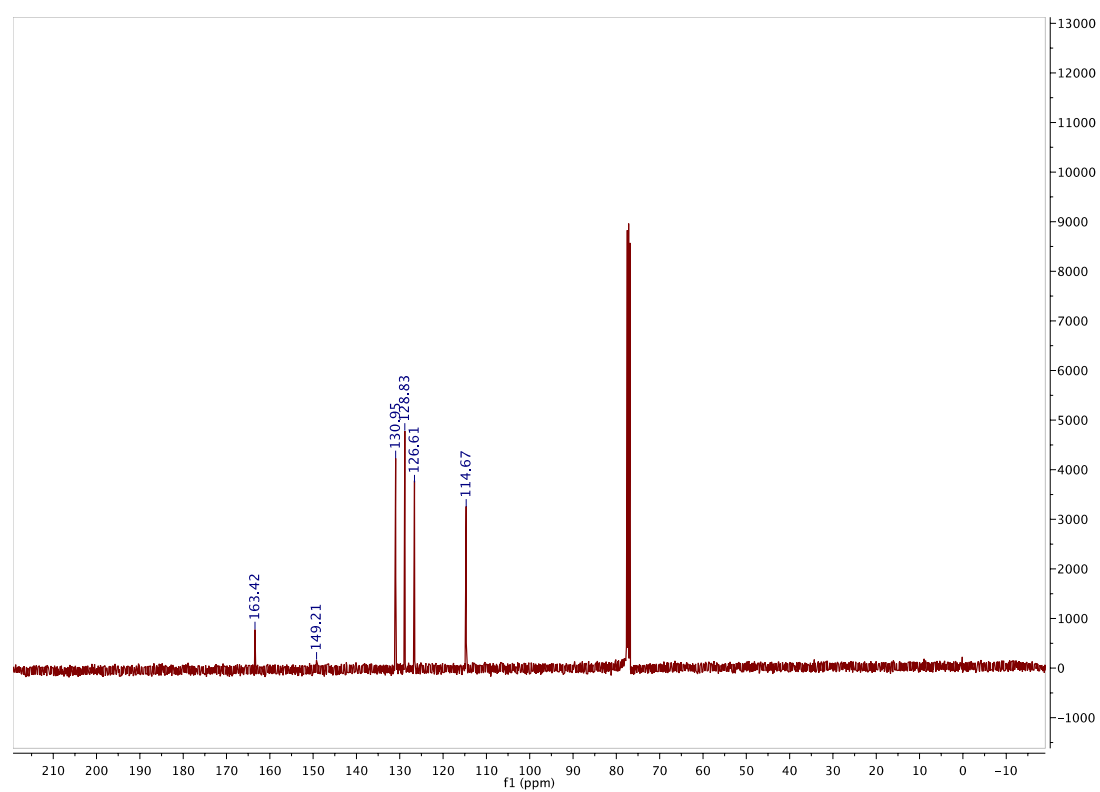
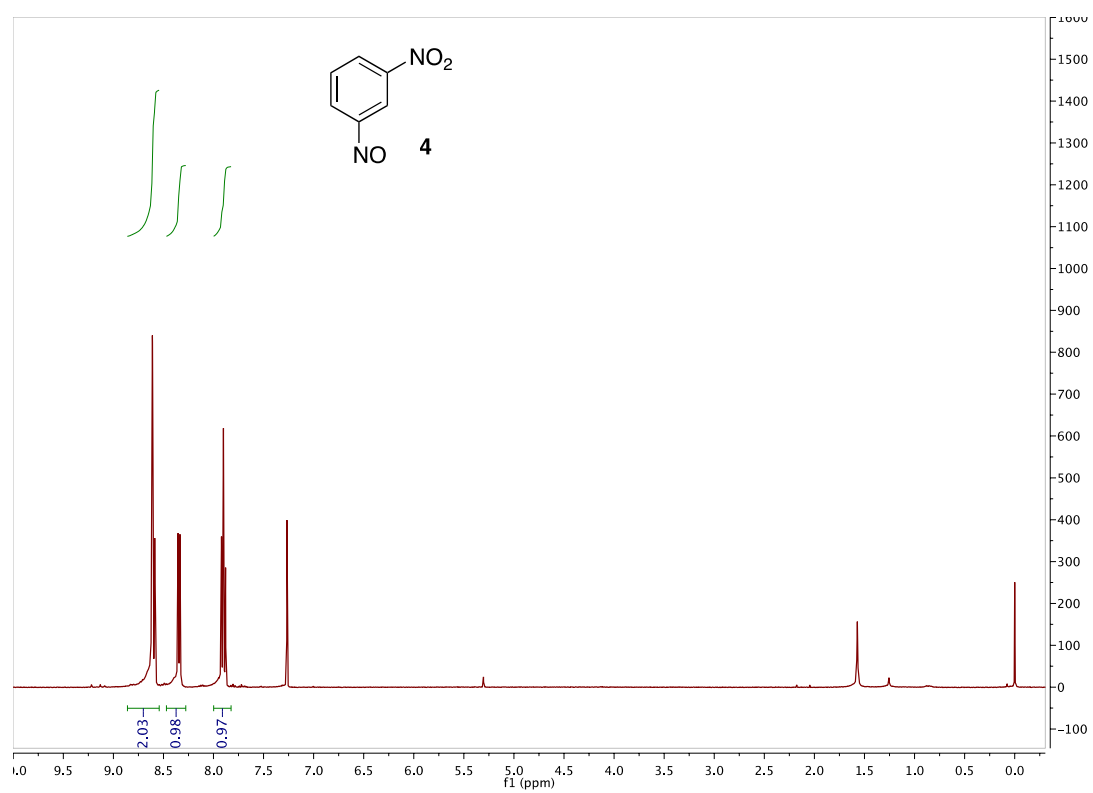


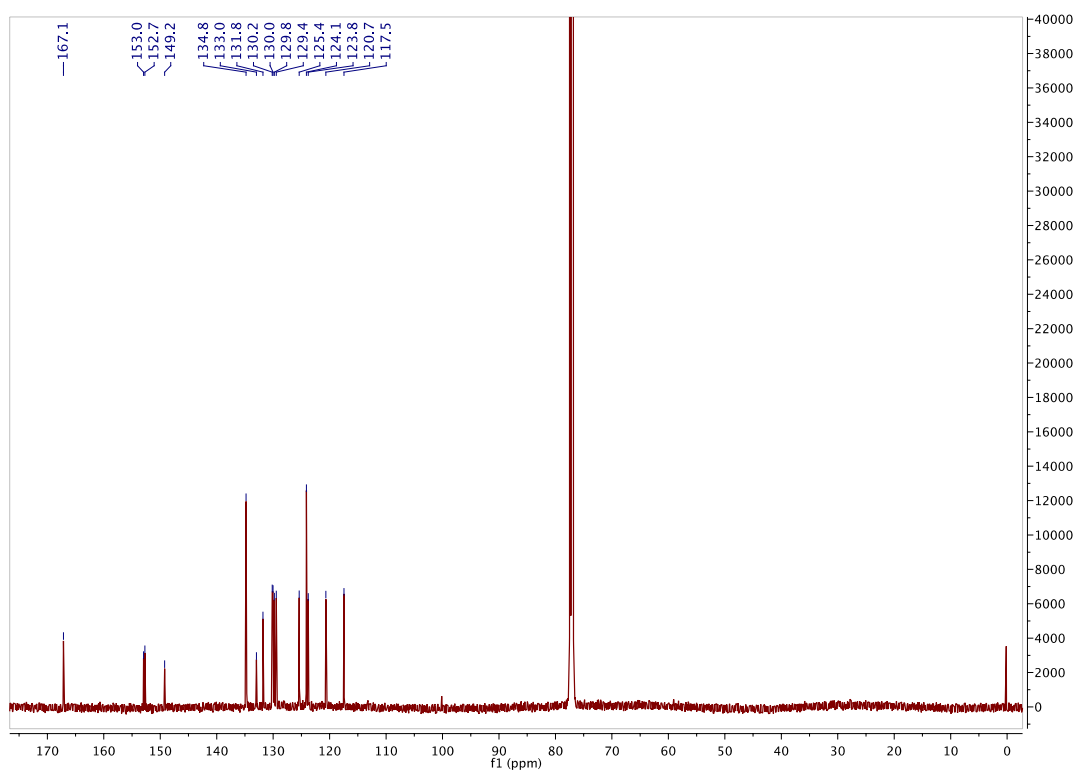
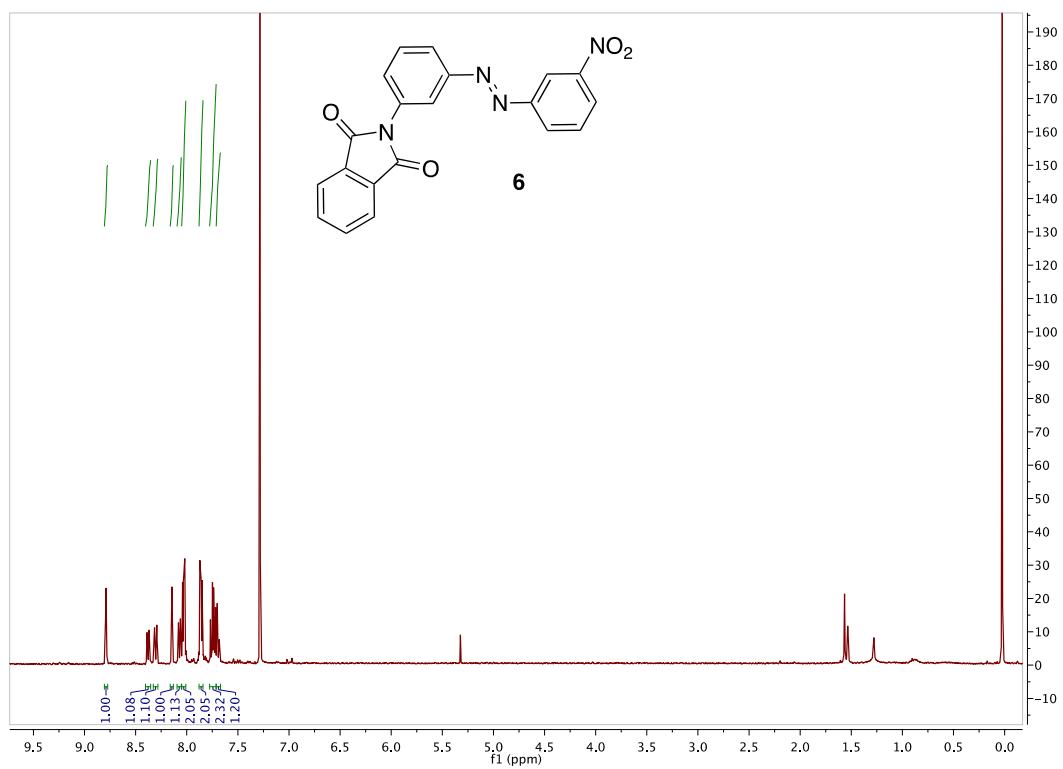
Figure S3. Selected region of the ^1H NMR spectra of a $\text{CH}_2\text{Cl}_2\text{-}d_2$ solution of $2\text{C1b}\cdot\text{1b}$ in the presence of 0.25 equivalents of **2** before irradiation (red), after 1 h irradiation at 380 nm (green) and after 2 h irradiation at 380 nm (blue).

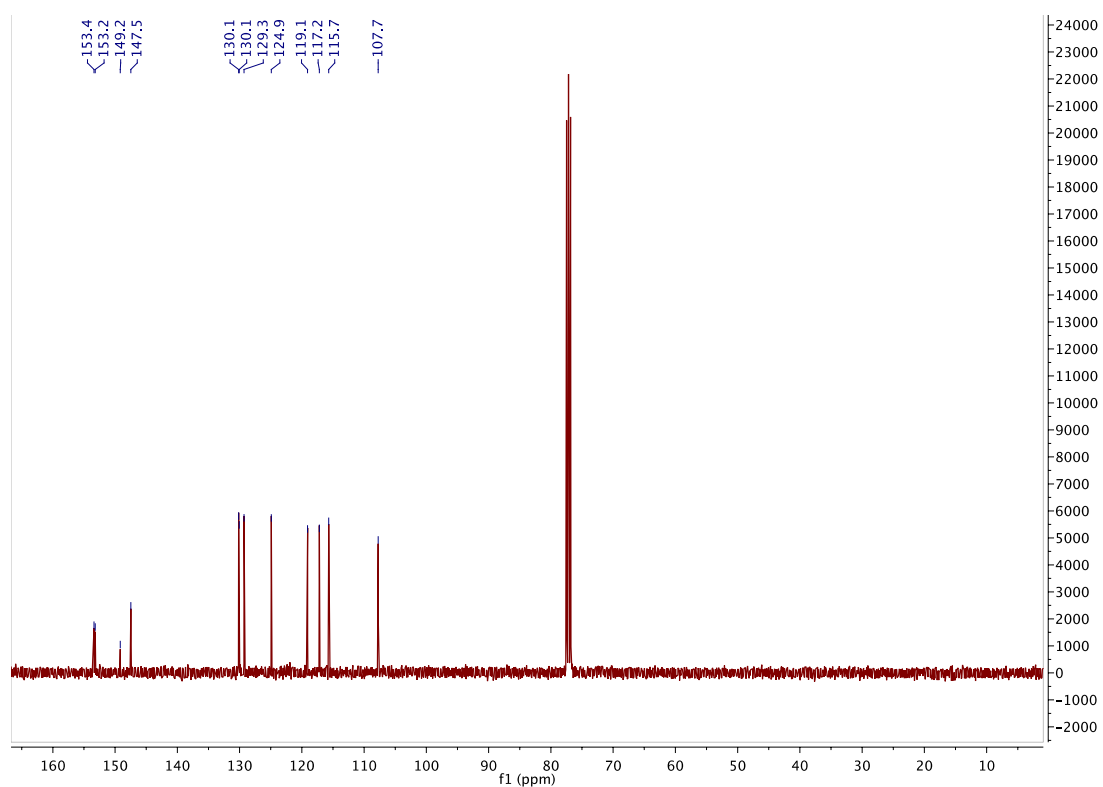
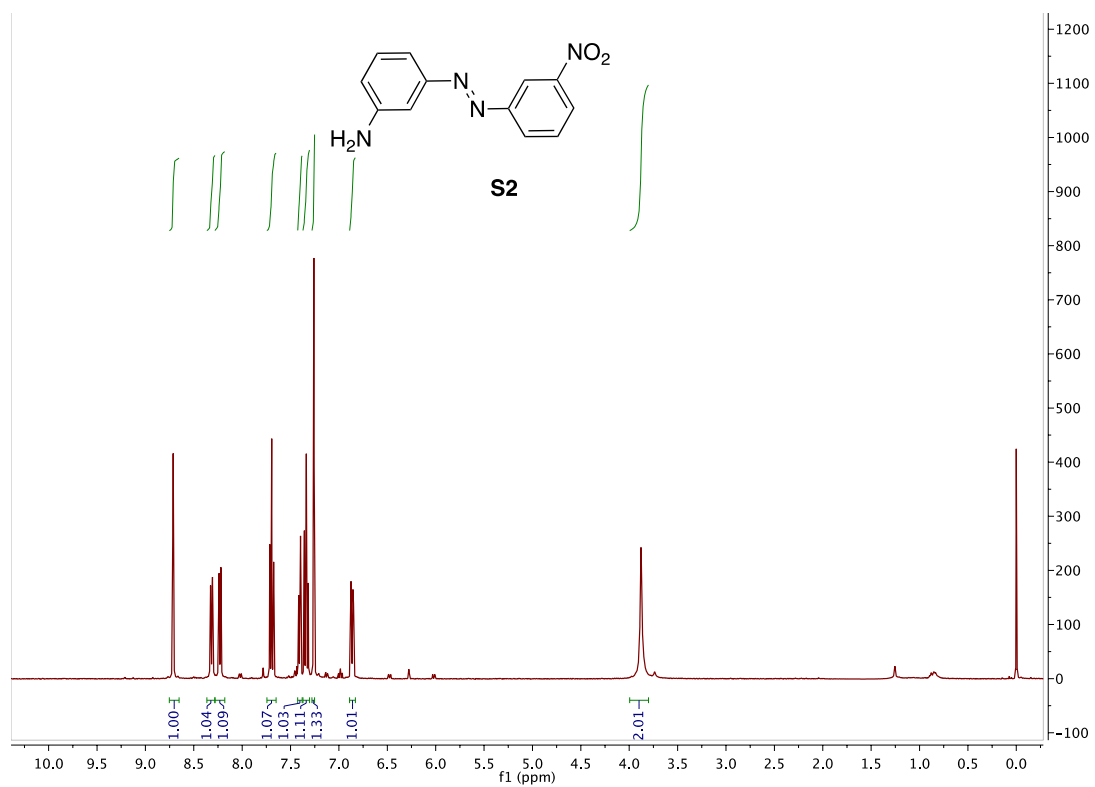
5. UV/Vis spectrum of guest **2** (0.1 mM in CH_2Cl_2)



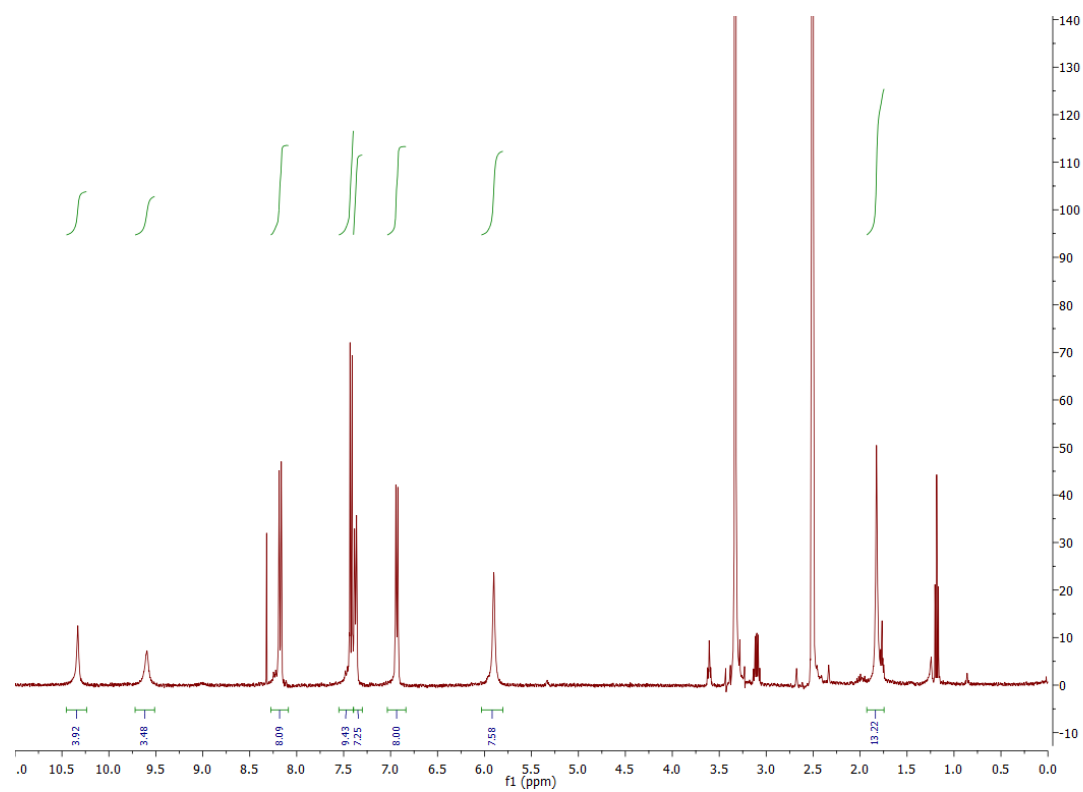
6. NMR spectra



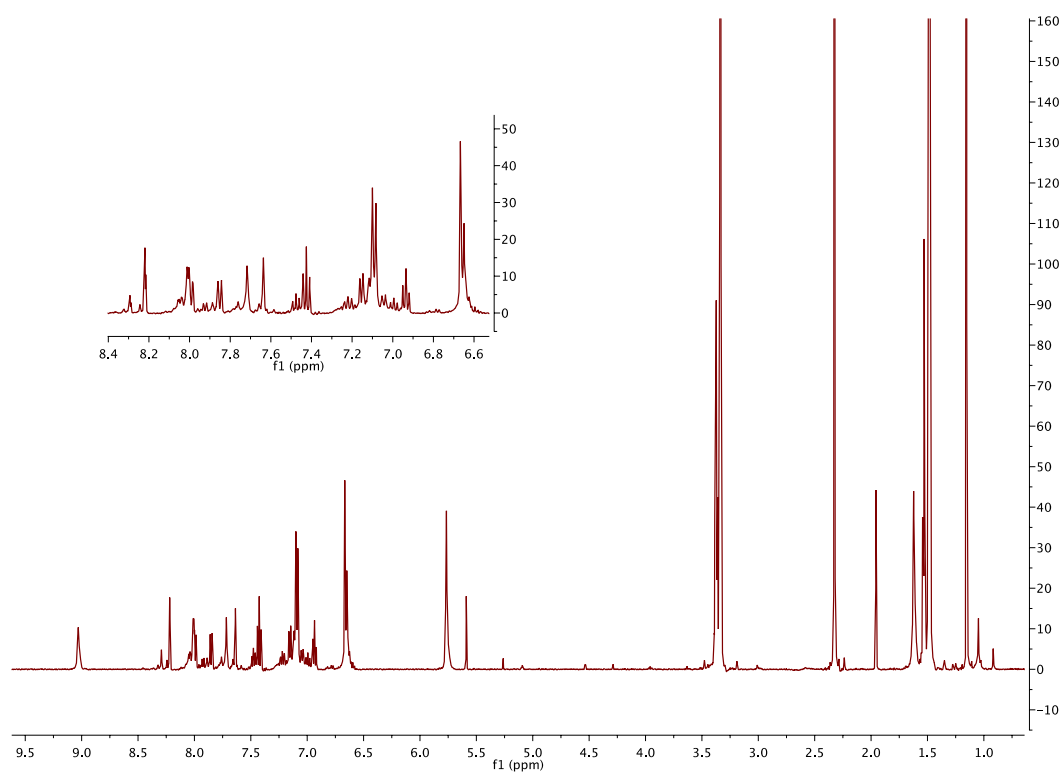




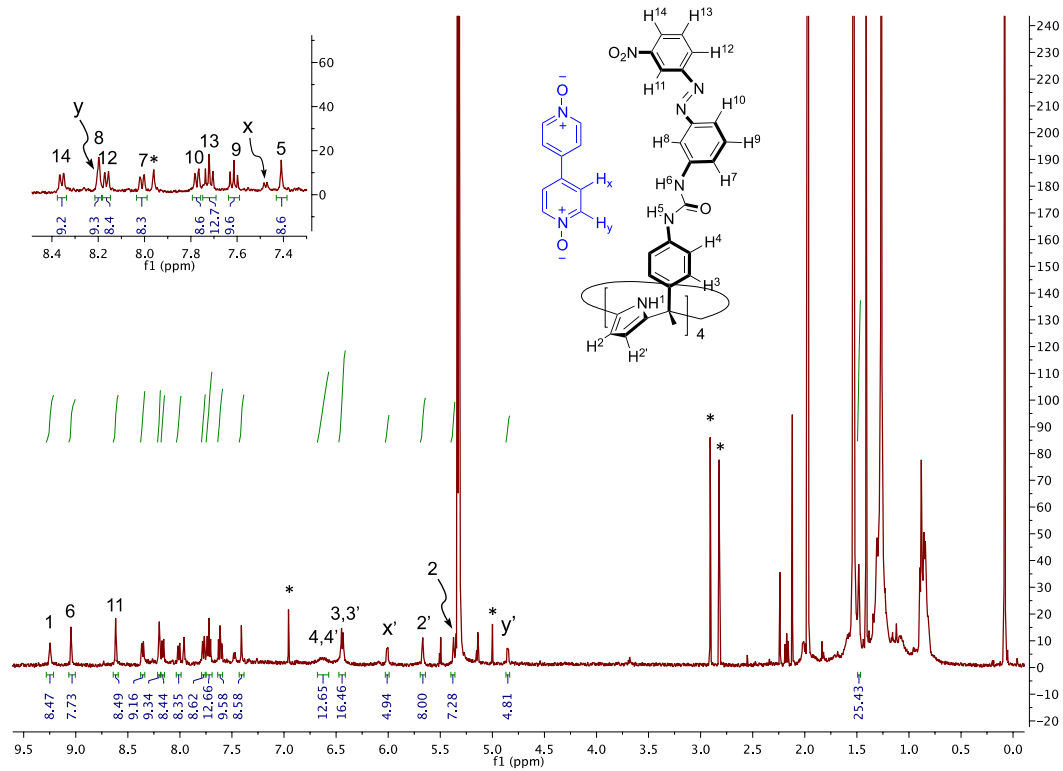
Activated urethane calix[4]pyrrole S1



Azo-calix[4]pyrrole 1b (THF-d₈)

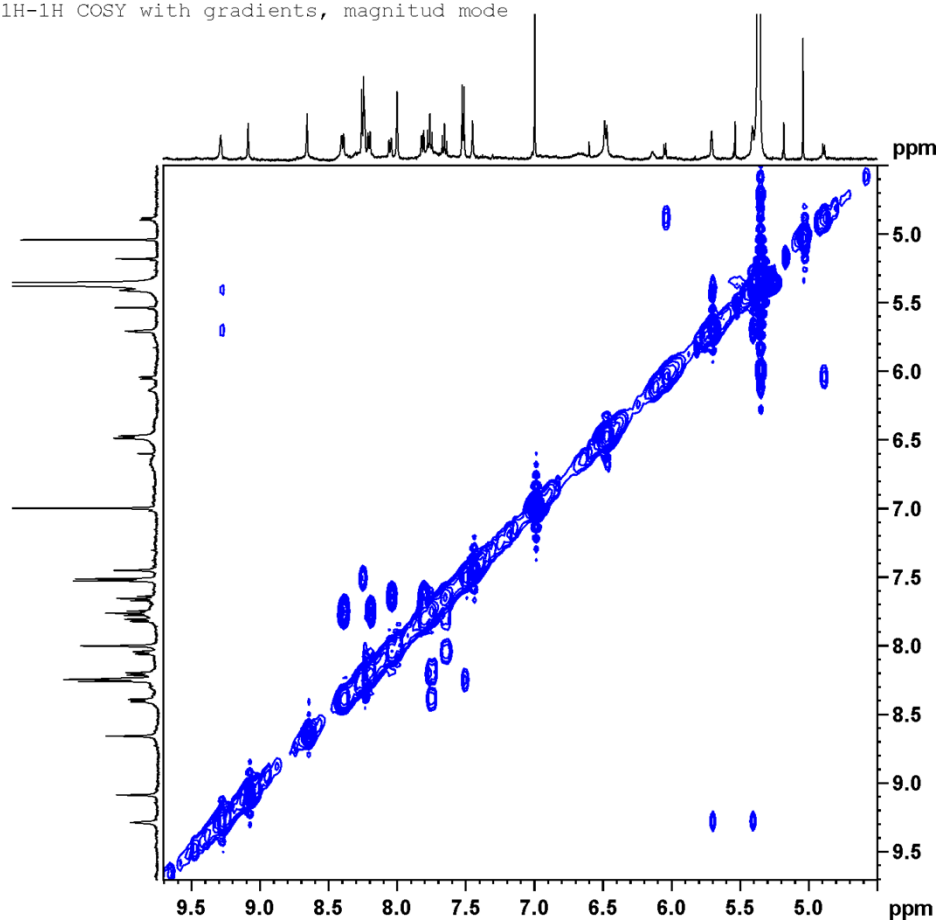


^1H NMR spectrum of the capsule 2 $\subset$ 1b•1b



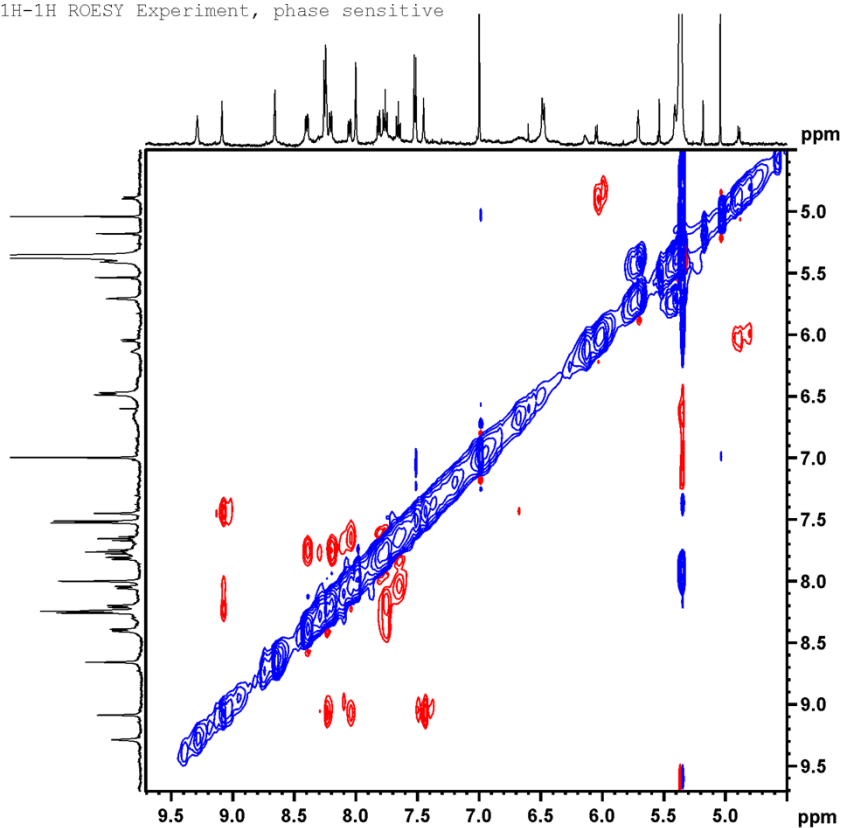
Selected area of the COSY spectrum of the capsule 2-1b•1b

2D ^1H - ^1H COSY with gradients, magnitud mode

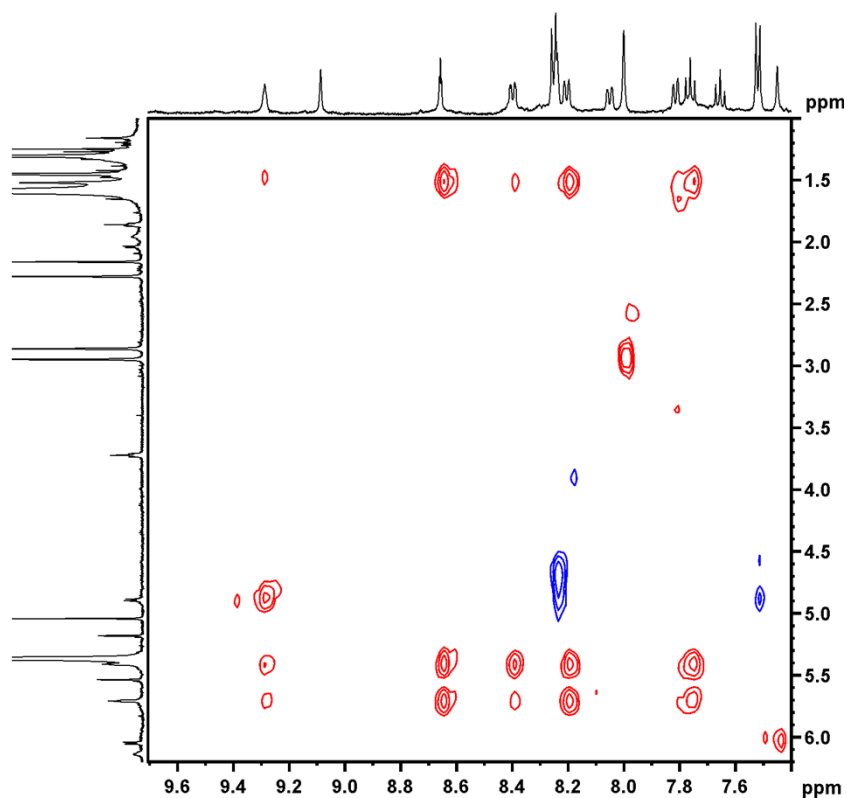


Selected areas of the ROESY spectrum of the capsule 2 $\subset$ 1b•1b

2D 1H-1H ROESY Experiment, phase sensitive



2D 1H-1H ROESY Experiment, phase sensitive

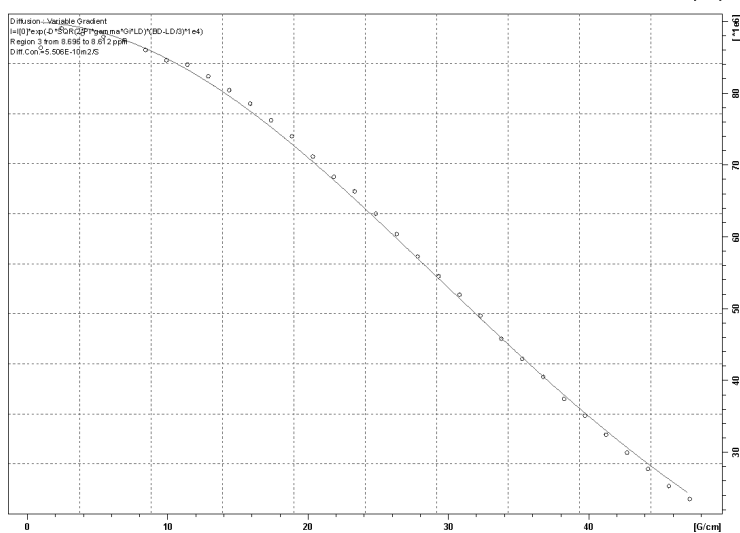
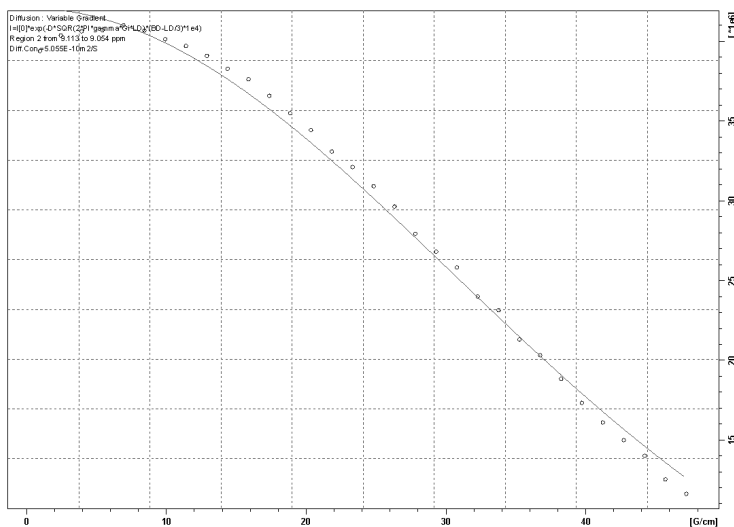
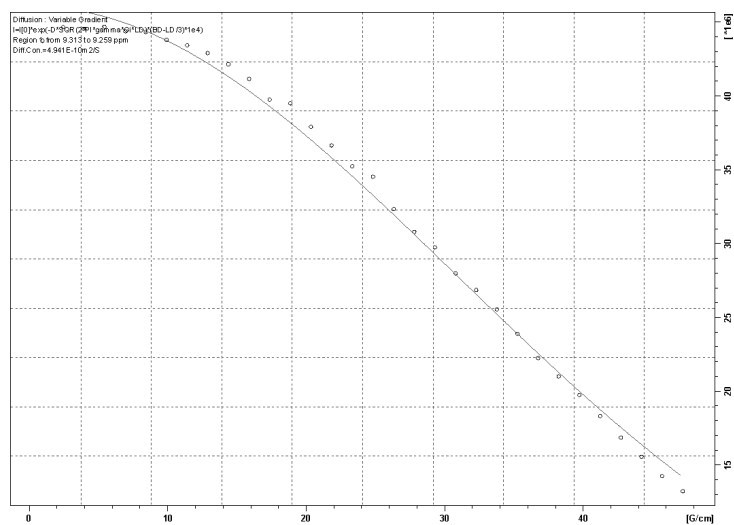


^1H pseudo-2D DOSY plot of the capsule 2c1b•1b. The horizontal scale shows ^1H NMR chemical shifts in ppm and the vertical scale shows $\log(\text{diffusion coefficient})$ values.

Diffusion coefficient = $5.28 \pm 0.14 \cdot 10^{-10} \text{ m}^2/\text{s}$



Plots of the DOSY data processing for the three further downfield signals corresponding to the pyrrole NHs (1), the urea proton (6) and the aromatic proton (11) alpha to the nitro group in the azobenzene unit.



MS spectrum of the capsule 2 $\subset$ 1b•1b (ESI+)

